Masibambisane:
Couple-Based Motivational Interviewing with Mobile Breathalyzers to Reduce Alcohol Use in South Africa

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Design: Formative qualitative phase followed by pilot randomized controlled trial

Population: Heterosexual couples with at least one heavy alcohol drinker on antiretroviral therapy

Study size: 40 key stakeholders and 90 couples/180 individuals (220 people total)

Study duration: 36 months

Aim 1: To develop a couple-based Motivational Interviewing intervention with mobile breathalyzer technology to deliver real-time feedback on blood alcohol content (BAC) levels. We will target heavy alcohol users with HIV and enroll their primary partner.

Aim 2: To develop and pilot test the study procedures for a future randomized controlled trial (RCT) of the couple-based intervention. We will develop and pilot test: a) training procedures; b) randomization procedures; c) the pilot study procedures; and d) data collection instruments.

Aim 3: To determine the feasibility and acceptability (F&A) of couple-based MI as a standalone intervention and when combined with mobile breathalyzers with couples to provide real-time feedback and support.

Study Site: Vulindlela/Sweetwaters community, KwaZulu-Natal, South Africa

1.0 INTRODUCTION

In sub-Saharan Africa (SSA), alcohol use is described as "adding fuel to the fire" for people living with HIV (PLWH)[1], threatening the success of HIV treatment programs and progress towards UNAIDS goals.[2-5] Our research in SSA suggests that primary partners are key to the success of alcohol interventions given their critical role in helping drinkers reduce alcohol use and the couple dynamics that intersect with alcohol use.[6-9] Harnessing this powerful form of social support is critical in a setting where clinical services for alcohol misuse are inadequate and can be costly for patients. One approach that has been effective at reducing alcohol use among PLWH is motivational interviewing (MI) that incorporates mobile technology for real-time feedback.[10-17] MI is a collaborative, goal-oriented style of communication with particular attention to the language of change. It is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion.

In this study, we propose to develop and test a couple-based MI intervention with mobile breathalyzer technology to provide dyadic support around drinking for HIV-affected couples in KwaZulu-Natal, South Africa.

Few couple-based MI approaches have been developed for alcohol use, particularly in the African context. In the US, there is evidence that couple-based MI is feasible, acceptable, scalable, and efficacious at reducing substance use.[9, 18-20] In studies with individuals, daily monitoring of drinking levels, when paired with MI, has a greater effect on drinking than MI alone[15-17] and we hypothesize that monitoring may have additional benefits with couples. Although primary partners are generally aware of a drinker's alcohol use, they have inaccurate knowledge of drinking amounts and frequency, in part, because drinking often occurs in gender-segregated spaces in SSA. Accurate knowledge of drinking levels in real-time is critical to trigger couple communication, and timely and tailored social support. Mobile breathalyzers have been shown to be a feasible and acceptable strategy for self-monitoring alcohol use in studies with individuals[21-23] and new products have been developed for dyads that share blood alcohol content (BAC) levels with support partners via a mobile app. Our scientific premise is that mobile breathalyzers to provide real-time feedback and support can be synergistic with a couple-based MI approach that fosters couple communication and problem-solving skills to effectively engage with the breathalyzers and work together to reduce alcohol use. We hypothesize that this combination will have a greater effect on drinking reductions than couple-based MI alone.

2.0 Study objectives and Design

2.1 Intervention Feasibility

Preliminary data to support proposed intervention: Couple-based MI interventions for substance use have demonstrated feasibility, acceptability and preliminary efficacy. Co-I Starks developed a couple-based MI intervention with US male couples called *We Test* to enhance the effectiveness of couples HIV testing and counselling (CHTC) by including structured components to address substance use and couple communication skills. The RCT findings showed that completion of a substance use module led to immediate decreases in drug use, and when combined with training in couple communication, resulted in reductions in drug use at 3- and 6-month follow-up.[19] Co-I Starks also developed a three-session MI-based intervention with US male couples to reduce HIV risk and drug use (*Couples Health Project*).[19, 20] A pre-pilot RCT of the intervention prototype with 20 couples showed that: 1) 19 out of 20 couples completed all three MI sessions; 2) retention was high at 1-month (95%) and 3-month (93%) follow-up; 3) and couples found the intervention highly acceptable. In the pilot RCT that followed, the intervention significantly reduced drug use at the 3-month follow-up among participants with high levels of baseline drug use.[20] We acknowledge that US male couples and those in South Africa may differ (e.g., higher rates of IPV and heavy drinking in South Africa), which our adaptation plan will take into account.

Our team's research in KZN suggests that a technology-based intervention will be feasible. In South Africa, smartphone penetration rates are high (82%) and of all provinces, KZN has the second highest number of 4G/LTE subscribers.[24] Mobile phones have been successfully incorporated into interventions in South Africa and elsewhere in the region.[25-27] Multiple studies at the proposed site have demonstrated the feasibility of digital interventions in HIV care. Site PI van Heerden demonstrated the feasibility of using an mHealth system to improve linkage-to-care after home-based testing[28] and a conversational agent (chatbot) to provide counselling for HIV self-testing.[29] These studies rely on high smartphone penetration rates and a strong mobile network. Pilot data from 2016 with PLWH in KZN (n=101) found that 96% of participants reported using a cell phone.[28] The research area is serviced by a strong network of mobile phone towers and in speed tests conducted at 14 sites spanning a distance of 60 km, we achieved an average download speed of 22.6 Mbps (3.5– 54.5 Mbps) and upload speed of 6.2 Mbps (0.05–14.2 Mbps). Although network conditions vary, speed tests show that we will have ample bandwidth to use the mobile breathalyzer technology for this study.

2.2. Aim 1

In the <u>first phase</u> (months 1-12), we will adapt our team's interventions to address alcohol use in South African couples living with HIV and incorporate the mobile breathalyzers.

2.3. Aim 2

As part of the first phase, we will develop the intervention manual, training procedures, randomization procedures, implementation procedures, and data collection instruments for the pilot RCT.

2.4 Aim 3

In the <u>second phase</u> (months 13-36), we will recruit 90 couples who will be randomized to a control arm, couple-based MI arm, and couple-based MI plus mobile breathalyzers arm. Couples will be assessed at baseline, , 2, and 6-months post intervention initiation and a subsample of 15

couples will complete exit interviews. In months 31-36, we will analyze the F&A data, discuss the findings as a team, and identify modifications to the intervention in preparation for a future trial.

2.5 Study design

For Aim 1, we will adapt a couple-based MI framework and interventions developed by co-I Starks (*We Test* and the *Couples Health Project)* to address alcohol use in heavy alcohol users and their primary partners and incorporate the mobile breathalyzer component. We will follow the ADAPT-ITT framework by conducting focus group discussions (FGDs) with around 40 key stakeholders to gain feedback on the intervention and then refining the intervention. For Aim 2, we will develop training procedures, study procedures, and data collection instruments that will be pilot tested during the RCT. For Aim 3, we will conduct a three-arm RCT with 30 couples randomized to the following arms (90 couples total): 1) an enhanced usual care control condition; 2) couple-based MI; and 3) couple-based MI with mobile breathalyzers for real-time feedback. For arm 2 and 3, couples will receive 3 MI sessions over a 60-day period with an experienced counselor to help strengthen communication and problem-solving skills around alcohol use. For Arm 3, couples will use the mobile breathalyzers and app for 60 days and receive the same MI sessions, which will also incorporate feedback on BAC levels (prior 30 days) and teach couples how to effectively engage with the breathalyzers. This design will allow us to assess the effectiveness of couple-based MI alone and the added synergistic effect of the mobile breathalyzers on alcohol use and HIV outcomes (e.g., adherence to antiretroviral therapy (ART), viral suppression). Our F&A outcomes will include enrollment and retention rates, satisfaction with both intervention arms, MI session attendance rates, and follow-up survey completion rates. We will also conduct qualitative interviews with a subset of 15 couples to contextualize F&A data and refine the intervention and procedures for a future full-scale efficacy trial.

3.0 Study Population

3.1. Couple Eligibility

Inclusion criteria:
(1) In a primary relationship for at least six months
(2) Aged 18-49
(3) Have at least one partner (the "index patient") with a positive AUDIT-C screen (score of 4 for men and 3 for women; prior 3 months) and on ART for at least six months (a time when alcohol use is found to rebound) who has disclosed their HIV status to their partner in the study
(4) Both partners separately agree to participate in the study for the couple to be enrolled.

Exclusion criteria:
We will exclude participants with an AUDIT-C score greater than 12, indicating risk of severe alcohol use disorder. Participants with severe drinking issues may not benefit from a brief counseling-based intervention and may need more intensive treatment that our study can provide.

Considering the intervention has a technology component and there may be a difference in acceptability between younger/older participants, we will impose an upper age limit of 49 (an age in which smartphone ownership and internet connectivity drops off in South Africa). We will not exclude those without phones or with incompatible phones to avoid widening the digital divide and excluding those who could really benefit from the intervention. We have budgeted for

phones to be provided. Our intervention may not be appropriate for couples experiencing severe IPV. We will exclude those who fear for their safety by participating in the study and/or report severe IPV in the past 3 months using the WHO measure for South Africa, which assesses physical, sexual, and emotional violence, and determines whether it is mild, moderate, or severe. The WHO measure for IPV contains 8 questions that assess perpetration and victimization of 4 types of severe violence including physical (kicking, punching, hitting, beating, scalding, burning), threats using weapons such as a gun or a knife, and restraint (i.e. holding down) in the past three months. The WHO questions on IPV will be administered to both members of the couple. Couples-based interventions in South Africa have successfully employed this approach. We believe this approach balances sample generalizability with safety. If couples report any IPV (mild, moderate, or severe) during screening or over the study, we will follow an established protocol to assess safety, provide emotional support, and provide intervention and/or linkage to psychological and/or medical services. If either person in the couple declines to participate, the couple as a whole will be ineligible.

Dr. Conroy's prior work with couples in this community in KZN showed that less than 1% of female partners reported any alcohol use, with the primary drinker almost always being the male partner. As such, we will not exclude dual-drinking couples since these couples could really benefit from the intervention. However, should we enroll couples with two heavy alcohol drinkers, our couple-based MI approach is designed to be flexible to handle cases where both partners are heavy drinkers, and will consider change behavior in both partners. The software for the breathalyzer is not optimized for both partners being "testers" and "accountability partners." Therefore, in couples with two qualified drinkers, whichever one is screened first will be considered the "index patient" and get the breathalyzer. In couples with two heavy drinkers on ART, both partners will have blood draws for viral load and/or alcohol use at follow-up visits.

3.2. Recruitment Process

Aim 1: For the two FGDs with couples (3-4 couples per group), we will recruit couples using procedures from our prior studies with couples in South Africa and Malawi. A team of recruiters will approach index patients at HIV clinics while waiting to attend appointments. We will announce the study during the daily health information talks in the waiting rooms and interested patients can approach the recruiters. If the patient is interested and eligible, we will provide them with a study information card to give their primary partner and will set up a phone appointment to screen the partner. If both partners are interested and eligible, the couple will be invited for a secondary screening to verify that the partnership is legitimate (e.g., confirming partner names, relationship length, etc.). To ensure we capture primary partnerships, both partners will be asked, "Of all your romantic partners, who are you the closest with?" Screenings will be interviewer-administered using tablet devices. If the couple remains eligible, both partners will provide written informed consent and be invited to participate. Partners will be consented separately to ensure a lack of coercion. Couples who are ineligible will be informed that they are ineligible but will not be given a specific reason why (i.e. which eligibility criteria they did not meet). Recruiters may deflect questions about eligibility by saying, "the computer program determines eligibility but does not provide a specific reason." Similarly, couples who are ineligible because one or the other does not want to participate will not be informed that this is the reason for ineligibility to avoid disclosing each partner's decision to provide consent.

Couples may also be identified from previous or current studies who have consented to be contacted for other research studies, and through our community partners and associated HIV testing/care services.

For the three FGDs with stakeholders (6-8 per group), which will consist of HIV care providers (nurses, clinic volunteers, clinicians), community representatives and religious leaders who interact with couples who drink, and alcohol vendors (e.g., shebeen owners, local brewers), we will recruit them using our professional networks in this region of KZN.

Aims 2 and 3: We will recruit couples using a combination of community-based and clinic-based recruitment approaches. Index patients who are heavy drinkers on ART for at least 6 months will be targeted first, followed by their primary partner. We will recruit around 120 couples to achieve the desired sample size of 90 couples (180 individuals). This assumes we will lose around 25-30% after randomization based on other studies at this site.

We will use a combination of active and passive recruitment strategies to enroll the sample.

Community-based recruitment: Index patients will be identified through community-based organizations or through locations in the community where drinkers can be found. Recruiters will use procedures established at HSRC to identify and recruit participants using a community mobilization approach. Individuals and couples will be targeted by a team of recruiters, who will approach potential participants in public areas in the community, such as alcohol venues (e.g., shebeens, bottle shops), markets, sports grounds, taxi ranks, HIV clinics, and community events. Recruiters will target couples together if possible, although our other studies have shown that couples are not often together in public. Potential participants will also be recruited passively (i.e., through fliers in the community). These fliers describe the study and invite interested individuals to contact the project staff by calling or sending a free "call me" SMS to the telephone number listed. Recruiters will return these messages as soon as possible and no later than the next working day.

Clinic-based recruitment: We will also actively recruit index patients at HIV clinics during morning health talks when patients are attending appointments. Recruiters will screen index patients in the waiting rooms immediately following the talks or distribute fliers/information cards so interested patients can later contact the study team if interested. We will also passively recruit index patients using fliers placed at the clinics. Clinic-based outreach teams and care providers will also help to identify HIV patients who are heavy alcohol drinkers and on ART for at least six months and refer patients to the HSRC recruiters.

Recruitment from other studies: There are other studies at the HSRC site that may be able to refer participants to the study team, for example, if they were ineligible for another study but may be interested in participating in research.

In either approach, recruiters will ask potential participants if they would like to hear about the study and explain the nature of the study using standard recruitment scripts.

If the index patient is interested and eligible, we will provide them with a study information card to give their primary partner and will set up a phone appointment to screen the partner. If both partners are interested and eligible, the couple will be invited for a secondary screening to verify that the partnership is legitimate (e.g., confirming partner names, relationship length, how the

couple met) and assess the risk for violence by participation in the study. To ensure we capture primary partnerships, both partners will be asked, "Do you have a primary partner, meaning a person who you are committed to above anybody else and with whom you have had sexual relations?" Screenings will be interviewer-administered using tablet devices either in-person or via phone. If the couple remains eligible and is a legitimate couple, both partners will provide written informed consent and be invited to participate. Partners will be consented separately to ensure a lack of coercion.

3.3. Participant Retention

Aim 1 requires only a single interaction with participants. The intervention period for Aim 2 and 3 will last 60 days with assessments at baseline, 2-months and 6-months post intervention initiation. Upon enrollment, we will obtain contact information (e.g., two cell phone numbers, directions to households, and contact information for up to three other individuals) to facilitate tracking. For the pilot study in Aim 3, participants will also be provided with phones allowing us the capability to reach them via SMS or calls as an alternative to their main phone number. Participants will be contacted regularly (e.g., twice a month) to update contact information and check on location. Prior to the assessment visits, reminder calls and SMS messages will be made to both partners one week before the appointment and again 1-2 days prior. For participants who miss appointments, we will limit the number of phone call attempts to 3-4 to respect privacy and the right to refuse. There may be special circumstances when outreach workers will be dispatched to participants' homes (with their prior consent) such as when calls do not go through.

We anticipate that we will lose a very small percentage of couples due to break-ups, deaths, and migration (<5% in another study at the site called *Uthando Lwethu*), which we have accounted for in recruitment and analysis plans. One assessment will be conducted with each partner separately following the break-up to understand when the couple broke up, whether study participation contributed to the break-up, and if not, other reasons for why the couple broke-up. The breakup assessment will also allow us to identify any negative effects of participation on couples. If the study contributed to the break-up or the break up was a negative experience, we will follow the adverse event logging process. We will continue to follow each partner individually and administer study assessments given that our study outcomes (e.g., alcohol use) are at the individual level. This will allow us to explore whether participation in the intervention, despite the break-up, still had an effect on their alcohol use. However, couples who break-up before participation in the intervention will exit the study.

3.4. Participant Withdrawal

Couples or individuals are free to leave the study at any time. If a participant notifies a staff member of their desire to withdraw from the study the staff member will ask if the couple or individual would like to share the reason they are withdrawing from the study. If the couple shares this information, the staff member will include that in their file and store their file in the "withdrawn participants" section of the filing cabinet. The project coordinator or project director must be notified of the situation.

4.0 Intervention Description

The two intervention arms consist of standalone MI (arm 2) and MI *Plus* (arm 3), which consists of MI sessions in arm 2 plus use of the mobile breathalyzer and app for two months. Both intervention arms are conducted with the couple as a unit.

MI *Plus* will consist of: 1) manualized MI sessions with couples and a counselor; 2) handheld breathalyzer with accompanying mobile app to deliver real-time feedback on drinkers' BAC levels to both partners. BAC data collected will be also used to provide personalized feedback based on summarized displays (e.g., calendar) of BAC levels in the MI sessions.

MI Sessions: We will aim for around 3 in-person sessions over a 60-day period with each session lasting 60-75 minutes – consistent with the format used in the Couples Health Project. We will administer MI sessions that are structured and manualized, as a roadmap for moving through content. MI is a collaborative process between a counselor and client, aimed at exploring and resolving ambivalence towards changing a behavior. Our approach will center around four MI processes (engagement, focusing, evoking, and planning)[30] and a fifth process around relationship quality based on co-I Starks' MI framework for couples[19, 20]. Starks recently published a paper using qualitative data from a couple-based MI intervention that supports the necessity of including relationship quality as a fifth MI process when working with couples.[31] An exploration of dyadic strengths is necessary to support couples with divergent views in the resolution of interpersonal ambivalence and the development of shared goal. Starks developed structured activities for exploring couples' shared goals and a lexicon of counselor skills that are effective in responding to dyadic ambivalence and achieving accommodation.[20]

Outline of MI Sessions: The first session will occur within two weeks after baseline and the two subsequent sessions will be delivered at 30 and 60 days after couples have used the breathalyzer app. In the first session, the counselor will establish rapport and draw out the couples' communication strengths and weaknesses. The counselor will review baseline alcohol levels using this as a starting point to evoke change talk. The session ends with the creation of a goal to reduce alcohol use. Session 2 will review the BAC data (or self-reported alcohol use if in the non-breathalyzer arm) from the past 30 days using a calendar approach, a check-in on goals set in Session 1, and a review of communication successes and challenges. The session ends with the creation of a behavioral goal for the next session. Session 3 begins with a review of BAC data (or self-reported alcohol use if in the non-breathalyzer arm) from the past 30 days using a calendar approach, a check-in on goals set in Session 2, and ends with a discussion of long-term goals and related planning. If both partners are heavy drinkers, then couples will develop goals in each session for both partners.

Mobile Breathalyzer for Couples: We will use BACtrack View®, which consists of a handheld commercial-grade breathalyzer and mobile app. To avoid disruptions in cellular service by having to manually purchase data, we will automatically replenish participants' data when running low. To reach those who could greatly benefit from the intervention and to avoid

widening the digital divide, we will provide phones to participants who do not have compatible smartphones.

5.0 Study Procedures

5.1 Procedures for FGDs with couples: We will conduct two FGDs with 3-4 couples (6-8 individuals) each. We will recruit couples using procedures from our prior studies with couples in South Africa and Malawi. A team of recruiters will approach index patients at HIV clinics while waiting to attend appointments. We will announce the study during the daily health information talks in the waiting rooms and interested patients can approach the recruiters. If the patient is interested and eligible, we will provide them with a study information card to give their primary partner and will set up a phone appointment to screen the partner. If both partners are interested and eligible, the couple will be invited for a secondary screening to verify that the partnership is legitimate (e.g., confirming partner names, relationship length, etc.). To ensure we capture primary partnerships, both partners will be asked, "Do you have a primary partner, meaning a person who you are committed to above anybody else and with whom you have had sexual relations?" Screenings will be interviewer-administered using tablet devices. If the couple remains eligible, both partners will provide written informed consent and be invited to participate. Partners will be consented separately to ensure a lack of coercion.

5.2 Procedures for FGDs with key stakeholders: We will conduct three FGDs with 6-8 stakeholders each. Key stakeholders will consist of HIV care providers (nurses, clinic volunteers, clinicians), community representatives and religious leaders who interact with couples who drink, and alcohol vendors (e.g., shebeen owners, local brewers). Stakeholders will be recruited using our professional networks in this region of KZN.

5.3 General procedures for the FGDs: FGDs will be conducted in private rooms at community halls or at the HSRC Sweetwaters office. Dr. Conroy will train research assistants on the study objectives, interview guide, and FGD methods using a decade's worth of training materials from studies in SSA. Research assistants will conduct the FGDs in isiZulu or English using a structured guide. FGDs will elucidate ways to make the intervention more feasible and acceptable to the target population and to obtain feedback on the curriculum. We will ask: What are your overall impressions of this program? What aspects of the program will people like/dislike the most? What types of couples and drinkers will be most/least likely to participate? How can we improve the program to increase participation among couples? If this service was offered today, would you recommend it to couples? To assess how to implement the intervention in the future, FGDs with stakeholders will elicit feedback on strategies to increase uptake of the breathalyzers by local agencies. FGDs will be audio-recorded, transcribed, and translated to English.

5.4 Training. Given the skills required to deliver MI, we will hire certified HIV testing counselors with 2+ years of counselling and/or facilitation and community experience. Facilitators and the HSRC research manager will attend a multi-day didactic training workshop (in-person, at HSRC) with Dr. Starks, following a curriculum based on workshops at the Motivational Interviewing Network of Trainers and Dr. Starks' prior research on couples MI. The next few weeks will consist of role-plays, practice, coaching and feedback, including mock sessions with peers and pilot couples which will be recorded for Dr. Starks. A follow-up training session will be held to cover more advanced MI skills with Dr Starks. This will be held online

(Zoom) several weeks after the initial training and facilitators have had time to practice. To minimize intervention drift, facilitators will be required to conduct two additional mock counseling sessions per month in English, which will be video-recorded and used in monthly booster sessions with Dr. Starks (remotely on Zoom). The project manager at HSRC will also be trained by Dr. Starks on coaching techniques to help oversee the training and role playing in Zulu and provide feedback as needed.

Before being cleared to interact with participants, facilitators will be required to demonstrate competency through three mock sessions in English.

We will also train a pair of interviewers to recruit couples and conduct assessment visits. Drs. Conroy and van Heerden will lead additional training with staff, covering topics on couples counseling, the mobile breathalyzer technology, how to handle ethical issues with couples, health education around alcohol use and HIV, the intervention manuals and procedures, and professional conduct.

5.5 Supervision. Supervision of facilitators will occur as follows. Following each session, facilitators will listen to the audio-recording in Zulu and complete a self-assessment, identifying areas they did well, struggled with, or faced challenges with couples. The HSRC research manager or their peer facilitator will also listen to audio-recordings and complete an assessment form. Study investigators will meet with the research manager to discuss the self-assessments, and supervisor/peer assessments to assess competency and identify areas for further coaching. If budget allows, we will translate and transcribe a random set of MI sessions into English for Dr. Starks to provider further training.

Dr. Starks will provide monthly supervision to staff on intervention delivery. Dr. Conroy will meet quarterly with van Heerden to provide strategic direction and support. PI Conroy will take primary responsibility for the design, implementation and analysis of the qualitative data, working with the other co-Investigators.

5.6 Fidelity monitoring of intervention. After each session, facilitators will complete a checklist to ensure each section of the intervention was covered. Intervention sessions will be audio-recorded. The HSRC manager will listen to audio files of sessions and also complete a checklist for the sessions. Self-assessment forms described above will contain rating for key MI components (e.g., collaboration, respect, etc.). A separate space on the checklist and self-assessment forms will be provided for written comments. Completed forms will be discussed in regular Zoom calls with the team to discuss areas where further guidance is needed and to help problem-solve challenges.

5.7 Recruitment and retention. We will recruit and randomize around 120 couples to meet our target sample size of 90 couples, assuming that we will lose around 25-30% of couples after randomization. We anticipate that we will lose a very small percentage of couples due to break-ups, deaths, and migration (<5% in Uthando Lwethu), which we have accounted for in recruitment and analysis plans.

5.8 Randomization process. After informed consent and the baseline assessment, couples will be randomized to either the control arm, the couple-based MI arm, or the couple-based MI with

mobile breathalyzers arm (MI *Plus)*. We will use randomly permuted block sizes (e.g., 3, 6, and 9) generated using a computerized and secure process. The UCSF project coordinator and the HSRC data manager will use the table that the statistician created to print documents that assign participants to one of the three arms. These documents will be placed in sealed envelopes and maintained by the HSRC data manager. HSRC interviewers will take a small subset of envelopes into the field with them. At the end of the baseline survey, the index patient will be given the envelope that contains the random assignment. Couples will receive an appointment card with a date for their next study visit following randomization.

5.9 Control condition. Participants will receive the Usual Care (UC) defined by the South African national 2019 ART Clinical Guidelines (updated in March 2020). The harms of alcohol use are briefly discussed during the morning health talks in the waiting rooms of HIV clinics. HIV clients are advised that alcohol intake should be reduced to <2 standard drinkers/day for men and <1 for women for 5 out of 7 days per week. After randomization, couples in the control arm will receive brief alcohol counseling modeled off WHO guidelines and Dr. Conroy's intervention in Malawi, which uses participants' baseline AUDIT scores for messaging around alcohol reduction and lasts 5-10 minutes. In selecting the control, we chose to balance our ethical obligation to provide basic health information on alcohol use (minimal in this setting), while maximizing the generalizability of our findings to inform a future RCT, which will employ a UC control group. Clinical trial experts recommend the UC condition over other designs such as a time-and-attention control (TAC) when the long-term goal is to inform implementation science and scale-up. Our long-term goal will be to test the effectiveness of a scalable alcohol intervention. Moreover, because TAC designs have an active but different intervention, there is the risk of positively-biased intervention results because the comparison arm can distract participants from making reductions in alcohol use they would have otherwise made.

5.10 Procedures for mobile breathalyzers with couples in MI *Plus* arm. Drinkers will be provided with handheld breathalyzers and both partners will receive access to the breathalyzer results. Drinkers will receive SMS requests to take a breathalyzer test twice per day (e.g., in the morning at 11 am and in the evening at 8 pm). After the drinker completes each breathalyzer test, the partner receives a notification that the drinker completed a test and can view the test results. Partners will receive a unique login username and password linked to their study ID. Dr. Conroy and the research manager(s) will facilitate a 1-2 hour training for couples how to use the breathalyzers/phones (e.g., charging, Wi-Fi, Bluetooth), complete breathalyzer tests, app functionality, trouble-shooting issues, and technical support. Couples will be instructed to use the breathalyzers for a 60-day period. Assessments at 60 days will allow us to assess the effects on alcohol use immediately following the 60-day intervention period.

A technology navigator will monitor daily compliance and check-in with participants to assist with login credentials, lost or damaged devices, cellular connectivity, difficulties using the phones or breathalyzers, and intentional non-use of the breathalyzers—with close monitoring during the first week. Navigators will monitor for safety issues and IPV (interpersonal violence) during routine check-ins and will provide assistance should a safety/IPV issue arise.

5.11 Survey assessments. Assessment visits will be held in community-based locations such as youth centers or in our team's mobile caravans used in other couples' studies. To minimize loss-

to-follow-up, we will administer follow-up surveys over the phone in the case that a participant moves out of the area or is unavailable for an extended period of time. For the pilot study, surveys will be administered at baseline and 2-months (after receiving all MI sessions and/or using the breathalyzers for 60 days), and 6-months post-intervention initiation. Measures collected will be the same across visits with the exception of time-invariant variables such as demographics (collected at baseline only). All measures will be pre-tested, tailored for South Africa, and translated to *isi*Zulu and back-translated to English. See Appendix with full survey instrument. Survey assessments will be interviewer-administered on tablet devices using REDCap mobile, last around 90 minutes, and uploaded to a secure web-based storage system. Partners will be assessed separately, but simultaneously, in private interview rooms.

	Domain	**Measure** (alphas noted are from prior studies with couples)
Primary outcomes (future trial)	Alcohol use	Number of drinking days in past 21, assessed using the three-week timeline follow-back method (TLFB) confirmed with the PEth biomarker.[32] AUDIT-C positive (score of ≥4 for men and ≥4 for women) and/or PEth positive (≥35 ng/ml).[33, 34]
Secondary outcomes (future trial)	Viral suppression and ART adherence	Viral suppression will be defined as less than 1000 copies/mL for DBS viral load. ART adherence will be captured using the bean method for low-literacy populations[35], by placing beans in a bowl for the number missed pills in the past 30 days. We will dichotomize adherence using a 95% cutoff, based on data showing that patients who miss ≥5% of doses have worse virologic outcomes.[36]
	Couple communication	Constructive, avoidant, and demand-withdraw communication (communication patterns questionnaire; α=0.69-0.72).[37]
	IPV	Physical, sexual, and emotional violence (WHO domestic violence measure; validated among PLWH; α=0.75-0.83).[38, 39]
	Relationship dynamics	Trust (dyadic trust scale; α=0.82).[40] Intimacy (emotional intimacy subscale of Sternberg love scale; α=0.90).[41] Unity (inclusion of self-in-other measure).[42] Relationship satisfaction (couple satisfaction index, single item).[43] Sexual satisfaction (couple sexual satisfaction scale; α=0.89).[44]
Mediating variables (future trial)	Shared illness appraisal	Single item that asks: "When you think about problems related to your [or your partner's] alcohol use, to what extent do you view this as "our problem" [shared by you and your partner equally] or mainly your [your partner's] own problem?".[45]
	Communal coping	Dyadic coping inventory, modified for alcohol use.[46, 47] Partners are asked how often they, as a couple, engage in activities to deal with alcohol (e.g., "We try to cope with alcohol issues together and search for solutions").
	Alcohol social support	Alcohol-specific partner support (to be adapted from the Social Provision Scale).[48]
Covariates (future trial)	Socio-demographics	Gender, age, marital status, relationship length, religion, living children, education level, household asset index.[49]

5.12 Medical record extraction. For participants living with HIV, we will access their medical record information including recent HIV results. We will obtain this information from electronic HIV registries (e.g., Tier.Net) or online databases (e.g., National Health Laboratory System), or

by requesting clinical files from patients' HIV clinic. Participants will be asked to bring their clinic cards to study visits, which contain identifiers that can be used to look up HIV test results.

5.13 Blood samples. At screening, we will obtain consent to confirm HIV status for all participants who report being positive using a point-of-care test. We will have results in 10-15 minutes. We will base eligibility on the result of this test. We will only test potential participants who report living with HIV. We will not return test results. ***At the two-month follow-up visit, we will collect blood samples via finger pricks for testing using DBS cards. Participants who are heavy drinkers will be tested for PEth. Participants who are heavy drinkers and living with HIV will have their viral load tested.*** PEth is 95% sensitive and 73% specific for detecting heavy drinking in the past 21 days and is highly correlated with number of drinking days among PLWH in SSA. PEth samples will be processed at the United States Drug Testing Laboratories using liquid chromatography tandem mass spectrometry. PEth samples on DBS cards will be stored at the HSRC research center until they can be batch transported to the US laboratory. PEth results will be reported as positive/negative and in ng/ml. Viral load DBS samples will be processed at the Universal Pathology Laboratory (UPL) in South Africa or an HPTN Network Laboratory certified laboratory facility. Viral load DBS samples will be processed using the Aptima HIV-1 Quant Dx Assay (DBS supplement) with a lower limit of detection of 30 copies/ml. In line with standard clinical practice in South Africa, less than 1000 copies/ml will be the threshold for viral suppression.

5.14 Exit interviews

Sampling: To contextualize the feasibility and acceptability data, we will conduct 60-90 minute exit interviews with 15 couples at the 2-month follow-up. Around five couples will be recruited from each arm, purposively sampled by participation level. For Arm 2, participation will be categorized as: low=attended one MI session, medium=attended two sessions, and high=attended all three sessions. For Arm 3, we will aim to enroll couples with varying test completion rates, categorized as low=completed less than 70% of breathalyzer tests, medium=completed 70-85% of tests, and high=completed>85% of tests. We will also try to interview couples in which both partners were heavy alcohol users to further understand how the intervention impacts dual drinkers.

Interview questions: We will elicit information on intervention preferences and satisfaction with domains of the intervention (e.g., frequency of breathalyzer tests and MI sessions, length, content, format of MI sessions). To explore dyadic mechanisms of change, we will elicit information on whether and how the breathalyzers and MI sessions enhanced communication, communal coping, and support. We will also elicit information on technology issues (e.g., user app experience, network connectivity, load shedding and power outages, battery life, trouble with logins) and contextual issues (e.g., literacy, alcohol stigma). Given the central question of whether the mobile breathalyzer technology can be used with couples to trigger support, we will assess how knowledge of BAC levels impacts the relationship (e.g., increases in couple conflict, changes in communication), how both partners interpret and respond to BAC levels, and the types of partner support provided and when.

Procedures: Given the gender-power dynamics in this setting, the PI Conroy's prior qualitative research, and the potential bias (e.g., women not feeling comfortable voicing their opinions in front of male partners) and increased risk for violence that could result from interviewing partners together, we will interview both partners separately, but simultaneously. Interviews will be audio-recorded, transcribed word-for-word, and translated from *isi*Zulu to English, and imported into Dedoose for analysis.

Analysis: We will use our successful analysis approach developed for dyadic qualitative data. This consists of coding one couple at a time by assigning new and *a priori* codes to both partners' transcripts. We will write an analytic memo for each couple that summarizes key factors involved, key themes or constructs, and within-couple consistencies and discrepancies. We will code the next set of couple transcripts and write an analytic memo for that couple and repeat this process until all transcripts are coded and 15 couple memos are written. We will construct data matrices to compare and contrast codes and themes between couples. An investigator meeting will be held to review the emergent patterns/themes, in conjunction with the quantitative findings, and to identify any final modifications to the intervention.

6.0 Safety monitoring and adverse event reporting

6.1. Safety monitoring

Safety-related risks could consist of: 1) loss of confidentiality; 2) loss of privacy; 3) couple tension, conflict and/or violence, and coercion; 4) discomfort or distress as a result of the personal and sensitive nature of the interviews or intervention sessions on alcohol, relationship dynamics, and violence; and 5) risks associated with finger pricks to collect blood samples for viral load and alcohol biomarkers (Phsphatidylethanol, or "PEth").

Any incidents involving subject safety will be reported to both institutional IRBs (Human Sciences Research Council and The University of California, San Francisco by the PI within 10 working days. The following information will be included in any report: 1) all serious adverse events associated with study procedures and/or 2) any events or problems involving the conduct of the study or patient participation, including problems with the recruitment or consent processes. The US PI will also provide a description of any problems or issues observed in the course of the study to each IRB on an annual basis.

Safety monitoring procedures. All safety-related risks will be monitored routinely at the time of assessment or intervention sessions. Procedures are in place to protect the confidentiality of information from one's partner and to monitor any confidential information. Interviewers and intervention staff will be trained to increase their sensitivity and present a caring and non-threatening manner regarding topics such as sexuality, HIV, and relationship issues. At any sign of discomfort or distress, or by request, interviews will be stopped. Confidentiality will be assured to participants at the time of consent, and they will be assured their answers or responses cannot be used against them for any reason, or for denial of any medical treatment. Standardized procedures will be documented and reviewed with staff regarding the possibility of tension, conflict or violence between partners. Procedures will be in place to monitor and respond to any instances reported by the participants of any type of negative relationship event, and proper action will be taken, including staff intervention and/or provision of referral for services depending on the level of the event (e.g., relationship conflict, an episode of domestic violence,

etc.). If a participant is referred to outside services, they will be provided with a formal referral letter.

Safety-related risk reporting and action plan. Interviewers and intervention staff at HSRC will report any breach of confidentiality incurred by the participants to the UCSF project coordinator, who will then inform the site PI and the US PI. Any participant in need of treatment due to distress, relationship conflict, or alcohol issues will be referred for appropriate services following staff completing the study protocol pertaining to these situations. As indicated above, in the event that a participant is referred to outside services, they will be provided with a formal referral letter. The US PI will ultimately be responsible for informing the IRBs and the DSMB through the IRB adverse event reporting procedure, and the Project Office through immediate email of any life-threatening incident, and through annual reports of other incidents. In the event of any adverse or life-threatening events occurring at an unacceptable level, the US PI will take appropriate action to halt the study, release a participant from the study, or modify the study procedures to reduce or eliminate the identified risk.

6.2. Adverse events

Any adverse events following participation will be tracked via referral and clinician follow-up. We will adapt the standard HSRC adverse event form adverse event form to document the incident, actions taken, supervisor notes, and follow-up steps. This form, supplemented by any additional staff notes will be provided to the appropriate agencies, including the University of California, San Francisco and HSRC Research Ethics Committees and the funding agency (NIH, USA). Any resulting recommendations from the IRB will be communicated to NIH. The site PI will be responsible for monitoring and reporting of any adverse events to the US PI, and will involve the DSMB as described below.

6.3. Data Safety and Monitoring Board

The level of risk from this behavioral intervention trial is minimal. We have developed the following plan to monitor the trial and to deal with data and safety monitoring. A Data and Monitoring Safety Board (DSMB) consisting of HIV behavioral and international research experts will be assembled.

The DSMB will meet using a video-conference platform such as Zoom. The DSMB will approve the overall protocol, assessments, and consent forms. All reports of adverse events (AE) will be reported to them, as well as to the IRBs (UCSF and HSRC). Severe adverse events (SAE) will trigger an immediate meeting of the DSMB. Additional meetings will be arranged as needed, following any emergent AE issues. The DSMB will review all accrued data to assess whether the study aims were met and to ensure that the benefits of the intervention outweigh any harm.

7.0 STATISTICAL CONSIDERATIONS

7.1 Analysis of FGDs to refine the intervention. Using a template analysis approach [50], we will develop a pre-determined template based on elements of the intervention to retain or refine, and new elements to add to address the needs of the target population. Study investigators will generate a draft of the template with thematic codes for relevant domains of the intervention, and will independently code the FGD transcripts. The investigative team will then discuss the emerging themes, identify areas for further adaptation, and refine the intervention manual. Depending on the extent of the changes, we may hold a meeting with HSRC's CAB to review

the FGD findings and identify intervention content and procedures that need to be added, removed, or refined.

7.2 Feasibility and acceptability data analysis. Our primary objective is to evaluate F&A of the intervention and study procedures. The primary analyses will include descriptive statistics of F&A indicators, comparing each statistic (e.g., percent retained) to the threshold listed in Table 4. Above-threshold findings will suggest a reasonable level of F&A while below-threshold findings would suggest that remedial modifications to study procedures and/or design would be required prior to moving forward with a full-scale trial. We will stratify the statistics by gender to consider sex as a biological variable.

Table 4. F&A Domain	Measure	Threshold	Arm(s)
Recruitment	Number of couples enrolled per week	Average 5 per week/20 per month	All
Enrollment	Proportion of eligible couples who enroll and complete baseline assessment	80% of eligible couples will complete enrollment	All
Randomization	Proportion of enrolled couples who complete randomization process	90% of enrolled couples will complete randomization	All
Participation	Proportion of couples who attend 66% and 100% of MI sessions	100% of couples will attend 66% (2 out of 3) of sessions; 75% of couples will attend all 3 sessions	2, 3
Engagement with mobile breathalyzer technology	Proportion of breathalyzer tests taken after prompted; number of partner SMS messages sent and received on BAC results; number of drinker SMS reminders to take breathalyzer tests sent and received; average length of time to take breathalyzer tests after prompted; average number of app logins per week to access BAC data (for both partners); average user session length; number of lost/stolen phones and breathalyzers	70% completion rate	3
Retention	Retention rates; reasons for dropouts	85% retention at 2-month follow-up	All
Process outcomes	Length of MI sessions in minutes	≤90 minutes per session[9]	2, 3
Intervention fidelity	Expert ratings of quality of intervention using audio-recorded intervention sessions (checklists)	>80% inter-rater reliability	2, 3
Assessment procedures	Length of surveys; proportion of couples who complete baseline, 1, 2, and 6-month surveys	90 minutes; 75% of all couples will complete all assessments	All

Acceptability	Proportion of couples satisfied with the intervention. Couples will decide their satisfaction together since this is a dyadic intervention.	75% of couples reporting being satisfied or very satisfied	All

7.3 Hypotheses and methods for preliminary/exploratory analyses. Although the purpose of this study is to determine F&A rather than to conduct formal hypothesis tests, we will evaluate exploratory hypotheses as part this assessment process. For example, we expect that: H1) participants in the couples MI-only group (arm 2) will report a greater reduction in the number of drinking days (confirmed with PEth) than participants in the control group (arm 1); H2) participants in the couples MI with mobile breathalyzers group (arm 3) will report a greater reduction in the number of drinking days than participants in the couples MI-only group (arm 2). Secondarily, we also anticipate that intervention participants will report a higher odds of adherence to ART and viral suppression than those in the control arm. We also anticipate the intervention participants will report higher (indicating more positive) scores on communication and relationship dynamics and less intimate partner violence than those in the control arm. Reflecting the exploratory nature of these analyses, alpha will be set at .05 for all inferential analyses.

7.4 Power analyses. Formal tests of health outcomes or attempts to obtain valid estimates of effect sizes are not statistically justified for the proposed study. Pilot studies, by design, cannot definitively test hypotheses due to their smaller sample sizes and the frequent design adjustments necessary to maximize recruitment, retention and quality assessment of outcomes. Effect size estimates are not sufficiently reliable given the breadth of the confidence intervals. However, to supply additional information, we conducted several power analyses using NCSS PASS. In sum, our study is powered to detect small to medium distances to confidence limits for descriptive statistics and medium to large longitudinal analysis effects, though, as noted above, formal hypothesis testing will not be the focus of this F&A study.

8.0 Human Subjects Considerations

8.1 Ethical Review

The study protocol, informed consent forms, and other requested documents — and any subsequent modifications — will be reviewed by the Human Sciences Research Council Research Ethics Committee in South Africa, and the Institutional Review Board at the University of California, San Francisco. Subsequent to initial review and approval, the responsible IRBs/ECs will review the study at least annually.

Each site Investigator will make safety and progress reports to the IRBs/ECs at least annually, and within three months after study termination or completion. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, all SAEs, and all unanticipated problems involving risks to human subjects or others.

The results of all DSMB reviews of the study also will be provided to the IRBs/ECs.

8.2 Informed Consent

Consent for participation in pilot RCT. Couples will arrive together for their appointments which will begin with the informed consent process. Partners will be consented individually in a private interview room by a gender-matched interviewer in the local language. The consent process will cover topics on the purpose of the study, potential risks and benefits, how confidentiality will be

ensured, voluntary participation, the funding agency and study investigators, and contact information for the study PIs. The study's consent form will be read and explained to them by the interviewer. A detailed description of the study procedures will be included. The consent form will include the information that they have the right to refuse or withdraw from participation at any time. The consent form will provide detailed descriptions of the expectations of being a participant in either of the study groups, along with the accompanying potential risks and benefits of each. Information will be presented on randomization, following procedures used to describe randomization in our prior studies in the region. A paper version of the information sheet will be offered to participants with the goals of the research, the study procedures, and the names and contact info for the principal investigators will also be provided, and a contact number for the local PI. The consent process will also ask respondents if they agree to be contacted to participate in additional study activities beyond what is required for the proposed study and whether it is acceptable to track them at their homes if phone calls do not go through.

Consent for biomarker collection. The main consent form will include consent for obtaining biomarker specimens, detailing the appropriate risks, procedures involved, and any benefits. Respondents will be informed of the risks/benefits and that the results of the HIV and alcohol biomarker (PEth) tests will not be made available to them.

Consent for qualitative data collection. For the qualitative phases (FGDs for Aim 1 and exit interviews for Aim 3), we will use separate consent forms. For the FGDs, the process will inform respondents that others in the group will learn of their HIV status (although all group members will be HIV+) and confidentiality cannot be assured so they must choose carefully the information that is shared with other group members.

Electronic signatures for consent will be obtained for all participants; for those who cannot write their names, they will place an "X," their thumbprint, or their mark on the consent form. The interviewer and an impartial witness, who the participants knows and trusts, will also sign the consent form. All consent forms will be translated into isiZulu (the predominant local language) and then back translated by a separate individual in order to ensure proper translation. Given the high levels of illiteracy in this context, study staff will read the written version of the consent form and test for an understanding at the end with a series of simple questions (e.g., "can you tell me what will happen if you agree to participate in the study?"). Respondents will be offered a copy of the consent form in isiZulu (or in English, if preferred). All consent forms will be approved by the IRBs of both UCSF and HSRC in South Africa.

8.3 Risks

This study is considered minimal risk. However, participation requires at least one partner to be HIV+ and thus respondents may be identifiable to others in the community by their participation in the study. The risks associated with knowledge of a respondent's HIV+ status in the community include social stigma (e.g., rejection, isolation) and discrimination (e.g., loss of employment or status in the community). The potential risks of the study can be grouped into five categories: 1) loss of confidentiality; 2) loss of privacy; 3) couple tension, conflict and/or violence, and coercion; 4) discomfort or distress as a result of the personal and sensitive nature of the interviews or intervention sessions on alcohol, relationship dynamics, and violence; 5)

risks associated with finger pricks to collect blood samples for viral load and alcohol biomarkers (PEth); and 6) risk of COVID-19 infection.

The intervention may not be appropriate for couples experiencing severe current IPV. We will exclude couples in which one or both members report concerns about their safety or report experiencing or perpetrating severe IPV in the prior 3 months. IPV measures will be adapted WHO measure for South Africa, which assesses physical, sexual, and emotional violence, and determines whether it is mild, moderate or severe. This approach was chosen to minimize exacerbation of potentially volatile situations while participating in a relationship-focused intervention. Given that we are not excluding couples based on ever experiencing severe IPV, and including those couples reporting any mild- to moderate IPV, we believe that this balances sample generalizability with participant safety.

Loss of confidentiality. The loss of confidentiality may lead to disclosure of HIV infection and alcohol use disorder. Stigma associated with disclosure may include social harms such as discrimination (e.g., lost of employment or status in the community), physical harm (e.g., acts of violence being committed against people who have HIV), and psychological harm such as embarrassment (e.g., being questioned by family members about alcohol use). To protect participants' confidentiality the following steps will be taken: 1) all staff will receive training at the initiation of the study and ongoing supervision to ensure their understanding of any and all confidentiality-protecting procedures; 2) participants' names will not be associated with any research instruments; 3) only research identification numbers will be used on data; 4) any tracing or other contact information, including signed consent forms will be stored separately from the data; 5) all records will be stored in locked file cabinets in study offices at HRSC; 6) the files linking research identification numbers and names will be stored in a separate locked file cabinet, and a computer file only accessible by the Research Manager, PI and Co-Is; 7) all computers/tablets/phones on which any data are stored will be password protected.

As this is a study involving couples, additional measures are needed to protect each participant's confidentiality from their partner. From our prior work, we have developed procedures to minimize risk. For the study assessment interviews, all participants will be interviewed by a gender-matched interviewer who will conduct the interview in a private room. Couples will arrive together but be consented and interviewed separately. Prior to their separation, study staff will inform them that they may contact the staff member who interviewed them, but they will not be permitted to have contact with the interviewer who administered the survey to their partner. This procedure will enhance the participants' confidence that the information they disclose will be kept confidential and not disclosed to their partner. Each study staff member will only interact with one participant, and the interviewers will be instructed not to compare answers between them regarding a couple's answers.

The consent form will include specific language regarding the confidentiality of the partner's study data: "Please be aware that you will not be told any information that your partner says in his or her interview. This includes any information your partner might say about his or her health, even if we think you do not know this information. Likewise, no information you say in your interview will be told to your partner, even if we think your partner might not know this information." Interviewers will be trained to ensure that participants understand this condition during the informed consent process, including information about the confidentiality of their own

and their partner's data. As mentioned above, systematically providing this information will eliminate partner's surmising that it is being provided due to information disclosed during the interview. It is possible that partners might ask each other about their responses to certain questions or issues discussed. Interviewers will be trained to discuss with participants ways of coping with this situation.

Loss of privacy. We will screen and interview couples in private locations and will take additional measures to protect respondents' HIV+ status. Although most activities will take place in the HIV clinics or other central community-based location, it will be important that interviewers maintain respondents' privacy if visiting the communities of respondents. To protect individuals' privacy, we will utilize language such as "Healthy Living" rather than referring to HIV or alcohol use when discussing the study.

There is the potential for additional privacy risks related to use of the breathalyzers in public, which could be stigmatizing if others in the community learn about their association with an HIV and alcohol study. When training participants on how to use the technologies for the study, we will counsel participants on how to best respond to questions from others on the breathalyzers and strategies to maximize privacy (e.g., finding a private space at drinking establishments to record BAC levels). During the consent process, we will explain these risks to participants to ensure they feel comfortable using the breathalyzers in the public space and participating in the study. We will provide a pouch to cover the breathalyzer and a phone cover to disguise the phone brand so these devices are not identifiable to the community and linked to the study.

During the FGDs which also utilize a group format, we will take additional measures to protect privacy. We will discuss the risks to confidentiality due to participating in FGDs in the informed consent processes. We will emphasize the fact that comments made during FGD sessions are to be kept confidential. However, it is possible that participants may repeat comments made or heard during FGDs in a different context in the future. They may also disclose the identity of other participants in the group. We will ask participants to not to talk specifically about themselves, but more generally about people they know who are like them or live in their communities. Although personal information and experiences may be discussed, the FGDs will primarily serve to obtain opinions on the proposed health intervention. The FGDs will be conducted in English/isiZulu by trained qualitative researchers with extensive experience in ensuring the safe conduct of group discussions. As with the interviews and survey, respondents will have the right at any time to decide not to participate or answer questions.

Couple tension, conflict, and/or violence, and coercion. It will be communicated in the consent form that while study staff members will not reveal participant information to their partner, it is possible that their partners might ask them about their responses to certain questions or issues they discussed. Interviewers will be trained to discuss with participants' ways of coping with this situation if the participant expresses concern or distress about this matter during consent, the administration of the survey, or after it is completed.

Although we have not had problems in the past in South Africa with participants reporting coercion, staff members will be trained to be sensitive to the possibility that one member of the couple was pressured or coerced by the other partner to participate in the study. Questions may be posed such as "Did you come here freely?" or "Will something bad happen to you if you say

no?" Should the staff member have this suspicion, s/he will be trained to immediately terminate the survey or session and provide the participant with appropriate referrals and the study incentive. Any data collected will be destroyed. The staff member will also be trained to offer the participant the opportunity to remain in the interview room for the appropriate amount of time that it would have taken to complete the survey or interview so that the study partner would not be alerted to the fact that the interview was terminated. If necessary, back-up staff members who are clinicians can be contacted to assess the appropriate immediate steps, should intervention be needed. Should evidence of coercion/violence arise in the intervention sessions, assessment visits, or exit interviews, the counselor will provide the appropriate clinical intervention regarding participation of the couple, including assessing the level of safety and whether immediate medical/psychological attention is needed, and/or provide community referrals. Depending on the situation, procedures as described above will be followed in terms of determining next appropriate steps.

Interviewers and other intervention staff will also be trained in the identification of, and proper response to, issues of coercion or abuse, and will be familiar with how to facilitate referrals for intimate partner violence assistance (either for the violent partner or the victimized partner). For example, staff will assess the degree of threat, whether the participant's life is currently at risk, or whether the crisis is not of an imminent nature. Depending on the degree of threat, the participant could be referred immediately to a district crisis center, or, in lesser threat situations, could be provided with referrals for community-based services.

As stated in the inclusion criteria, couples will be excluded if they report a history of severe intimate partner violence in the past three months or feel their safety would be at risk. We do not wish to exclude a lifetime experience of violence from our sample, as that would potentially exclude participants who could benefit the most from the alcohol intervention. By screening out recent episodes (past three months) of severe intimate partner violence and/or women who feel their safety could be jeopardized by participation, we aim to have a sample that balances potential benefit with relatively low risk from a couples-based intervention. Incident risk for IPV will be assessed at all follow-up visits and intervention sessions. If IPV is reported during these visits, we will follow an established protocol to document the situation, assess safety for the partner(s), provide emotional support, and appropriate intervention and/or linkage to psychological and/or medical services.

We will also use a combination of actively and passive monitoring for violence during the intervention sessions and while the couples are independently using the breathalyzer devices. For active monitoring, a designated technology navigator will routinely check in with participants (separately with each partner) to ensure compliance and to troubleshoot any technical issues with using the breathalyzers/phones and will discretely monitor for violence. For passive monitoring, the technology navigator or another staff member at HSRC will be paired to participants and will be available to be contacted via phone should a safety issue arise during the study period. If a violence or safety concern is reported, the staff member will follow an established protocol to assess the degree of threat, whether the participant's life is currently at risk, or whether the crisis is not of an imminent nature. Depending on the degree of threat, the participant could be referred

immediately to a district crisis center, or, in lesser threat situations, could be provided with referrals for community-based services.

Should a participant specifically request an IPV referral during a study visit, the staff member will immediately terminate the interview, provide the participant with the study reimbursement, offer to let the participant remain in the interview room for the approximate time of completion, and the assessment protocol for determining participant safety will be triggered. In addition, our resource list given to all participants will include intimate partner violence programs, clinicians, and support groups specializing in relationship abuse and violence.

Discomfort/distress. There could be some discomfort with the sensitive nature of the interviews on topics including alcohol use and couple conflict. Interviewers and study staff will be trained to minimize distress/discomfort to respondents, to recognize any signs of distress, and to make appropriate referrals to community-based services, if necessary. Our research team has a significant amount of experience conducting behavioral surveys and interviews within the field of HIV prevention and treatment, and with couples, including in the proposed setting. It has been our experience that it is rare for a participant to find the interview upsetting. We have infrequently encountered episodes of mild embarrassment or awkwardness, which quickly dissipate. Experienced lay counselors will be available on the study staff for consultations or referrals, should a respondent exhibit severe symptoms of mental distress. All couples' counseling sessions will be conducted by lay counselors, but who have received significant training pertaining to couples, so any distress during an intervention session will be able to be processed and dealt with appropriately. All staff will be trained in the proper referral procedures, and will be provided with ongoing supervision of such issues by the Research Manager. Through our work in this community, we have compiled a list of community-based resources, including mental health counseling, general health services, domestic violence, and substance use. This list of referrals will be continually updated, and systematically provided to every individual at every visit, which will reduce the likelihood that any one couple or individual would be identified as needing a particular service. Informed consent documents will inform research participants of potential discomfort around certain interview topics and the option to refuse to answer or skip any questions on the surveys that they are uncomfortable answering.

Blood draw injury. Viral load and PEth tests require participants to provide a blood sample through finger pricks. The physical risks associated with finger pricks are low, but could include pain and rarely, bruising and/or infection. All study staff will be crossed trained in how to collect DBS samples and in good clinical practice (GCP). GCP protocols will be followed for the handling and storage of DBS samples. Research assistants will report any complications resulting from the blood collection to the field study coordinator, who will make an immediate report to the local and UCSF PIs. The PIs will take responsibility for reporting serious adverse events to the IRBs.

Procedures for handling alcohol dependency. This is a pilot study of a behavioral intervention to reduce customary levels of alcohol consumption. Study staff will be clear in instructing participants not to drink alcohol in excess of their customary amounts such that study participation does not incur any increased risk above that of their customary alcohol consumption. Control arm participants will receive brief advice on alcohol use as part of the enhanced care control condition. However, our screening and follow-up visits may uncover

possible alcohol dependence, using an AUDIT-C score of greater than 8. Our electronic data collection instruments will flag these participants in real-time and alert the interviewer to take action. In this case, we will provide simple advice to help participants cut down slowly on their alcohol use and avoid the negative effects of alcohol withdrawal. For example, participants will be advised: "If you are a heavy drinker, we advise you to gradually reduce your alcohol consumption. We advise that you do not stop drinking suddenly because you may feel alcohol withdrawal symptoms that may seriously affect your health." We will continue with study activities but will have procedures in place to refer patients to several private alcohol and substance use referral centers/services in the local area (SANCA, LifeLine, and SADAG). At any point in the study, participants who request or ask about services to help them with their alcohol dependency will be referred to such services. If significant alcohol problems are encountered during the couples' MI sessions or other intervention activities, study participants will be encouraged to discuss these problems with their health care providers and will be referred to alcohol and substance use services in the community.

Procedures for handling severe depression and suicidality: If a participant shows signs of severe depression (e.g., score ≥20 on the PHQ-9 scale) or suicidality (e.g., indication on PHQ item 9) during the study assessments or intervention sessions, study staff will follow an established protocol to assess risk and make the appropriate referrals and linkages into services. In the case of suicidality, staff will be trained on how to conduct a suicide risk assessment including how to differentiate between potential suicidal ideation and non-suicidal ideation. In the case of suicidal ideation, staff will assess past and current suicidal episodes and screen for other risk and protective factors to determine the appropriate safety plan. Referrals and linkage into services will be made in consultation with the broader HSRC clinical and community outreach teams using internal procedures for handling cases of distress and poor mental health.

COVID-19 safety management plan: To protect study participants, their families and research staff from the risk and spread of COVID-19, the study will adhere to all Kwa-Zulu Natal Department of Health directives aimed at mitigating the spread of COVID-19. We will inform research participants of requirements to undergo COVID-19 screening and reporting of screening results to the local public health authorities whenever the results may point at a possible infection with the disease, for their benefit. We will also provide participants and staff with 3 ply face masks, avail hand washing stations at the study sites, and provide hand sanitizers. We will pre-screen participants before physical contact, check temperature and observe social distancing requirement of 1.5 meters during face-to-face interaction with participants. We will inform the participants of the measures that we will be taking during any form of face-to-face contact. We will also have daily mandatory screening for staff who are making contact with participants, and only those without any COVID-19 symptoms will be allowed to make contact with participants. The staff will also disinfect furniture and sanitize their hands after every contact with a participant. Finally, we will select a large conference room with good ventilation (open windows and fans) to further reduce risk of transmission for COVID-19.

8.3.1. Minimizing risks

We will handle risks associated with couples research by following similar procedures from our team's prior work with couples in southern Africa. Any risks to respondents that stem from

participation in the intervention, assessment visits, exit interviews, or focus group discussions will be minimized by: 1) training of staff in the ethical conduct of research; 2) training of staff in issues specifically pertaining to couples in this setting (i.e., potential for couple tension/conflict/violence, or coercion); and 3) close monitoring of any adverse events with appropriate IRB reporting; and 4) referrals to professional or community agencies providing mental health (including alcohol use disorders) or other appropriate services, when necessary. Refresher trainings on ethical procedures will be held as needed and ongoing adherence to all ethical practices will be closely monitored by the Research Manager and site PI.

During the screening process, we will have established procedures in place for ensuring that HIV+ individuals have verbally disclosed their HIV status to their primary partners in order to minimize risk associated with unintended disclosure (e.g., distress, conflict or arguments, break-ups, violence). If we cannot establish that disclosure has occurred, the screening process will be terminated due to ineligibility. We will consider HIV status disclosure to have occurred from the patient to their partner only if verified by the partner. If both partners are HIV-positive, both partners will be required to have disclosed to the other. Should the situation arise where we identify that HIV+ individuals have not disclosed their HIV status to their partner, we will have resources available (e.g., study HIV counselors) and referral pathways in place. Screening will be an interactive process and study staff will pause and check for understanding of all eligibility criteria.

As this is a study involving couples, additional measures are needed to protect each participant's confidentiality from their partner. From our prior work, we have developed procedures to minimize risk. For the ongoing assessment interviews, all participants will be interviewed by a gender-matched interviewer who will conduct the interview in a private room. Couples will arrive together but be consented and interviewed separately. Prior to their separation, study staff will inform them that they may contact the staff member who interviewed them, but they will not be permitted to have contact with the interviewer who administered the survey to their partner. This procedure will enhance the participants' confidence that the information they disclose will be kept confidential and not disclosed to their partner. Each study staff member will only interact with one participant, and the interviewers will be instructed not to compare answers between partners unless required for the study (e.g., confirming the couple is eligible).

In sum, the proposed 3-year project is a pilot study for a couple-based motivational interviewing intervention aimed towards reducing heavy alcohol use and improving adherence to ART among HIV-positive alcohol users. We will collect data using surveys, focus group discussions, exit interviews, biomarkers, tracking logs, mobile app data, and intervention forms to address the specific aims. The assessments and interventions pose no more than minimal risk to participants, and we have taken steps to minimize risk. The data and safety monitoring plan identifies the PI (Dr. Conroy) as the primary individual responsible for monitoring the risks to human subjects with regards to data and safety related issues. We will use available mental health professionals and medical procedures to address any psychological or physical risks that may arise. Serious adverse events will be reported promptly to the UCSF and HSRC Research Ethics Committee, the DSMB, and project officer of the funding source.

8.4 Benefits

8.4.1. Overall benefits to participants

There are no direct benefits to the study participants. However, they may gain motivation and skills to reduce alcohol use and engage in communication better with their partner around alcohol use. Some participants might find it therapeutic to discuss alcohol and issues in their relationships, as we found in our formative research with this population. The larger public health community could benefit if the intervention is found to be feasible and acceptable, and later shown through a full-scale trial to be efficacious at reducing alcohol use and improving HIV treatment outcomes, and potentially, reducing the burden of HIV and heavy alcohol use in the community. While there are some risks to participating in the study, based on prior experience, we feel that the likelihood of participants experiencing negative events due to participation is low. The risk to individual participants is small, and the potential to provide information that could benefit the target population outweighs the risk.

8.5 Confidentiality

See section on risks for discussion of confidentiality and steps taken to protect it and consequences if violated.

8.6 Incentives

Participants will be reimbursed based on the time, inconvenience and expense model of reimbursement in research. Each person screened will be given R40 for completing the screener. Each participant will be given R100 for participation in study assessment visits and R100 for exit interviews. We propose R50 as a token of appreciation for participants attending each intervention session. Participants selected for focus group discussions will be reimbursed with R210 per session. Participants in the MI plus breathalyzer arm will be reimbursed R5 for each breathalyzer test completed, for a maximum of R10 per day or R300 per month. Reimbursements proposed are for participant time and inconvenience. No participant incurred expenses are anticipated – sessions will be scheduled in community venues and all study related consumables will be provided by the study team. At the end of the study, all participants in all arms of the study who completed their participation, will be entered into a lottery to win a second-hand iPhone. We will use this method to distribute the iPhones used in the study.

8.7 Study Discontinuation

This study may be discontinued at any time by the Protocol Chairs, government or regulatory authorities, and/or site IRBs/ECs.

9. ADMINISTRATION

9.1 Compliance

9.1.1. Training, Quality Assurance (QA) and Supervision

The investigative team has experience in staffing, training, and supervising clinical research studies, including behavioral intervention trials. Our proposed QA protocol is based upon experience in other studies at University of California, San Francisco, University of California-San Francisco, and in sub-Saharan Africa. The QA protocols will be led by the PI and Dr. Conroy, given their additional experience with clinical trials.

9.1.2. Assessment training

Assessment interviewers will be selected based on a minimum of one-year experience with HIV-research quantitative standardized interviews. We have developed a detailed training manual for the training and ongoing supervision of assessment staff which will provide specific information on study policies and procedures. Initial training, led by the Dr. van Heerden and Dr. Conroy, will occur in an intensive workshop in which the following are covered: 1) general interviewing skills; 2) specific training relevant to this study, particularly with regard to conducting research with couples; 3) extensive training in research ethics; and 4) observed practice and certification as interviewers. The training will include specific modules regarding domestic violence, especially as pertains to any report of partner violence by a participant, and the proper response to a disclosure**.**

9.1.3. Assessment Quality Assurance

Given the structured format of the assessments there is less concern with interviewers veering from the protocol than in other interviewing situations. However, we recognize the importance of internal validity of assessment procedures and have developed the following procedures: (1) A supervisor (Project Director or Lead Interviewer) will sit in on random interviews to ensure standardization of administration; (2) a standardized evaluation form will be used, based on the specifics of the assessment; and (3) the PD will oversee the QA of assessments and provides feedback and supervision as appropriate.

9.1.4 Data Entry and Management

The mobile application displays questions on the screen and then gives interviewers the ability to enter responses directly into the mobile phone or tablet. Once complete, the research instrument (i.e. survey, baseline interview) is temporarily stored in a non-readable encrypted file on the device/tablet. When in an area with network coverage, completed forms are uploaded and removed from the handset approximately every 60 seconds. If no network signal is present, the data is stored on the phone until such time that phone detects a network signal. Checks will be placed to ensure correct information has been entered. Information from the research instruments will be uploaded to a secured server. The UCSF Research Manager will monitor incoming data on a daily basis and generate data queries for unusual or unexpected entries and communicate with the HSRC team to resolve queries.

9.2 Study monitoring

9.2.1. Data monitoring procedures.

Recruitment goals will be carefully monitored by the Project Director, and the PI. We will also monitor the presence of any missing data and loss to follow-up. Co-I, Neilands, will serve as the study's biostatistician and will provide ongoing monitoring of the study progress. We will also provide this information to the DSMB on a consistent basis.

9.2.2. Data-related risk reporting and action plan.

We will closely track incoming numbers of participants via ongoing recruitment activities, and weekly and monthly reports will be compiled by the study staff. We will utilize similar procedures to monitor any missing data or missed follow-up assessments. Recruitment and missing data reports will be monitored weekly by the Project Director, statistician, Co-Is, and PI. All data will be protected on firewall-protected servers at University of California San Francisco and HSRC. Any identification of recruitment rates or follow-up rates that represent threats to our

ability to sufficiently answer the research questions will be met with action by the PI to intervene to remedy the shortcomings. Should a situation arise of insufficient power or early detection of research questions the investigators will discuss halting the study, when and if needed, and would report such action to the IRBs at the University of California, San Francisco and HSRC, the DSMB, and project officer. Completion rates of intervention activities will be monitored in parallel fashion.

9.2.3. Safety monitoring procedures.
All safety-related risks will be monitored routinely at the time of assessment or intervention sessions. Procedures are in place to protect the confidentiality of information from one's partner and to monitor any confidential information. Interviewers and intervention staff will be trained to increase their sensitivity and present a caring and non-threatening manner regarding topics such as sexuality, HIV, and relationship issues. At any sign of discomfort or distress, or by request, interviews will be stopped. Confidentiality will be assured to participants at the time of consent, and will be assured their answers or responses cannot be used against them for any reason, or for denial of any medical treatment. Detailed protocols will be in place regarding the possibility of tension, conflict or violence between partners. Protocols will be in place to monitor and respond to any instances reported by the participants of any type of negative relationship event, and proper action will be taken, including staff intervention and/or provision of referral for services depending on the level of the event (e.g., relationship conflict, an episode of domestic violence, etc.)

9.3 Study Records

Consent forms will be stored separately from questionnaire data and data collection forms, and will not be linkable to study data (surveys and follow-up visits). Special permission will be obtained for audio files to be digitally recorded of the couples' counselling sessions, but this material will only be used for quality control procedures. All individuals will be given a confidential study identification number and all data will be labelled only with this identification number. There will only be one master list linking participants' names and study identification numbers. We will keep this list separate from all other materials in a locked file in a locked office at the HSRC study site. We will keep a back-up file of this list on a password protected computer file, and select HSRC study staff (site PI, Project Director, and Interviewers) will have access. Access will be necessary by HSRC staff for tracking purposes. Digital audio files from the couples' counselling sessions (again for QA purposes only) will be kept in a password protected, encrypted computer file.

All data – electronic and paper – will be kept for a period of up to 5 years. The data will be stored through REDCap and Dropbox, and destroyed after 5 years.

9.4 Use of information and publications.

We plan to focus our dissemination efforts in the following contexts:

1. *Scientific community*: We plan to communicate our results to other researchers through published papers in peer-reviewed journals and through scientific presentations given at national and/or international conferences.

2. *HIV care providers (clinicians, nurses, counselors, and other providers):* It is possible that our intervention may be of interest to HIV care providers who work with couples and/or HIV-positive individuals as a potential strategy to reduce alcohol consumption and improve treatment engagement and clinical outcomes. We will aim to disseminate salient findings to HIV care providers as they become available. Our prior research made use of monthly HIV grand rounds in the hospitals as a forum for dissemination and encouraging feedback on the findings, and we will explore other forums such as regular staff meetings with providers, and national conferences in South Africa which are widely attended by HIV care providers.

3. *Community members:* We will aim to communicate the findings to the study participants and communities represented by the study participants. The findings could be disseminated during the daily health information talks given in the waiting rooms at the HIV clinics or at other large meetings for people living with HIV such as support groups. We will also communicate the findings to key stakeholders in the communities (e.g., religious leaders, tribal leaders, etc.). We have successfully completed this type of outreach in our prior studies in this setting (e.g., community forums). The information disseminated will be available in English and in the local language of isiZulu, in either written or verbal form. To facilitate access to our work, we will make study materials available online and in print format. Any published results will not identify any participants.

10.0 References

1. Hahn JA, Woolf-King SE, Muyindike W. Adding fuel to the fire: alcohol's effect on the HIV epidemic in Sub-Saharan Africa. Curr HIV/AIDS Rep. 2011;8(3):172.
2. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: review and meta-analysis. J Acquir Immune Defic Syndr. 2009;52(2):180-202.
3. Wu ES, Metzger DS, Lynch KG, Douglas SD. Association between alcohol use and HIV viral load. Journal of acquired immune deficiency syndromes (1999). 2011;56(5):e129.
4. Shuper PA, Neuman M, Kanteres F, et al. Causal considerations on alcohol and HIV/AIDS—a systematic review. Alcohol Alcohol. 2010;45(2):159-66.
5. Baliunas D, Rehm J, Irving H, Shuper P. Alcohol consumption and risk of incident human immunodeficiency virus infection: a meta-analysis. International journal of public health. 2010;55(3):159-66.
6. Conroy AA, McKenna SA, Ruark A. Couple interdependence impacts alcohol use and adherence to antiretroviral therapy in Malawi. AIDS Behav. 2019;23(1):201-10.
7. Conroy AA, McKenna SA, Leddy A, et al. "If She is Drunk, I Don't Want Her to Take it": Partner Beliefs and Influence on Use of Alcohol and Antiretroviral Therapy in South African Couples. AIDS Behav. 2017;21(7):1885-91.
8. Conroy AA, Ruark A, McKenna SA, et al. The Unaddressed Needs of Alcohol-Using Couples on Antiretroviral Therapy in Malawi: Formative Research on Multilevel Interventions. AIDS Behav. 2019:1-13.
9. Starks TJ, Millar BM, Doyle KM, et al. Motivational interviewing with couples: A theoretical framework for clinical practice illustrated in substance use and HIV prevention intervention with gay male couples. Psychology of sexual orientation and gender diversity. 2018;5(4):490.
10. Wandera B, Tumwesigye NM, Nankabirwa JI, et al. Efficacy of a single, brief alcohol reduction intervention among men and women living with HIV/AIDS and using alcohol in Kampala, Uganda: a randomized trial. Journal of the International Association of Providers of AIDS Care (JIAPAC). 2017;16(3):276-85.
11. Murphy DA, Chen X, Naar-King S, Parsons for the Adolescent Trials Network JT. Alcohol and marijuana use outcomes in the Healthy Choices motivational interviewing intervention for HIV-positive youth. AIDS Patient Care STDS. 2012;26(2):95-100.
12. Velasquez MM, von Sternberg K, Johnson DH, et al. Reducing sexual risk behaviors and alcohol use among HIV-positive men who have sex with men: a randomized clinical trial. J Consult Clin Psychol. 2009;77(4):657.
13. Naar-King S, Wright K, Parsons JT, et al. Healthy choices: motivational enhancement therapy for health risk behaviors in HIV-positive youth. AIDS Educ Prev. 2006;18(1):1-11.
14. Naar-King S, Lam P, Wang B, et al. Brief report: maintenance of effects of motivational enhancement therapy to improve risk behaviors and HIV-related health in a randomized controlled trial of youth living with HIV. J Pediatr Psychol. 2007;33(4):441-5.
15. Hasin DS, Aharonovich E, O'leary A, et al. Reducing heavy drinking in HIV primary care: a randomized trial of brief intervention, with and without technological enhancement. Addiction. 2013;108(7):1230-40.

16. Hasin DS, Aharonovich E, Greenstein E. HealthCall for the smartphone: technology enhancement of brief intervention in HIV alcohol dependent patients. Addict Sci Clin Pract. 2014;9(1):5.
17. Kahler CW, Pantalone DW, Mastroleo NR, et al. Motivational interviewing with personalized feedback to reduce alcohol use in HIV-infected men who have sex with men: A randomized controlled trial. J Consult Clin Psychol. 2018;86(8):645.
18. Robles G, Bosco SC, Dellucci TV, Starks TJ. Integrating intra-individual and dyadic factors in examining health among gay and bisexual men: A narrative review of recent literature. LGBT Family Studies. In Press.
19. Starks TJ, Dellucci TV, Gupta S, et al. A Pilot Randomized Trial of Intervention Components Addressing Drug Use in Couples HIV Testing and Counseling (CHTC) with Male Couples. AIDS Behav. 2019:1-14.
20. Starks TJ, Robles G, Doyle KM, et al. Motivational Interviewing with Male Couples to Reduce Substance Use and HIV Risk: Manifestations of Partner Discord and Strategies for Facilitating Dyadic Functioning. Psychotherapy. In Press.
21. Wang Y. Real-time assessment of alcohol use: The potential of wrist-worn alcohol biosensor. Oral presentation given at the NIAAA ART/PrEP Meeting. 23-24 September 2019. Bethesda, MA 2019.
22. Lauckner C. Harnessing mHealth Technologies to Deliver a Behavioral Alcohol Reduction Intervention: The TRAC Study. Oral presentation given at the NIAAA ART/PrEP Meeting. 23-24 September 2019. Bethesda, MA 2019.
23. Fairbairn CE, Kang D. Temporal Dynamics of Transdermal Alcohol Concentration Measured via New-Generation Wrist-Worn Biosensor. Alcoholism: Clinical and Experimental Research. 2019.
24. Independent Communications Authority of South Africa. The state of the ICT sector report in South Africa. Last accessed from https://www.icasa.org.za/pages/sector-forecasting on November 3, 2019. 2019.
25. Beratarrechea A, Lee AG, Willner JM, et al. The impact of mobile health interventions on chronic disease outcomes in developing countries: a systematic review. Telemedicine and e-Health. 2014;20(1):75-82.
26. Opoku D, Stephani V, Quentin W. A realist review of mobile phone-based health interventions for non-communicable disease management in sub-Saharan Africa. BMC Med. 2017;15(1):24.
27. Peter J, Benjamin P, LeFevre AE, Barron P, Pillay Y. Taking digital health innovation to scale in South Africa: ten lessons from MomConnect. BMJ Specialist Journals; 2018.
28. Comulada WS, Wynn A, van Rooyen H, et al. Using mHealth to deliver a home-based testing and counseling program to improve linkage to care and ART adherence in rural South Africa. Prevention Science. 2019;20(1):126-36.
29. van Heerden A, Ntinga X, Vilakazi K, editors. The potential of conversational agents to provide a rapid HIV counseling and testing services. 2017 international conference on the frontiers and advances in data science (FADS); 2017: IEEE.
30. Miller WR, Rollnick S. Motivational interviewing: Helping people change: Guilford press; 2012.
31. Starks TJ, Robles G, Doyle KM, et al. Motivational interviewing with male couples to reduce substance use and HIV risk: Manifestations of partner discord and strategies for facilitating dyadic functioning. Psychotherapy. 2020.

32. Hahn JA, Dobkin LM, Mayanja B, et al. Phosphatidylethanol (PEth) as a biomarker of alcohol consumption in HIV-positive patients in sub-Saharan Africa. Alcoholism: clinical and experimental research. 2012;36(5):854-62.
33. Bush K, Kivlahan D, McDonell M, Fihn S, Bradley K. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Arch Intern Med. 1998;158:1789-95.
34. Hahn JA, Emenyonu NI, Fatch R, et al. Declining and rebounding unhealthy alcohol consumption during the first year of HIV care in rural Uganda, using phosphatidylethanol to augment self-report. Addiction. 2016;111(2):272-9.
35. Conroy AA, Leddy AM, Darbes LA, et al. Bidirectional violence is associated with poor engagement in HIV care and treatment in Malawian couples. Journal of interpersonal violence. 2021:Advance online publication.
36. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med. 2000;133(1):21-30.
37. Christensen A, Shenk JL. Communication, conflict, and psychological distance in nondistressed, clinic, and divorcing couples. J Consult Clin Psychol. 1991;59(3):458-63.
38. WHO. WHO Multi-country Study on Women's Health and Domestic Violence: Core Questionnaire and WHO Instrument – Version 9 World Health Organization, Geneva, Switzerland: 2005.
39. Jewkes R, Dunkle K, Nduna M, et al. Factors associated with HIV sero-status in young rural South African women: Connections between intimate partner violence and HIV. Int J Epidemiol. 2006;35:1461-68.
40. Larzelere RE, Huston TL. The Dyadic Trust Scale: Toward Understanding Interpersonal Trust in Close Relationships. Journal of Marriage and the Family. 1980;42(3):595-604.
41. Sternberg RJ. Construct validation of a triangular love scale. Eur J Soc Psychol. 1997;27(3):313-35.
42. Aron A, McLaughlin-Volpe T, Mashek D, et al. Including others in the self. European Review of Social Psychology. 2004;15(1):101-32.
43. Funk JL, Rogge RD. Testing the Ruler With Item Response Theory: Increasing Precision of Measurement for Relationship Satisfaction With the Couples Satisfaction Index. J Fam Psychol. 2007;21(4):572-83.
44. Conroy AA, Ruark, A., Neilands, T.B., Darbes, L.A., Johnson, M.O., Tan, J.Y., Mkandawire, J. . Development and Validation of the Couple Sexual Satisfaction Scale for HIV and Sexual Health Research. Arch Sex Behav. In Press.
45. Helgeson VS, Jakubiak B, Van Vleet M, Zajdel M. Communal coping and adjustment to chronic illness: Theory update and evidence. Pers Soc Psychol Rev. 2018;22(2):170-95.
46. Bodenmann G. Dyadic coping-a systematic-transactional view of stress and coping among couples: Theory and empirical findings. Eur Rev Appl Psychol. 1997;47:137-40.
47. Bodenmann G. Dyadisches coping Inventar: DCI; Manual: Huber; 2008.
48. Cutrona CE, Russell DW. The provisions of social relationships and adaptation to stress. Advances in personal relationships. 1987;1(1):37-67.
49. Filmer D, Pritchett LH. Estimating wealth effects without expenditure data--or tears: An application to educational enrollments in states of India. Demography. 2001;38(1):115-32.
50. King N. Template analysis. 1998.