Study Protocol & Statistical Analysis Plan for ClinicalTrials.gov

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Siyakhana Peer: Evaluating a Peer Recovery Coach Model to Reduce Substance Use Stigma in South African HIV Care

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Ethics Information

IRB:	South African Medical Research Council (SAMRC) Human Research Ethics Committee (HREC)
Study Name (Ethics):	Evaluating the Role of Peers to Reduce Substance Use Stigma and Improve HIV Care Outcomes in South Africa: Aim 3. SIYAKHANA – P.
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Multiple Principal Investigators

Bronwyn Myers, PhD
South African Medical Research Council (South Africa) | Curtin University (Australia)

Jessica Magidson, PhD
University of Maryland, College Park (United States of America)

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Primary Research Support

South African Medical Research Council – Cape Town, Western Cape, South Africa
Kim Johnson, MA
Sibabalwe Ndamase, BA
Nonceba Ciya

University of Maryland – College Park, Maryland, United States of America
Kristen Regenauer, MS
Rithika Baskar, BS
Imani Brown, MPH

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LIST OF ABBREVIATIONS

3MFU	3-Month Follow-Up Assessment
6MFU	6-Month Follow-Up Assessment
AE	Adverse Event
AOD	Alcohol or Other Drug use
APA	American Psychological Association
ART	Antiretroviral Therapy
BL	Baseline Assessment
CFIR	Consolidated Framework for Implementation Research
CHW	Community Health Worker
COPC	Community Oriented Primary Care
ETAU	Enhanced Treatment As Usual
GCP	Good Clinical Practice
HCW	Health Care Worker
HREC	Human Research Ethics Committee
LMIC	Low- and Middle-Income Countries
MPI	Multi-Principal Investigator
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health (US)
PI	Principal Investigator
PLWH	People living with HIV
PPE	Personal Protective Equipment
PRC	Peer Recovery Coach
SA	South Africa
SAE	Serious Adverse Event
SAMRC	South African Medical Research Council
SANCA	South African National Council on Alcoholism and Drug Dependence
SDS	Social Distance Scale
SU	Substance Use
SU-SMS	Substance Use Stigma Mechanism Scale
SUD	Substance Use Disorder
UMD	University of Maryland
US	United States
WBOT	Ward-Based Outreach Team

1. OVERALL AIM AND SPECIFIC OBJECTIVES

1.1 Overall Aim

The overall aim of this study is to assess the feasibility, acceptability, and preliminary effectiveness of integrating peer recovery coaches (PRCs) into Community Oriented Primary Care (COPC) teams to help people living with HIV (PLWH) and problematic substance use (SU) better engage in health care.

PRCs are lay people with lived SU experience who are trained to help people with current SU problems. They have been lauded as an innovative, acceptable, and cost-effective strategy for supporting SU outcomes in some high-income settings. PRC models are scaling in the US, but their implementation in HIV care in low- and middle-income countries (LMICs) has been limited. To adapt a PRC model to this context, we previously conducted qualitative interviews with stakeholders and patients about their attitudes towards integrating PRCs into COPCs (Protocol ID #EC046-10/2020). From these interviews, we were able to assess barriers and facilitators to this integration, which informed our development of a draft model. We then conducted workshops with stakeholders and patients (Protocol ID #EC049-11/2021) to obtain stakeholder feedback on our proposed model. Based on workshop feedback, we then further adapted the model and received confirmatory feedback on the final proposed model. In the present study, we propose to test this final co-designed model by comparing health care engagement outcomes for PLWH and SU who are seen by a COPC with an integrated PRC to those who are seen by a matched COPC without an integrated PRC.

1.2 Specific Objectives

To evaluate the feasibility, acceptability, and preliminary effectiveness of this PRC COPC integrated model (called *"Siyakhana"*), we will:

1. **Primary:** Evaluate the pilot effectiveness of *Siyakhana* reducing healthcare worker stigma towards substance use (SU), compared to a control condition (COPC enhanced treatment as usual (ETAU)):
    a. Healthcare worker stigma towards SU at the three-month follow-up, measured using the Social Distance Scale (SDS[2–4]; *n*=30)
2. **Secondary:** Evaluate the implementation of Siyakhana using the following measures:
    a. Feasibility and Acceptability (COPC perspective)
        1. Feasibility and Acceptability subscales of an adapted Implementation and Dissemination measure,[1] completed by healthcare workers (HCWs) in the Siyakhana condition at the six-month follow-up (*n*=15)
        2. Semi-structured qualitative interviews with HCWs in the Siyakhana condition after the six-month follow-up (*n*=15)
3. **Other:** Additionally evaluate the following outcomes using the following measures:
    a. Feasibility and Acceptability (patient perspective)
        1. Feasibility and Acceptability subscales of an adapted Implementation and Dissemination measure,[1] completed by patients (HCWs) in the Siyakhana condition at the three-month follow-up (*n*=25)
        2. Semi-structured qualitative interviews with patients in the Siyakhana condition after the six-month follow-up (up to *n*=25)
    b. Feasibility and Acceptability (other stakeholder perspectives)
        1. Semi-structured qualitative interviews with key stakeholders (e.g., policymakers, organization and clinic heads, etc.,) at the end of the study (up to *n* = 15)
    c. Pilot effectiveness of Siyakhana patients (intervention) re-engaging in HIV care, compared to patients in the ETAU (control) condition, over three-months
        1. Patient engagement in clinic-based HIV care between baseline assessment and three-month follow-up assessment from medical records (dichotomous yes/no)

2. INTRODUCTION

Background and Rationale

South Africa (SA) is home to the highest burden of HIV globally, with over 7.7 million PLWH.[6,7] SA has scaled up its response to the HIV epidemic, including expanding access to antiretroviral therapy (ART) so the virus can remain undetectable and untransmittable. Yet, over 60% of PLWH have not achieved viral suppression largely due to poor ART adherence and disengagement from care.[7] This lack of engagement in care contributes to HIV morbidity and mortality, as well as ongoing transmission of the virus.[8]

Substance use disorder (SUD) is prevalent among PLWH and contributes to poor engagement in HIV care.[9,10] There have been alarming increases in SUD among PLWH in SA, including methamphetamine, heroin, and other opioid use.[11] SA also has one of the highest global rates of per capita alcohol consumption,[12] with approximately one-third of PLWH on ART reporting problematic drinking.[13] Untreated SUD is associated with worse engagement in HIV care, lower likelihood of being on ART,[14] worse ART adherence, and lower rates of viral suppression.[9,10,15,16] **Identifying PLWH who use substances and supporting them to stay retained in HIV care is critical for increasing rates of adherence and viral suppression.**

Recent innovations in SA to improve access to and engagement in HIV care for PLWH include the use of Community Oriented Primary Care (COPC) teams, previously called ward-based outreach teams (WBOTs). The goal of COPC teams is to reach vulnerable, out-of-care patients in communities and re-link them to facility-based services.[17,18] COPC teams include community health workers (CHWs), one supervisor, and one nurse team leader. Each COPC works in a specific "indawo" (i.e., place/community), and CHWs receive one week of HIV/TB training.

Untreated SUD undermines recent innovations to improve engagement in HIV care for PLWH, including the success of COPC teams. In Cape Town, the success of COPC teams in improving engagement in HIV care is limited by untreated SUDs. Currently SUD screening and interventions are not part of COPC services**—a missed opportunity to address a key barrier to patient re-engagement in HIV care.**

SUD stigma among health care workers (HCWs) is a barrier to integrating SUD screening and brief interventions into HIV care. Preliminary qualitative work by our team[19] and others[20] suggests that HCWs have stigmatizing views towards PLWH with SUD. This can result in HCW reluctance to provide SUD screening and interventions, less time spent with patients who use substances, and lower likelihood of providing evidence-based practices and patient-centred care.[20] SUD stigma among HCWs is a significant barrier that must be addressed for COPC teams to successfully reach and improve care outcomes for PLWH with SUD.

SUD stigma also contributes to patients' poor engagement in HIV care. Our preliminary work has shown that patients with SUD anticipate being stigmatised, scolded, and disrespected, and this anticipated stigma is a barrier to initiating and engaging in HIV care.[19,21,22] When stigma is internalised, SUD stigma is also a barrier to engagement in care.[23,24] The impact of internalised SUD stigma on care engagement is worsened by the presence and intersection of internalised HIV stigma, which persists even in the context of a generalised epidemic.[25] Following evidence that supports measuring HIV, SUD and other stigmas separately, we will explore the contribution of SUD stigma to treatment engagement for PLWH as well as how SUD stigma intersects with other stigmas to impact engagement in care. **Given SUD stigma's pervasiveness, its impact on health care engagement, and that members of COPC teams are likely to hold SUD stigma, COPC teams may therefore have limited success re-engaging PLWH in care without strategies to reduce SUD stigma.**

However, stigma reduction interventions for SUD are rare and under-researched in low- and middle-income countries (LMICs). Strategies for reducing HIV stigma have been researched in LMICs and have been efficacious for reducing discriminatory practices among HCWs and improving engagement in HIV care.[26–29] Intervention efforts to reduce SUD stigma and/or the intersection of HIV and substance use stigma have however been limited. Although strategies for reducing SUD stigma have rarely been evaluated, the limited evidence available suggests that social contact with peers is essential to reduce mental health and substance use stigma among HCWs.[26,30,31] Interventions that incorporate social contact with peers during HCW training have been tested, but this contact is often limited to the training period and has not focused on SUD.[32] Although prior work has shown that the effects of short-term peer contact are unlikely to be maintained, it is unclear how to sustain social contact between HCWs and peers in a way that does not interfere with health service delivery. In response to this gap, we propose testing whether introducing peers into COPC teams could enable sustained peer contact and reduce SUD stigma among these HCWs.

Peer Recovery Coaches (PRCs) may offer a solution for addressing SUD stigma while also improving HIV care engagement among PLWH with SUDs. Our team has found that PRCs—trained individuals with their own lived experience with SUD integrated into health care teams—allow for sustained social contact with other HCWs that can shift SUD stigma among HCWs.[33,34] PRCs can also help patients address internalised stigma and structural and health system barriers to care engagement.[34] Our preliminary work in the United States (US) has shown that PRCs can be integrated into health care teams with the peer contact associated with a significant increase in outpatient care engagement and increased substance use treatment engagement.[33,34] Further, in other preliminary work in a low-income setting of the US, a PRC we trained was able to successfully link 89% of individuals who were not engaged in care to care.[35]

Our previous qualitative work also suggests that PRC-delivered services are likely to be acceptable to PLWH in SA. For instance, we found that PLWH with SUD in Khayelitsha had an overwhelming preference for peer-delivered SUD screening and interventions.[19] These patients expressed that peers may be more likely to understand them, work with them in a non-judgmental and supportive way, and feasibly address barriers to care, including stigma, compared to other HCWs. We have also found that many individuals who receive SUD interventions begin acting as "informal" PRCs by sharing the information and materials with others,[36,37] supporting the feasibility of recruiting peers for a more formalised PRC role that includes training, structure and support. Yet, the *feasibility* and *acceptability* of incorporating PRCs into community-based teams in a setting with a generalised HIV epidemic like SA and into an already constrained health care system is in a nascent stage.

We previously conducted two studies (SAMRC HREC Protocol IDs: EC046-10/2020, EC049-11/2021) to adapt a PRC model to a South African HIV context. In EC046-10/2020, we conducted (N=40) qualitative interviews with PLWH and SUD and stakeholders. Key themes that emerged in these interviews included that HIV and SUD stigmas negatively impacted patient HIV care engagement; participants believed integrating PRCs into community-based services like COPC teams would be highly acceptable; and participants believed that PRCs' lived experience could enhance the quality of services and shift stigma among patients and providers. Based on these qualitative findings, in EC049-11/2021, we showed a general PRC model to N=24 PLWH and SUD and stakeholders, gathered their feedback, adapted the PRC model based on their feedback, and presented the model to them again for final feedback. Based on this feedback, we have now adapted the final PRC model, which we hope to test.

Therefore, the purpose of this study is to test this final adapted PRC model by comparing a COPC team with an integrated PRC to COPC usual care without an integrated PRC. Using a pilot Type 1 effectiveness-implementation design,[38] we will examine whether the PRC model is feasible, acceptable, and potentially beneficial (preliminary effectiveness) for improving patient re-engagement in healthcare and reducing SUD stigma.

3. Research Work Plan

Aims:

The overall aim of this study is to examine the feasibility, acceptability, and preliminary effectiveness of our adapted PRC-COPC model "Siyakhana". The main goal of this model is to increase engagement in HIV care for PLWH with SU and decrease HCW stigma towards SU.

Using a pilot hybrid Type 1 effectiveness-implementation design,[38] we will explore whether our adapted Siyakhana model is feasible, acceptable, and potentially beneficial for improving engagement in health care for PLWH with SU, and reducing SUD stigma among HCWs. We will compare two matched COPC teams (i.e., similar in HCW makeup and patient population). Both COPC teams will provide treatment as usual, which we will enhance by providing a brief psychoeducational training on SU and SU screening (enhanced treatment as usual; ETAU). One of the COPC teams will also be randomized to receive the PRC model integration (described more below).

Study Sites

At the time of initial ethics submission, COPC teams were active in four clinics in the Western Cape: Asanda, Nomzamo, Ikhwezi, and Lwandle. Through ongoing conversations with Masincedane—the nonprofit organization that oversees these COPCs—Nomzamo and Ikhwezi were selected as our two COPC sites.

Both Nomzamo Community Health Centre and Ikhwezi Clinic are located within the larger community of Nomzamo, in the Helderberg Basin and Eastern Suburbs of the Cape Town Metropolitan Area. The clinics are located approximately 1.5km apart.

Study Design

The present study is a pilot study with the intent to establish the pilot effectiveness (not efficacy; primary), feasibility, and acceptability (secondary) of a PRC model ("Siyakhana"). The study uses a pilot hybrid Type 1 effectiveness-implementation design.[38] In this study, a COPC team using our integrated Siyakhana PRC model will be compared to a COPC team without an integrated PRC.

Additional patient-level measures will be collected through this study (patient-level implementation) and NIDA grant R36DA057167 (patient-level stigma; PI: Regenauer). However, the primary focus of the present study is on the COPC staff level (i.e., HCW level).

Participants and Eligibility

3.1.1 COPC HCW: Eligibility

A minimum of *N*=30 HCWs will be enrolled in this study.

Rationale for Enrolment Numbers.

Exact enrollment numbers will depend on the size of each COPC team at the time of enrollment.

At the time of initial ethics submission—based on feedback from the Western Cape Department of Health—the largest COPC team was comprised of approximately *n* = 24 HCWs (22 CHWs, 1 outreach team leader (supervisor; often a nurse by training), and 1 clinic-based nurse). The HCW numbers on each COPC may vary slightly at the time of enrollment due to staff members leaving and new hires. However, based on these numbers, we feel confident that each COPC team will employ at least *n*=15 HCWs at the time of enrolment.

Therefore, we expect to enroll a minimum of *N* = 30 HCWs (approximately 15 HCWs per COPC).

HCW Eligibility
HCW eligibility criteria consists of:

Inclusion:
- Employed as a HCW (e.g., nurse, supervisor, CHW) for one of the COPC teams partnered with this study
- 18 years or older (expected for all HCWs employed by COPCs)

Exclusion:
- Unable or unwilling to complete informed consent and study procedures (i.e., brief trainings, self-report assessments) in English, isiXhosa, or Afrikaans

3.1.2 COPC Patient: Eligibility

We aim to enroll *N*=50 patient participants in this study (*n*=25 patients per COPC team).

Rationale for Enrolment Numbers.
As this is a pilot study with the primary goal of establishing feasibility and acceptability, we view our effectiveness effect size as preliminary. However, based on prior work in this population and with PRCs, we expect to find a small improvement in patient re-engagement in care in enhanced treatment as usual (ETAU; previous studies have found about 14% re-engagement in ETAU[39]) and a larger improvement in the PRC condition (previous studies have found 66-89% improvement[7,34]). Assuming ETAU re-engages at an even higher rate (i.e., 24%), and Siyakhana (PRC condition) re-engages at the low end of previous studies (i.e., 66%), enrolling 50 patients will give us approximately 85% power to detect a difference in patient re-engagement after accounting for up to 20% attrition and/or missing records.

Patient Eligibility.
Patients will be eligible if they meet the criteria in the table below.

Patient Eligibility Criteria

Inclusion Criteria	Exclusion
1. 18 years or older	1. Unable or unwilling to complete informed consent or study procedures in a language spoken by members of our team (i.e., English, isiXhosa, Afrikaans)
2. Living with HIV	
3. Problematic alcohol or other drug use (AOD) defined a CAGE score ≥2	
4. Seen by a HCW from one of the COPC teams partnered with this study	

3.1.3 Stakeholders (Qualitative Interviews): Eligibility

Participants will be up to n=15 HCWs (not previously enrolled in the study), leaders, policymakers or others involved in administration/supervision at COPCs, clinics, the Department of Health, or other relevant organizations.

Rationale for these numbers
This number of participants will allow us to represent a wide range of perspectives. The study team will identify stakeholders by asking people working in the health care system to refer stakeholders that are involved in NGO managed COPC and CHW services. We anticipate this number will allow us to reach theoretical saturation for qualitative analysis.

Eligibility Criteria
To be eligible, stakeholders must meet the following criteria:

Inclusion:

- Employed in a HCW role (not previously enrolled in the study), a leadership role, a policymaking role, or other administrative/supervision role for an organization associated with the COPC teams with whom this study partnered (e.g., partner non-profit organization, affiliated clinics, Department of Health)
- 18 years or older (expected for all employed in the abovementioned positions)

Exclusion:

- Unable or unwilling to complete informed consent and study procedures (i.e., brief training(s), brief self-report assessments) in English, isiXhosa, or Afrikaans

Recruitment

3.1.4 COPC HCWs: Recruitment

Based on ongoing conversations with the Western Cape Department of Health, we will select two of the four COPC teams to partner with for this study. These teams will be located at two of the following four sites: Asanda, Nomzamo, Ikhwezi, Lwandle.

All members of the two chosen partner COPC sites will be invited to join the study. Study staff will work with COPC supervisors to determine an appropriate time to approach the COPC members, tell them about the study, and ask them if they are interested in participating. Due to the nature of the study procedures (i.e., group COPC training delivered during normal work hours), HCWs colleagues will know whether they participate in the training. However, we will make it clear that colleagues will never see each other's answers to assessment questions. We will also work with the supervisors to ensure that participation, or lack thereof, will not affect the HCWs employment.

3.1.5 COPC Patients: Recruitment

After receiving the ETAU training (i.e., SU psychoeducation and screening), HCWs in both COPCs will be asked to screen their HIV patients for SU using the CAGE. HCWs will be trained on these screeners during ETAU training. If a participant screens positive on alcohol or other drug use (AOD), the HCW will ask the patient if they would be willing to be contacted by a researcher at the SAMRC about potentially participating in the study. If the patient says yes, the CHW will pass on any relevant contact information (e.g., phone number, address) to the study team. If a HCW on a COPC chooses not to screen a patient, they will be told they can still tell the patient about the study, and ask the patient if they would like to be contacted by a researcher at the SAMRC about potentially participating in the study. If the patient says yes, the CHW will pass on any relevant contact information to the study team. Finally, HCWs will be given study flyers that they can choose to hand out to their patients. These flyers have study contact information so that interested patients can contact the study team directly.

It will be made clear to all potential patient participants that joining or not joining the study will in no way affect treatment from their COPC HCWs, from their clinic, or from anyone else.

3.1.6 Stakeholders (Qualitative Interviews): Recruitment

NGO leaders, policymakers and other stakeholders (n=15) referred from health system leadership will be recruited. Trained study team members will approach stakeholders and tell them further about study procedures and ask if they would be interested in participating in a qualitative interview.

Study Procedures

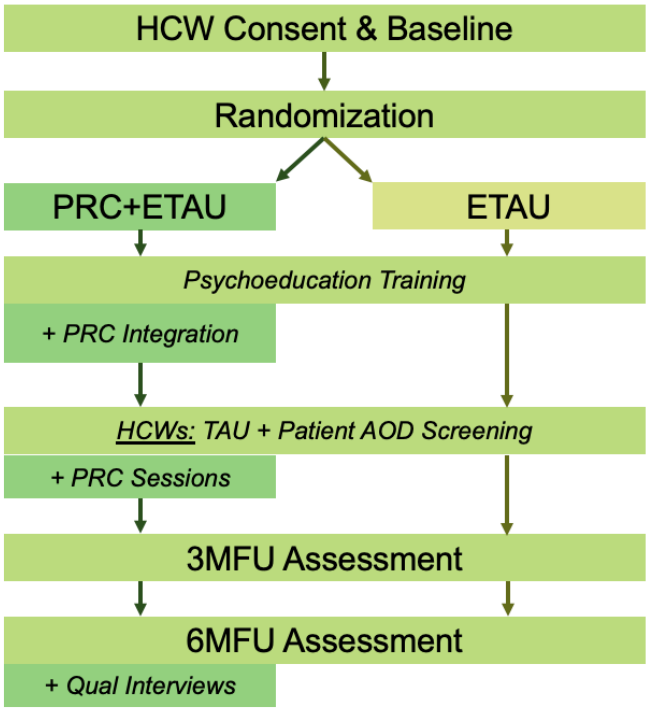
3.1.1 COPC HCWs: Procedures

Study procedures for HCWs in the Pilot PRC Study are described below and illustrated in Figure 1.

HCW Enrollment and Baseline Assessment: Eligible and interested HCWs in the two partner COPC teams will be enrolled upon completed the informed consent process. All HCWs will then complete an individual baseline assessment consisting of self-report measures to assess basic demographic and job information, and stigma towards SUD *(primary)*.

COPC Randomization & Training. After all HCW baseline assessments have been completed, one COPC will be randomly assigned to the ETAU condition (i.e., ETAU training only) and one COPC will be randomly assigned to the Siyakhana (i.e., ETAU and PRC integration training) condition. These trainings are described in more detail below.

Figure 1. HCW Procedures



Randomization will be determined by flipping a coin on a video-call with multiple study staff members (including at least one PI) in attendance.

ETAU Training (Psychoeducation): Both COPC teams will receive the ETAU training from our study team. This training will consist of psychoeducation around how to screen and refer for SU in HIV patients, the prevalence of SU in HIV, and the impact SU has on HIV care. This training will last for 1-2 days, depending on COPC availability. A brief psychoeducation refresher course (i.e., one afternoon a week or two after the original training) will also be offered. The purpose of this refresher will be to review how to screen and refer patients for substance use and answer any questions about screening and referring.

PRC Integration Training: Only the COPC randomized to the Siyakhana (PRC+ETAU) condition will receive the Siyakhana PRC Integration Training. In this training, the already trained PRC will be introduced to HCWs in the Siyakhana COPC. Together, the PRC and these HCWs will be trained on the PRC role (i.e., the difference between a PRC and a CHW) and how to refer to the PRC. This

training will last from 1-2 days, depending on COPC availability. After the training, the PRC will join this COPC (e.g., shadow team members before patients are enrolled, work closely with the COPC team, attend weekly COPC supervision) for the remainder of the study.

Active Treatment Phase: After the training(s), HCWs in both COPCs will continue visiting and treating patients as usual. The treatment as usual will potentially be enhanced (i.e., ETAU) by HCWs now being trained in how to screen patients for SU, and how to refer patients to local, publicly-funded SU treatment programs. The study team will provide each COPC with initial SU screeners, and let the COPCs know that the team can provide more screeners at any time during the active phase of the study.

Siyakhana: HCWs in the Siyakhana COPC will be aware that any patients who enroll in the study will be invited to meet with the PRC. This PRC will be present at COPC meetings, supervisions, etc.

HCW 3MFU: Approximately three-months after the PRC integration (i.e., enrollment of first patient participant), all HCW participants will be asked to complete a three-month follow-up (3MFU) assessment. This brief assessment will consist of the same self-report stigma measures as the HCW baseline assessment.

HCW 6MFU Assessment. Approximately six-months after the PRC integration, all HCW participants will be asked to complete a six-month follow-up (6MFU) assessment. This assessment will consist of the same self-report stigma measures as the HCW baseline and 3MFU assessments. Additionally, HCW participants in the Siyakhana condition will be asked to complete the Feasibility, Acceptability, and Appropriateness subscales of an Implementation & Dissemination measure.[1]

Qualitative Interviews. After the 6MFU assessment, all HCW participants in the Siyakhana condition will be invited to participate in a semi-structured, individual interview with a study team member. The purpose of this interview will be to assess the feasibility and acceptability of the PRC Model Integration. Ideally, these interviews will be conducted immediately after the 6MFU assessment. However, if it is not possible to conduct them on the same day as the 6MFU assessment, the interview will be scheduled for as soon as possible.

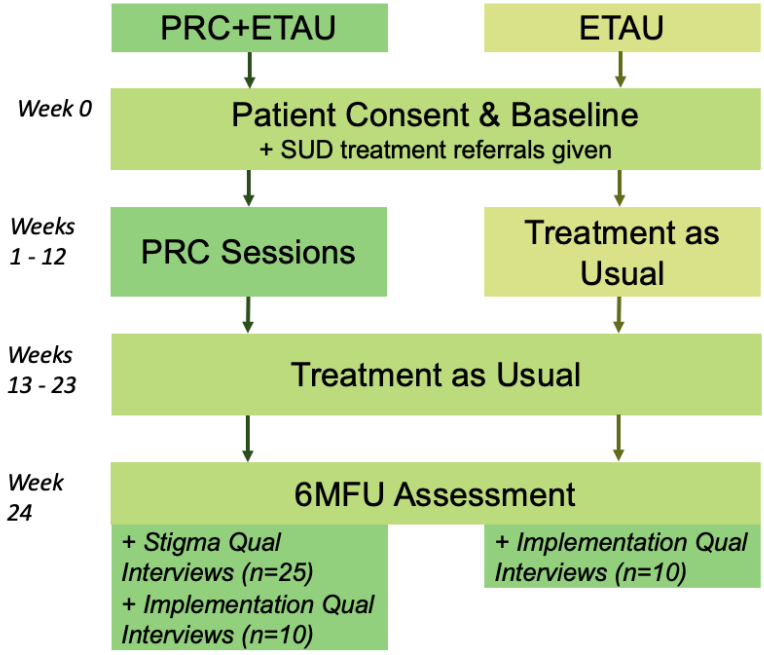
3.1.2 COPC Patients: Procedures

Study procedures for patient participants in the Pilot PRC Study are described below and illustrated in Figure 2.

Patient Screening & Enrolment. At least once a week, the study team will consult with enrolled COPC HCWs on patients who may be interested in participating in the study. The study team will contact these patients and briefly tell them about the study. If a patient is still interested in potentially participating, the study members will officially screen the patient. If the patient is still interested in participating after screening and met all eligibility criteria, a staff member will complete the informed consent process with the patient as soon as possible. The consent form will include all study procedures and state that we are seeking approval to extract information from medical records (i.e., information related to clinic visits (dates, attendance), HIV (viral load, CD4 count), care for other chronic diseases, referrals to other programs including SU treatment programs, etc.). It will also state that we are seeking approval to see if they attended local publicly funded SU treatment programs (date(s) of attendance, location(s) attended), provided through the South African Community Epidemiology Network on Drug Use (SACENDU). Finally, it will state that the study will only collect medical record and SU treatment program attendance data between the date of their baseline assessment and the date of 6MFU.

Patient Baseline Assessment: Upon completing informed consent, all patients will be asked to complete a self-report baseline assessment with a study team member. Ideally the baseline assessment will be completed immediately after informed consent is given. However, if the patient is unable to complete the baseline assessment immediately after consent, a time to complete the assessment will be scheduled for as soon as possible. The patient baseline assessment consists of self-report questions around demographics, SU, HIV, and stigma. After the baseline assessment, all patient participants will be given another referral to the nearest free SUD treatment program(s) (for example, the Help Me Network).

Figure 2. Patient Procedures



Patient Active Treatment Phase: 0 to 12 weeks post-baseline. Following the completion of the patient baseline assessment, the below procedures will occur.

ETAU Patients. Patients seen by the ETAU COPC will continue to receive normal treatment from their COPC HCWs (i.e., normal efforts to re-engage patients in HIV care). These normal visits will be enhanced through (1) their COPC HCWs knowing how to, and therefore, potentially screening them for problem SU, and (2) their COPC HCWs knowing how to give referrals to local SU treatment programs. It is also possible that they will receive enhanced care from their COPC HCWs due to their COPC HCWs now knowing more about SU in the context of HIV.

Siyakhana (PRC+ETAU) Patients. Patients seen by the Siyakhana COPC will be invited to attend sessions with a PRC after their baseline assessment.

The structure and content of PRC sessions were designed based on patient and stakeholder feedback about PRCs (Protocol IDs: EC049-11/2021, EC046-10/2020). Siyakhana patient participants will be invited to meet with the PRC on a regular basis for approximately 12-weeks (3-months). Each meeting will be scheduled to last approximately 30 minutes, although an hour will be allocated for each meeting. The PRC and patient together will decide where to meet in a venue that is physically and psychologically safe for both the PRC and patient. Options deemed safe by stakeholders and patient participants in our formative work included the library, the local clinic, community centers, and for some, their homes. The location that the PRC and patient chooses will be recorded so that we have this information for future iterations of this project. The goal of these meetings will be for the PRC to motivate the patient to return to HIV care and seek SUD treatment. In training the PRC, the PRC will have attained competence in providing brief education around SU and HIV, supporting the patient in their recovery, and helping the patient problem-solve barriers to accessing both HIV and SU care.

Frequency of PRC sessions, and an overview of their content, are described in the table below. The proposed contact schedule was co-designed with patient and stakeholder feedback in our formative work but is only meant as a guideline for the PRCs. While it is expected that most patients will follow the below structure, additional sessions can be added or removed if needed in this pragmatic implementation study. Similarly, while the PRC will be instructed to complete all sessions within the 3-month period after baseline, there can be some flexibility (e.g., if a patient is away for a month in December/January, they may have the option to pause sessions for a month and pick them back up in late January). The frequency that patients meet with the PRC, and the general content of each session, will be recorded and used to inform further refinements to the PRC model for future trials.

Flexible Guidelines for PRC Sessions (12-weeks)

Week(s)	Frequency & Content
1	First session: Introduction to PRC sessions. PRC and patient discuss meeting time and locations, boundaries, and what the PRC's role is and is not. The PRC may also share their own story and experiences to engage the patient.
2 – 4	Weekly sessions: The PRC and patient meet approximately weekly. The PRC's goal is to **help the patient navigate challenges they may be experiencing in engaging in HIV/SU care**. The PRC may do this by providing psychoeducation around SU and HIV, using basic counselling skills (e.g., motivational interviewing, problem-solving therapy, behavioural activation), and supporting the patient in their recovery journey. The PRC may also share his/her own experiences throughout to engage the patient.
5 – 8	Session every other week: The PRC and patient will meet approximately every other week. The PRC will continue to support the patient in their recovery and motivate them to re-engage in HIV care and engage in SUD treatment.
9 – 12	Sessions as needed: In the final month, the PRC and patient together will determine how many sessions are needed. The PRC's goal this month will be to help the patient re-engage in HIV care and SUD treatment (if needed, if they have not already) and help them transition to using resources other than the PRC to support them in their recovery (e.g. peer support groups in the community).

Patient 3MFU Assessment. Approximately 3-months after their baseline assessment, patient participants will be asked to complete a 3MFU assessment. The 3MFU assessment consists of the same self-report questions around SU, HIV, and stigma that were asked at the baseline assessment. Additionally, patients in the Siyakhana condition (i.e., patients who had the opportunity to meet with a PRC) will also be asked to complete the Feasibility, Acceptability, and Appropriateness subscales of an Implementation & Dissemination measure.[1]

12 to 24 weeks (3-6 months) post-baseline. Following the active treatment phase (which lasts approximately 12-weeks post-baseline), all participants will continue to receive their usual care. Participants in the intervention COPC will have the option to receive optional "booster sessions" with the PRC. These optional sessions will review material previously covered in normal sessions.

Patient 6MFU Assessment. Approximately 6-months after their baseline assessment, patient participants will be asked to complete a 6MFU assessment. The 6MFU assessment consists of the same self-report questions around SU, HIV, and stigma that were assessed at the baseline assessment. Additionally, patients in the Siyakhana condition (i.e., patients who had the opportunity to meet with a PRC) will also be asked to complete the Feasibility, Acceptability, and Appropriateness subscales of an Implementation & Dissemination measure.[1]

Qualitative Interviews. After their 6MFU, all participants in the Siyakhana condition will be invited to participate in an individual, semi-structured interview.

Stigma. As part of a sub-study (R36DA057167), one part of the interview will assess patient perspectives on internalized SU stigma, potentially intersecting stigmas (e.g., HIV, gender, religion, ethnicity) from multiple levels (e.g., self, providers, community), experiences with the PRC, engagement in HIV and SU care, and relations between all these topics. The key domains of these interviews are perspectives on: (a) internalized SU stigma; (b) intersecting stigmas from multiple levels; (c) the PRC; (d) engagement in care; and (e) how these domains relate.

Implementation. As part of the current study, the second part of the interview will assess patients' perspectives on the implementation of the study. The main domains of interest will be feasibility and acceptability. However, other implementation domains, such as reach, adoption, and appropriateness, will also be assessed.

3.1.3 Stakeholders (Qualitative Interviews): Procedures

Potentially eligible NGO stakeholders will be screened for eligibility. If eligible and interested in participating, they will undergo informed consent procedures. As part of this process, participants will be informed of all the potential risks and benefits to taking part in the one-time interview. Participants will be reminded that participation is voluntary and that they can decline to answer any questions that they are not comfortable answering and that they can withdraw from the study at any point. They will also consent to having the interview audio-recorded.

3.1.4 Additional Procedures

We recognize the importance of ongoing support to PRCs in their recovery. Therefore, we have come up with strategies to monitor and support PRCs' ongoing recovery and self-care. We have successfully used these and similar strategies in previous studies.[35,44–47]

Recovery Stability: All PRCs in this study will be well-established in their recovery (i.e., have been in self-reported recovery for at least one to two years, which is the threshold most commonly used in other settings for the PRC role). All PRCs hired will be selected based on their recovery length as well as supports for ongoing recovery.

Ongoing Supervision: The PRC(s) will receive regular (i.e., weekly or biweekly) supervision from the study team. The PRC(s) main supervisor will be a study team member who has previously worked with PRCs and is familiar on how to supervise this role. The supervisor will help the PRC monitor and reflect on their own recovery during supervision sessions, with ongoing attention to self-care following best practices for supervising PRCs.

Participant Compensation

3.1.1 COPC HCWs: Compensation

Initially, HCW participants did not receive monetary compensation for their trainings or assessments. The rationale for not providing monetary compensation for trainings was that participation in trainings is a regular part of their professional development, and trainings were conducted during usual working hours (time negotiated with organization that oversees COPC). Attendees were provided with meals during trainings and received reimbursement for travel (or were provided with travel) if they had to travel outside of their normal work commute for trainings. The rationale for not providing monetary compensation for assessments was similar – assessments were conducted during normal work hours and at their place of work. However, based on participant feedback, an amendment was approved so that HCW participants will be reimbursed R150 rand for completing a 6MFU, and for completing a qualitative interview.

3.1.2 COPC Patients: Compensation

Patients will be compensated 150 Rand for each assessment (baseline, 3MFU, 6MFU) they complete. They will be compensated an additional 150 Rand for completing a semi-structured interview after the 6MFU.

3.1.3 Stakeholders (Qualitative Interviews): Compensation

The stakeholders participating in the interviews will receive a 150 Rand gift voucher for consenting and completing the semi-structured qualitative interview.

Phone

All assessments and interviews may be completed in-person or over the phone. If over the phone, the research assistants will ask the participant if they feel free talking freely before beginning.

Allowing assessments and interviews to occur in-person or over the phone will allow for more flexibility around scheduling. As patients living with HIV who have disengaged from care and are using substances is a hard-to-reach population, this flexibility may allow us to recruit and retain more patients.

4. STATISTICAL ANALYSIS PLAN

Type and Purpose of Data

The purpose of this pilot hybrid Type 1 implementation-effectiveness trial is to examine the pilot effectiveness (primary) and implementation (secondary) of our adapted PRC model. This study will collect quantitative (self-report assessments) and qualitative (semi-structured interviews) data. Additionally, HIV and attendance-related data will be extracted from patients' medical records, and attendance data will be extracted from patients' SUD treatment records.

Effectiveness Outcomes

4.1.1 Primary Outcome: HCW Stigma Towards SU

HCW stigma towards SUD will be measured using the Social Distance Scale (SDS),[2,3,54] a well-validated measure of stigma used to capture health-related stigma across conditions and has been recommended for assessing mental health stigma among healthcare providers.

A total SDS score will be calculated to represent HCW stigma towards the target population at each time point, with higher scores indicating greater desire for social distance. First, we will conduct descriptive analyses (e.g., mean, standard deviation) to summarize the CHW stigma, using the continuous SDS score. The data distribution will be assessed to see whether the underlying assumptions are met (e.g., normality). Then we will examine the trajectory of HCW SUD stigma scores over time across the two conditions using a generalized linear mixed model, which includes all data points. The primary parameter of interest will be the interaction between time and condition to test whether changes in SUD stigma over time differ between the two groups.

Data will be analyzed over both three-months (3MFU) and six-months (6MFU). The primary timepoint is the 3MFU.

4.1.2 Other Outcome: Patient Engagement in HIV Care

Throughout the study, patients' medical records will be monitored and clinic attendance data will be extracted.

We will compare the rate of re-engagement in HIV care in the Siyakhana condition to rate of re-engagement in HIV care in the ETAU condition. Our primary analysis will be a logistic regression examining re-engagement in care by group. We will examine engagement both between baseline and the 3MFU, and between baseline and the 6MFU. To supplement this dichotomous measure, we will also conduct a Poisson regression model to examine number of clinic visits by group over 3 and 6 months, and a Cox Proportional Hazard survival analysis to model time to re-engagement by group.

Implementation Outcomes

4.1.3 Secondary Outcomes: HCW Feasibility and Acceptability

Feasibility is defined as the extent to which a HCW could engage with the PRC given their available resources such as time, money, and family or job responsibilities. Acceptability is defined as the extent to which HCWs found the tested PRC model satisfying and agreeable.

Quantitative Assessment: At their follow-up assessments (3MFU, 6MFU), HCWs will be given the Feasibility and Acceptability subscales (two separate scales) of a Dissemination &

Implementation measure based on the Consolidated Framework for Implementation Research (CFIR).[1] The measure will be adapted specifically to assessing the implementation of the PRC model for HCWs. We have used this subscale in previous studies in South Africa (for instance in Khayelitsha[44]). Items on this measure will be averaged for an overall feasibility rating from 0 to 3, with higher scores indicating higher feasibility. The primary Feasibility and Acceptability timepoint for HCWs is their 6MFU.

Qualitative Assessment: Brief semi-structured interviews assessing perceived feasibility and acceptability of the PRC model will be conducted with HCWs in the Siyakhana condition after their 6MFUs.

4.1.4 Other Outcomes: Patient Feasibility & Acceptability

Feasibility is defined as the extent to which a patient could engage with the PRC (including in PRC sessions) given their available resources such as time, money, and family or job responsibilities. Acceptability is defined as the extent to which patients found the tested PRC model satisfying and agreeable.

Quantitative Assessment: At their follow-up assessments (3MFU, 6MFU), patients will be given the Feasibility and Acceptability subscales (two separate scales) of a Dissemination & Implementation measure based on the Consolidated Framework for Implementation Research (CFIR).[1] The measure will be adapted specifically to assessing the implementation of the PRC model for patients. We have used this subscale in previous studies in South Africa (for instance in Khayelitsha[44]). Items on this measure will be averaged for an overall feasibility rating from 0 to 3, with higher scores indicating higher feasibility. The primary Feasibility and Acceptability timepoint for patients is their 3MFU.

Qualitative Assessment: Brief semi-structured interviews assessing perceived feasibility and acceptability of the PRC model will be conducted with patients in the Siyakhana condition after their 6MFUs. These interviews will be combined with interviews on stigma (conducted for R36DA057167).

5. ETHICAL CONSIDERATIONS

Potential Risks to Participants

There is minimal risk from the research procedures in the present study. However, the following risks are still possible:

5.1.1 Breach to confidentiality

As with any study, breach of confidentiality is a potential risk. Ways to minimize this risk are described below.

5.1.2 Psychological or mental discomfort

It is possible that participants will feel uncomfortable discussing certain topics in trainings, assessments, or PRC sessions. For instance, HCW participants may feel nervous discussing their judgments towards SU, patient participants may feel uncomfortable discussing sensitive topics related to SU and stigma with the peer or study staff, and peers may feel uncomfortable discussing these topics in their training.

5.1.3 COVID-19 transmission

Due to the current COVID-19 pandemic, there is a potential risk for COVID-19 transmission between project staff and participants. Efforts to minimize these risks are described below.

Protections Against Risks

Every effort will be made to minimize all study-related risks. These efforts include:

5.1.4 Informed consent

All participants will complete informed consent procedures. To join the study, participants must fully understand and sign the consent form (or, if over the phone, give verbal informed consent after going through the form with the study team member). All participants will have as much time as they want to review the consent form and ask questions. A study team member will also review the form with each participant. The consent form will include all study procedures, information about potential risks and benefits of participation, and information regarding whom they can contact for further questions. It will also state that participation is voluntary, that participants can refuse to answer any question, that participants can withdraw from the study at any time, and that participation (or lack thereof) is in no way related to their employment or care. All procedures and protocols will be approved by the South African Medical Research Council's (SAMRC) Human Research Ethics Committee (HREC) before study initiation.

Ensuring capacity to provide consent if a person uses substances. Ensuring that people are not intoxicated at the time of providing consent is important. If a potential participant appears acutely intoxicated, that person will not be consented into the study. The study team will be trained by Drs Myers and Magidson on how to detect simple signs of intoxication, such as impaired or slurred speech, smelling of alcohol, impaired co-ordination or balance- if any of these signs are present, we will not enrol a participant or continue with any research activities at subsequent appointments with those already enrolled in the study. To increase our confidence in potential participant's capacity to consent, we include a simple assessment of intoxication in our screening form and assess capacity to provide consent in our consent form, that has been used in other studies with populations of patients who use alcohol.

5.1.5 Preventing breaches to confidentiality

The confidentiality of each participant will be respected and maintained. Participant confidentiality will be ensured at all stages of the study.

All data will be kept confidential and only accessible to study staff. Participants' data will be identified by a study identification (ID) number only and a link between the names and ID numbers will be kept separately on a secure server and in a password protected document. This link will be destroyed after the study, including data analysis, has ended. The only individuals who have access to the link are the trained study coordinators on this project in South Africa. The study team at UMD will only have access to data identified with participant ID. Participant documents which include personal identifiers (such as signed consent forms) will be kept in locked files at SAMRC with restricted access. All other de-identified study documents will be kept in a secure location (such as UMD Box) and only study team members will have access to this location.

As part of the informed consent process, all participants will be advised that they may decline to answer any study questions. All study personnel working on the project will receive training about strictly adhering to study protocols regarding participant confidentiality.

Qualitative interviews and sessions will be audio-recorded for analysis. The purpose of the recording will be explained to all participants and informed consent and authorization for recording will be obtained. Digital audio recordings will be uploaded to the study computer immediately following session and the file will be deleted from the recorder/ recording program. Computer files will be secured by a password and will only be accessible to authorized study personnel. The digital recording will be uploaded and stored using a secure project drive (i.e., UMD Box). Following the South African good clinical practice (GCP) guidelines and guidelines set by the American Psychological Association (APA; APA Record Keeping Guidelines, Guideline #7), recordings will be maintained until seven years after the publication of the study. The ethics committee will review study procedures at least annually to review procedures pertaining to participant confidentiality.

5.1.6 Protections against psychological or mental discomfort

All study staff conducting trainings and assessments will be trained to recognize signs of discomfort, distress, or anxiety. Participants will take breaks when necessary to help alleviate any discomfort. Participants will also be reminded that they can refuse to answer any question that makes them uncomfortable and may take breaks whenever they are needed. They will also be informed that they have the right to decline participation in the study, or to withdraw consent at any time without adverse consequences. All patient participants will also be given referrals to local SUD services. HCW participants will be given information about SUD referrals. If needed, mental health referrals will also be given. We have a network of referral resources in the area, established through previous studies in this area.[14,16,32,38]

The PRC(s) will also be trained in recognizing signs of discomfort, distress, and anxiety in the patients they work with. The PRC(s) will be taught about local referral resources and taught to give patients the referrals when needed.

Additionally, there is a study protocol for managing distressed participants that all study staff will receive training in as well as regular supervision and debriefing. This protocol was developed by Dr. Myers and has been used across multiple studies with highly vulnerable populations, including traumatized women who use substances, people living with HIV, depression and problem alcohol use, and adolescents with alcohol and depression. In all her studies, Dr. Myers has successfully managed all incident cases of distressed participants and there have been no serious adverse or adverse events related to mental health or substance use harms. For participants who are distressed and at risk of harm, we will actively refer and link them to appropriate resources to help them cope with and deal with their

distress. Dr. Myers is a registered clinical psychologist (PS 007 1935) and given the size of this study, will be able to provide active and daily clinical oversight to determine the level of care needed for each distressed participant. Our strategies to actively link distressed participants to care include debriefing with the participant. Our study team includes registered psychological counsellors who are trained and have the correct competencies to do this Strategies will include making (and fast-tracking appointments) at the appropriate agency and accompanying the distressed participant to the agency for their appointment to ensure that they receive the recommended services. Dr Myers has worked in the target communities for more than 15 years and has an established network of mental health and substance use providers to whom we can refer participants should the need arise.

5.1.7 Health and safety: COVID-19

To reduce the likelihood of COVID-19 transmission, all staff members will be trained in COVID-19 safety protocols and the SAMRC standard operating procedures for the conduct of research during COVID-19. Staff members will have access to personal protective equipment (PPE) which will include masks. All staff members will wear PPE when required by the SAMRC, and can choose to wear PPE when it is not required by the SAMRC. When required by the SAMRC, social distancing (of 1.5m) between staff member and the participant will be practiced, and all surfaces used will be disinfected before and after any trainings/assessments are held. On a case-by-case basis (to be discussed with study managers and PIs), patients and PRCs may choose to have a session over a phone call rather than in-person.

Potential Benefits of Proposed Research to Human Subjects and Others

5.1.8 COPC HCW Participants

It is possible that HCW participants will not directly benefit from this study. However, HCWs may find that they benefit from the additional information they learn in the training(s), such as general information on SU, SU in the context of HIV, how to screen for problem SU, and how to refer to publicly-funded SUD treatment programs. HCWs in the Siyakhana condition may also enjoy the opportunity to share their feedback on the tested PRC model.

5.1.9 COPC Patient Participants

It is possible that patient participants will not directly benefit from this study. However, patients may find the treatment referrals—and their COPC HCWs potential increased knowledge of SU and referrals—helpful. Patient participants in the Siyakhana condition may find working with the PRC helpful in their recovery journey, and helpful in getting connected to services and re-engaged in HIV care. Finally, patient participants may enjoy the opportunity to share their feedback on this new PRC model.

5.1.10 Importance of the knowledge to be gained

From a broader perspective, the current study will be the first to our knowledge to test a novel, adapted PRC model in a low-resource setting for patients struggling with HIV care engagement. As SU stigma among HCWs and patients represent barriers to HIV care engagement, this project will help in understanding how to conduct outreach to people living with HIV and SUD and struggling with HIV care engagement. Further, since this knowledge is being generated within existing COPC teams managed by the Western Cape Department of Health, it has the potential for sustainability and scale-up. Finally, this research will inform future iterations of this model powered to measure effectiveness.

Protection of Personal Information (POPI) Act 4 of 2013

In the consent form, all participants will consent to: their personal information (data) being collected, processed, shared and stored in accordance with this research protocol as approved by the SAMRC HREC; their anonymised data being shared, processed, and transferred by third parties and between third parties

where relevant beyond the jurisdictional borders of South Africa (i.e., to the research team in the United States); and to the findings and results flowing from their anonymised data being broadly shared and published on the conclusion of the research.

In line with the South African POPI act, all data will only be shared securely as outlined in this research protocol. Researchers involved with this project at the University of Maryland in the United States will only have access to de-identified, anonymised data.

6. DATA MANAGEMENT

Data Storage

6.1.1 Data acquisition and transmission

Data collection occurs only in SA at the specified data collection sites. All quantitative data will be entered into an electronic REDCap database (described below). All participants will be given a study ID. Personal identifying information of study participants will be kept entirely separate from their coded data.

Data Integrity. All trainings and assessments will be facilitated by a trained member of the study staff who will be supervised throughout the study. The PRC(s) will also be trained before interacting with patients and will receive regular supervision from trained members of the study team.

Recordings. Qualitative interviews and sessions will be audio recorded for data analysis. The purpose of recordings will be explained, confidentiality will be respected, and informed consent, including the authorization for recording, will be obtained. All recordings will be uploaded to the secure study drive immediately after the interview is complete. Computer recordings will be secured by password and will be accessed only by authorized study personnel. Digital recordings will be stored and moved between sites using a secure, password-protected storage site, such as Box through UMD. In line with the guidelines of the American Psychological Association (APA; APA Record Keeping Guidelines, Guideline #7), recordings will be maintained until seven years after the publication of the study.

Identifiable Data. Consent forms and any other documents with identifiable information will be kept in a separate, secure filing cabinet at the secure SAMRC study site.

De-Identified Data. De-identified data will be kept in a secure electronic system, such as Box through UMD. Only authorized study staff will have access to this data.

Link. The link between the names and ID numbers of participants will be kept separate from all other data on a secure server at SAMRC and in a password protected document. The link will be destroyed after data analysis for the study has ended. Only trained study staff in South Africa will have access to this link.

6.1.2 Data entry methods

Qualitative.

Interviews. Qualitative data will be collected from in-depth interviews which will be recorded and transcribed. Transcripts will be transferred into MS Word files before being uploaded to NVivo[53] for analysis.

Sessions. PRC sessions will be recorded for ongoing supervision purposes.

Quantitative Assessments.

Data entry will occur as close to real time as possible to facilitate data management and monitoring of study operations. If assessments are done on paper, they will be scanned by a research assistant as soon as possible and sent to the study's secure server. The paper assessment will then be filed away at a secure location at the MRC and the scanned assessment will be entered on REDCap.

REDCap. Demographic and measure data will utilize REDCap through UMD, a secure software toolset and workflow methodology for electronic collection and management of research and clinical trial data in real-time. SAMRC also uses REDCap for data collection. REDCap provides a web-based application with an intuitive interface for users to enter data and have real time validation rules (with automated data type and range checks) at the time of entry. REDCap data collection projects data on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members

of the research team with planning assistance from UMD. All information entered on REDCap will be de-identified in order to protect participants' identities.

6.1.3 Quality assurance

Data Completeness. To ensure the usability of self-report data, a member of the research team will review all self-report measures to ensure their completeness. Using an electronic data capture system such as REDCap is meant to reduce errors in the data entry and management process. Using REDCap, missing data can be reduced by making items required to answer before moving on to the next item and effort and error associated with data entry can be reduced because there is no manual entering of data at a later timepoint by research assistants.

Confidentiality. Participant data on study materials (including electronic study materials saved on a secure study drive such as Box) will be identified only by participant number and date of visit. By recording the study data in this manner, the information can be considered 'de-identified.'

Data safety and monitoring plan

6.1.4 Regulatory issues

The procedures laid out in this document will be followed, in compliance with US National Institutes of Health (NIH) requirements as well as South African good clinical practice guidelines, to ensure the safety of study participants and the validity and integrity of data.

Before initiation of this study, the protocol, informed consent, and all other materials used with participants in this study will be reviewed and approved by SAMRC ethics committee. The study team will additionally submit a report to SAMRC ethics committee on an annual basis.

6.1.5 Amendments

Any changes to the protocol or amendments will be submitted to SAMRC ethics committee before they are implemented.

6.1.6 Reporting definitions

Unanticipated problems are any incidents/ experiences/ outcomes that are (1) unexpected (in terms of nature, severity, or frequency), (2) related or possibly related to participation in the research, AND (3) suggest that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously recognized.

Adverse events (AEs) are any untoward or unfavourable medical occurrences in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Serious adverse events (SAEs) are any adverse events that meet any of the following criteria: (1) results in death; (2) is life-threatening; (3) requires inpatient hospitalization or prolongation of existing hospitalization; (4) results in a persistent or significant disability/ incapacity; (5) results in a congenital anomaly/ birth defect; OR (6) may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

Labelling of AEs and SAEs.

Severity. AEs and SAEs will be labelled according to severity by one or both of the PIs, based on their impact on the patient. An AE will be termed "mild" if it does not have a major impact on the patient, "moderate" if it causes the patient some minor inconvenience, and "severe" if it causes a substantial disruption to the patient's well-being.

Relatedness. AEs will also be categorized according to the likelihood that they are related to participating in the study. Specifically, they will be labelled "definitely unrelated", "possibly related", "probably related", or "definitely related".

6.1.7 Protocol violations

Study staff will inform the Principal Investigators (PI) as soon as they are aware of any violations to the protocol. The South African PI will report any violations and the corrective actions taken to prevent further violations within 7 days to the SAMRC ethics committee.

6.1.8 Adverse events and unanticipated problems

As this study consists of low-risk meetings with a PRC, we do not anticipate having any study-related AEs, SAEs, or unanticipated problems. However, given that many participants in this study are from a vulnerable population (i.e., PLWH and SUD who have fallen out of HIV care), and are enrolled for about six-months, it is possible that AEs, SAEs, and unanticipated problems will arise. The plan for monitoring and reporting AEs, SAEs, and unanticipated problems is below.

Monitoring. At follow-up assessments, study staff will ask participants if they experienced any AEs or SAEs since the last assessment (e.g., hospitalizations). The PRC(s) will also be trained to let the study team know if they are aware of any AEs or SAEs.

Reporting to SAMRC HREC.

AEs. If any AEs occur, they will be reported to the SAMRC HREC during the yearly progress report.

SAEs. All SAEs will be reported to the SAMRC HREC within 48 hours of the team discovering the SAE, regardless of whether or not it is related to the study.

Responsibility

The Multi-PIs (MPIs) are ultimately responsible for data and safety monitoring. The processes described above ensure that the MPIs will be aware of important study related issues on a regular basis.

Disclosure of Any Conflict of Interest

Each investigator will complete a conflict of interest statement which will be kept on file by the study team. Any new investigators or key study staff will complete these forms, which will be stored and kept on record. At this time, there are no conflicts of interests in this study.

7. MANAGEMENT DETAILS

Management Approach

The present study will be led by the two PIs: Dr Bronwyn Myers and Dr Jessica Magidson.

7.1.1 SAMRC

Dr Myers (MPI) will take primary responsibility for SAMRC ethics protocols, training materials, staff training and management, and quality assurance. She will also oversee data collection.

7.1.2 UMD

Dr Magidson will oversee data management and the US based team who will support administrative coordination, oversight on regulatory issues and compliance, and all data management and cleaning.

7.1.3 Both Sites

Dissemination & Implementation. Drs Myers and Magidson will work collaboratively on the dissemination of findings. Specifically, each PI will take responsibility for gathering and coordinating resources and ensuring outputs for each area of primary responsibility. Leadership will be shared, as will responsibilities, authority, data, and credit. All final scientific and study implementation decisions will be made collaboratively between PIs, with inputs from the project team.

Communication. The PIs will communicate on a regular basis regarding study implementation and progress by telephone or video, in additional to regular email communication. Depending on travel guidelines (due to COVID-19 or other events), Dr Myers, Dr Magidson, and the US team will travel to Cape Town to support study training and implementation.

Conflict Resolution. All final decisions will be made collaboratively between Drs Myers and Magidson. In the case of conflicts, the two PIs will work diligently to resolve any issues and will draw on the expertise and inputs of the Co-Is and study collaborators to reach consensus. In the unlikely case that the two PIs cannot come to a consensus, they will seek out a third-party mediator (Dr John Joska at the University of Cape Town) to help resolve this conflict.

Staff and Scientific Collaboration

Dr Bronwyn Myers (MPI) will have the overall responsibility of ensuring procedural and scientific integrity of the SA-based study operations, including overseeing the team at the SAMRC. This will include supporting training and supervising research staff on study measures and assisting with regulatory requirements.

Dr Jessica Magidson (M PI) will have the overall responsibility of ensuring the procedural and scientific integrity of the US-based study operations, including data management and oversight. She will lead the team at UMD in coordinating research meetings, maintaining a study timeline, creating reports on study projects, handling ethics committee issues, and ensuring clear communication between all study members.

Facilities

7.1.4 Field Site

The present study team will be based on the SAMRC premises in Delft. This site has all the privileges of SAMRC office space and is the base for several studies located within the community. Project staff will be housed at this facility.

Please note that due to COVID-19, staff may work remotely. If working remotely, staff will still have access to SAMRC resources.

7.1.5 Data Management Site

Data management will primarily occur in the Global Mental Health and Addiction Program (Director: Dr Magidson) at UMD. The office space consists of shared office space, a conference room, individual offices, and locked file storage rooms. Data files will be saved to a secure network running the PI's laboratory.

Please note that due to COVID-19, staff may work remotely. If working remotely, staff will still have access to UMD resources including access to the secure network.

8. ADDITIONAL DETAILS

Research Translation

8.1.1 Manuscripts

We plan to publish the findings of this study in peer-reviewed journals. At a minimum we hope to publish a report of the implementation and preliminary effectiveness findings of this pilot study.

8.1.2 Scientific Conferences.

We plan to present findings from this study at scientific conferences, including Addiction Health Services Research (AHSR) annual meeting, the Dissemination & Implementation Science Annual Conference, and the College of Problems on Drug Dependence (CPDD).

8.1.3 Training Materials.

This study will allow for the final adaptation of our PRC model. If at the end of this future study the approach proves to be effective, feasible, and acceptable, we will offer capacity-building workshops to help the Department of Health scale-up peers and make our initial peer training and supervision available to all who would like it.

8.1.4 Data Sharing Plan.

We will make de-identified transcripts, codebooks, and quantitative data available to interested individuals (with appropriate training and approvals) after publication of the main outcome paper(s). Data will be released directly by the investigators providing evidence of their institution's ethics approval for planned analyses of the data. Our team will be available to address queries.

8.1.5 Clinical Trial Registration

In line with the requirements of the US National Institutes of Health (NIH), the Pilot PRC Study will be registered on ClinicalTrials.gov within 21 days of enrolment of the first participant.

Scientific Validity

This study has been peer-reviewed and approved by the US National Institute on Drug Abuse (NIDA), a division of the US NIH.

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