Home link:

Post hospital care to reduce HIV mortality in South Africa

Short title: Home Link

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Implementing Partner: PHRU, South Africa

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NCT04436289

Statement of Compliance

The study will be carried out in accordance with the design and specific provisions of this Human subjects ethics-approved protocol, with the ethical principles that are consistent with Good Clinical Practice (GCP) and the applicable regulatory requirements by the following:

- Declaration of Helsinki
- ICH GCP E6
- Completion of Human Subjects Protection Training

The Principal Investigator will assure that no deviation from, or changes to, the protocol will take place without prior agreement from the sponsor and documented approval from the Human Research Ethics Committee, except where necessary to eliminate an immediate hazard(s) to the trial participants. The Principal Investigator will promptly report to Human Research Ethics Committee any changes in research activity and all unanticipated problems involving risk to human subjects or others.

STUDY SUMMARY

Background: This is a pilot randomized clinical trial (RCT) to demonstrate the feasibility and acceptability of a structural and behavioral intervention to reduce mortality following hospital discharge for people with HIV (PWH) in South Africa. Our prior study showed that among 121 PWH discharged, 54% were readmitted and 26% had died by six months following discharge. In the prior study, we identified that missing clinic visits after discharge was associated with death. Here we are seeking to overcome key barriers in piloting a home-based post-hospital care intervention. Our approach is informed by a conceptual model of key barriers to the care transition along with a behavioral explanatory model, the Behavioral Model for Vulnerable Populations.
The overarching goal of this study is to tailor and pilot the intervention that shifts initial post-discharge care from the out-patient clinic to the home and provides patient-centered counseling (Home Link intervention). For the intervention to prove effective it will need to substantially reduce post-discharge mortality. Specifically, in the Home Link intervention, a team will conduct home visits to (1) provide a structured clinical assessment; (2) reconcile medications, (3) provide psychosocial support through patient-centered counseling, and (4) assess home needs (food security). These visits will start one week after discharge and be repeated every two weeks until the participant is stabilized and ready to initiate lower intensity clinic-based services or three months have elapsed.

Aims: The aims of the study are to pilot a randomized clinical trial of home delivery of health services during the post-hospital period for PWH.

Methods: This project is a pilot randomized clinical trial (RCT) to refine and test the feasibility, acceptability, and preliminary effectiveness of the HomeLink intervention. At the conclusion of the R34 grant period we will have a protocol and procedural manual ready for a full RCT powered for effectiveness.

Significance: The proposed study is consistent with NIH HIV/AIDS highest priority research and the South African National Strategic Plan on HIV, TB, and STIs 2017-2022. The research addresses the HIV/AIDS Research Priority of "retention and engagement in these services, and achievement and maintenance of optimal prevention and treatment responses."

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Glossary of Terms

AIDS	Acquired Immuno-deficiency Syndrome
ART	Antiretroviral Therapy
CAU	Care as Usual
CBO	Community Based Organization
CCMDD	Central Chronic Medicine Dispensing and Distribution (system or service)
CRF	Case Report Form
DOH	South African Department of Health
HIV	Human Immunodeficiency Virus
LTFU	loss to follow up
NIH	National Institutes of Health
PHC	Primary Health Clinic
PWH	People with HIV
PIS	Participant Information Sheet
RCT	Randomized Clinical Trial
SA	South Africa
STI	Sexually Transmitted Illnesses
TB	Tuberculosis
WBOT	Ward-Based Outreach Team

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1 INTRODUCTION

1.1 Background

A.3. Sub-Saharan Africa HIV mortality

In 2016 in South Africa approximately 154,000 PWH died.[1] Of these deaths, 110,000 have been characterized as excess mortality due to HIV (HIV associated deaths).[2,3] Overall, HIV-associated deaths are associated advanced disease defined by a low CD4 count.[4-6]

A.4. In-Hospital and Post-Hospital Mortality in Africa

Inpatient mortality among people with HIV (PWH) in Africa is uniformly high ranging from 17.2 to 29.6% across the continent, including in South Africa.[4-6] Following discharge from an index hospitalization the mortality is also high. In our preliminary work we have observed a 26% mortality in the 6 months after hospital discharge. This observation is consistent with mortality from other reports: 50% mortality at twelve months and 30% and 31% at six months reported from Tanzania, Kenya, and South Africa, respectively [7,8]

A.5. The contribution of Post-Hospital Mortality to Overall Death among People with HIV

In South Africa there are approximately 84,633 public sector acute care hospital beds of which approximately 25% are adult medicine beds.[9] By extrapolating the post-discharge mortality we observed to all discharges among PWH in South Africa we can estimate the annual mortality among PWH with a hospital discharge in the past six months. Considering the national proportion of all admissions that are for PWH, the average length of stay, and the annual readmission rate an estimated 240,000 PWH are admitted to medicine wards in South Africa annually.[10,11,12,13] A six-month post-hospital mortality of 26% suggests a total of 62,374 post-hospital deaths among PWH. This number of deaths represents 40% of the approximately 154,000 total annual deaths among PWH in South Africa.[1,2] A modest reduction in post-hospital deaths could substantially reduce overall HIV mortality in South Africa.

A.6. Causes of Post-Hospital Death

Some post-hospital deaths may be unavoidable due to advanced or incurable disease. Other post-hospital deaths may be avoidable with improved retention in care. A study from Johannesburg, South Africa assessed loss from care for HIV-TB co-infected patients; only 42% of patients discharged were known to have been to an HIV clinic within 30 days of hospital discharge (the time needed to obtain or refill ART prescriptions at the time of the study) [14] Similarly in our preliminary study, only 19% of participants attended a scheduled follow-up visit. Failure to attend a scheduled visit was associated with subsequent mortality in our preliminary study and in a report from Tanzania.[7] At present, there is limited research regarding approaches to retaining PWH in care during the post-hospital transition.[4,15,16]

A.7. The Hospital Admission and Re-admission Cost to the Medical System

In addition to the human toll of post-hospital mortality, there is a substantial cost to the health care system. The estimated average cost per medical admission in South Africa is USD1426 (USD364 per day).[17] Reducing the frequency of readmission and death (often during readmission) has the potential to reduce health system costs. Among the 121 PWH we observed in our preliminary study, 49 were readmitted once, 13 twice, and 2 three times within six months of discharge for an estimated hospital cost of USD115,506. Improving outpatient engagement in care may reduce this cost.

A.11. Factors Associated with Accessing HIV Care in Africa

Although little has been described regarding engagement in care following hospitalization in southern Africa, a great deal is known about failure to link to care. Study team members and other investigators in the field have identified factors associated with linkage to care and continued engagement in care on multiple socio-ecological levels.[18,19] On an individual level feeling healthy, not accepting an HIV diagnosis or allopathic care, internalized or anticipated stigma, fear, and food insecurity either diminish the perceived value of care or increase the perceived costs [19-22] Personal resilience and coping skills can reduce some of these potential costs while understanding or recognizing the role of ART can increase perceptions of value. On an interpersonal level, social support, acceptance, and encouragement of health seeking behaviors can contribute to care engagement. Clinic-level costs including travel, need for repeat visits, long wait times, needing to arrive very early in the morning, enacted stigma, inadvertent disclosure by attending a clinic, and demeaning behavior from health staff are barriers to care engagement.[23-27]Supportive health care workers can improve engagement. Strengths-based counseling and eliminating structural barriers have had demonstrated success in increasing linkage to care.[28-33] Furthermore, little is known about what impact, if any, COVID-19 has had on patient engagement in care following hospitalization.

A.8. Hospital Transition Programs in High Income Countries.

In the absence of hospital transition intervention studies from sub-Saharan Africa, studies from high income countries may provide useful lessons. Best practice guidelines regarding hospital discharge are largely focused on educating the patient and household members, medication reconciliation and pharmacy-based interventions, and communication between the discharging hospital and ambulatory care providers. Additional recommended or tested strategies include personal contact via telephone calls, home visits, or scheduled clinic visits shortly after hospital discharge.[34] Several studies have evaluated home medical visits following discharge. A recent meta-analysis of 47 randomized trials reported reduced readmission in five studies; 4 of these included home medical visits.[35,36] Post-hospital interventions that included home visits compared to those that did not were more likely to improve outcomes.

A.9. Home-Based ART Initiation or Maintenance in Africa

Home-based ART has been studied in sub-Saharan Africa to increase ART initiation, improve retention, or do both. A study in Uganda randomized participants to care at home or at the health facility starting at the first visit after ART initiation. Viral load suppression and mortality, to 24 months, was similar by study arm.[37,38] Studies of home ART initiation in Malawi and Lesotho reported higher ART initiation and improved or similar retention in care with household ART initiation followed by subsequent facility-based care when compared to standard facility-based ART initiation.[29,30] These studies suggest the acceptability, feasibility, and potential for better outcomes with home-care based interventions.

A.10. Public Health Sector Home Visit Model in South Africa

The National Department of Health, South Africa, began a process known as Primary Care Reengineering in 2010. An integral component of this initiative is community and household care. Specifically, each of the >5000 primary care clinics and community health centers will have a "ward-based outreach team" or WBOT. The teams are designed to be led by a primary care nurse and include enrolled nurses and lower level cadres including counselors. The primary mandate of the WBOTs is to improve health outcomes of South Africans through provision of

home and community-based health services.[39] At present, there is no defined approach for post-hospital follow-up nor is there a structured system of communication between the discharging hospital and clinics or WBOT teams.[40] The proposed intervention fits within the current initiative of the South African Department of Health and has the potential to provide valuable new knowledge to guide WBOT deployment.

1.2 Study objectives

The overarching goal of this proposal is to demonstrate clinical trial feasibility, acceptability, and preliminary efficacy of structured post-discharge medical home visits to reduce mortality following the transition from the hospital to home. We are proposing a pilot randomized clinical trial (RCT) to determine preliminary efficacy, feasibility of trial implementation and intervention delivery, acceptability of the intervention, the effect of the intervention on barriers to care, and to obtain detailed baseline psychosocial and medical needs to inform intervention refinement and explain outcomes (Figure 1).

The primary objectives of this study are:

1. To estimate 6 month mortality rates and assess for evidence of efficacy of the Home Link intervention compared to care as usual.
2. To determine the feasibility, acceptability, and effect of the Home Link intervention on identified barriers to care.
3. To characterize medical and behavioral needs among participants in the study.

The secondary objectives of this study are:

1. Determine post-hospital health care out-of-pocket costs for participants
2. Assess re-admission
3. Estimate 12 month mortality by study arm
4. To understand experiences around the time of the passing of the participant from the family members perspective

1.3 Significance

This study fits with the South African National Strategic Plan to increase effective HIV treatment. The study is also consistent with NIH HIV/AIDS highest priority research and the South African National Strategic Plan on HIV, TB, and STIs 2017-2022. Given the high post-discharge mortality findings from this study could contribute to approaches to reduce mortality for PWH.

2 METHODS

2.1 Study design

This is a pilot randomized clinical trial (RCT) to refine and test the feasibility, acceptability, and preliminary effectiveness of Home Link.

2.2 Study setting

This pilot operational research study will be conducted in Matlosana. All participants will be recruited from Tshepong Hospital. Eligibility will include residing within Matlosana sub-district.

2.2.1 Tshepong Hospital

Tshepong Hospital is a tertiary care hospital in Matlosana. An average of 30 patients are admitted to medicine wards daily. Nearly 50% are PWH.

2.2.2 Description of the geographical areas of study implementation

The proposed study will be conducted at the 500 bed Tshepong Hospital in the Northwest Province. Tshepong Hospital is one of 5 hospitals in Kenneth Kaunda District and the single tertiary care public hospital serving the population of 400,000 in Matlosana (Figure 1). This hospital was selected due to its size, heterogeneous catchment area (rural to urban), and long-standing working relationships with the research team. Tshepong Hospital currently provides discharge services that include (1) discharge counseling and education provided by counselors and (2) a medical record notebook with a discharge summary for the patient to take to his or her clinic visits.

2.2.3 Rationale for selecting geographical areas of study implementation

We selected Tshepong Hospital based on a long-standing working relationship between the PI, PHRU, and the Tshepong Hospital. This has included a prior study of post-hospital outcomes

2.3 Study Population

The population is comprised of adults (≥18 years old), either male or female, spending at least two nights in a medical ward of Tshepong Hospital. We will only include individuals with known HIV status, either HIV-positive or HIV-negative. We propose to recruit up to 180 HIV-positive and 60 HIV-uninfected participants. Randomization to the intervention vs control arms will be stratified by HIV status.

2.3.1 Inclusion criteria

- Tested for HIV (can be living with HIV or HIV-uninfected) – HIV negative partcipants should have a documented test from within the previous 3 months
- Residing within Matlosana sub-district
- Agree to post-discharge follow-up including home visit
- Able to provide informed consent or, if lacking capacity at the time of recruitment (if unable to answer basic orientation questions including name, month/year, and residence location), as determined by the study team, having a next of kin able to provide informed consent

2.3.2 Exclusion criteria

- <18 years of age
- Length of stay <2 nights
- Unknown HIV status at the point of study screening and enrollment
- Failure by the patient or next of kin to provide informed consent to be followed up by study staff after discharge
- Residing outside of Matlosana sub-district
- Not speaking any of the languages spoken by the study team

Late exclusions occurring after enrolment

- Death prior to hospital discharge
- Discharged too late for the study team to deliver the intervention
- Transfer to another hospital
- Relocation outside of Matlosana sub-district at the point of discharge or within 7 days of discharge

2.4 Sampling scheme

2.4.1 Participant recruitment and informed consent

In liaison with Tshepong Hospital staff, a list of names of all medicine ward patients will be generated on recruitment days. This list will be then be placed in random order (via random number generation on Excel worksheet). Recruitment will begin with the first individual and proceed down the list until the enrollment target for the day has been met. Patients on the list who are already enrolled, already declined, or do not meet enrollment criteria will be excluded. Patients who meet the enrollment criteria will be invited to participate (Appendix A: S001 Screening, eligibility and Enrolment). This process will take place any time after admission and prior to release.

2.4.2 Randomization

The total sample size is 180 HIV-positive and 60 HIV-uninfected adults. There will be a total of four study arms comprising of two arms for HIV uninfected and two arms for PWH. We will

perform individual randomization blocked by HIV-status to enroll 30 HIV-uninfected adults per arm and 90 PWH per arm (Figure 2).

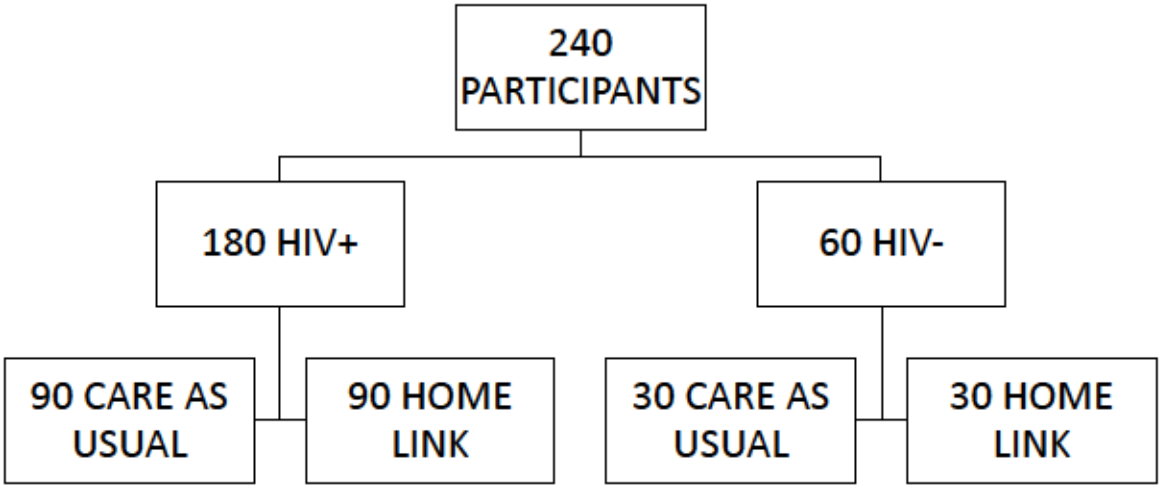

Figure 2: Randomization Study Arms for Home Link Intervention

1. Randomization of hospital patients for recruitment: On each participant recruiting day, a list of all medical ward patients will be generated, and each patient will then be randomly listed in order of planned recruitment. Patients will be approached at any time after admission if they are next on the list for recruitment until the enrolment target is reached for that day. A new list will be generated each day including only those patients admitted 2 days prior (or on Thursday, Friday and Saturday on Mondays).
2. Randomization to study arm: After informed consent and completion of baseline CRFs the participant will be randomized to care as usual or Home Link arm.

   Randomization will be conducted immediately after eligibility criteria for the participant has been documented and informed consent has been signed. Participants will be randomized 1:1 to either the care as usual or the Home Link intervention arms using computer-generated random numbers, stratified by HIV-status.

   A study staff member will SMS a dedicated study telephone number – staffed by someone not linked to any other aspect of the conduct of the study. Details of the eligible participant, including randomization group (1=living with HIV; 2=living without HIV), initials (first two letters of the first name and first two letters of the surname), age, and sex, will be sent via SMS to the randomizing team. A member of the randomizing team will then relay the allocation details (within 15 minutes) to the study staff member

who requested the randomization via SMS. Proof of randomization will be sent to the study staff member who will place the proof into the participants' study file.

2.5 Pre-discharge study procedures

All participants will have a baseline demographic health and psychosocial questionnaire (E001, E002).

2.5.1 Care-as-usual (CAU) study arm

Participants will receive standard discharge care as provided at Tshepong Hospital during the study. This currently includes discharge counseling from a trained discharge counselor and will be provided with a follow-up return date (usually two weeks post-hospital). Discharge counseling will include a review of discharge medications and instructions regarding follow-up care visits.

2.5.2 Home Link study arm

The Home Link intervention will be delivered by a **home visit team** including a primary care nurse and counselor trained in patient-centered counseling (Table 1). A rotating hospital-based doctor will be available for pre-home visit clinical file review and post-visit discussion, via cell phone, for decision making and input on patient care during a household visit. We have termed this individual a "**discharge officer**". The discharge officer will be a Tshepong clinician who is working in the hospital. Supporting Home Link is expected to take <30 minutes of the physician's time during the day. The team will also consult with a GCP-trained, PHRU research doctor based at Tshepong Hospital prior to household visits and for advice regarding referrals, discharge from home-based care, and other queries.

Table 1. Home Link intervention team key members

Team member	Training	Location of service	Role
Primary Care Nurse	Professional Nurse	Home visit team	Clinical assessment and management
Counselor	High school diploma	Home visit team	Patient-centered counseling & home needs assessment
Discharge officer	Medical doctor degree	Based at hospital	Clinical support (via cell phone)
PHRU research doctor	Medical doctor degree	Based at hospital	First point of contact for clinical support

The home care team will travel via car to the participant's house one week after discharge and every two weeks thereafter until completing 6 visits or the participant is discharged from the Home Link intervention based on the clinical assessments.

Home visits: Prior to team departure for a participant's home: the discharge officer and PHRU research doctor will review the participant's medical file, including retrieving laboratory results pending at the time of discharge or the prior home visit, and add any patient specific recommendations for assessments to the Patient Assessment Instrument (Appendix A) for the nurse to use at the household.

At the household, the team will use the Patient Assessment Instrument to document findings and guide decision making in the following areas:

Primarily provided by the primary care nurse

(a) Assess illness severity. The nurse will assess for symptoms of COVID-19 infection and active TB disease as well as general illness severity using temperature, blood pressure, pulse, respiration rate, pulse oximetry, and orientation. Use of these signs will be guided by an algorithm (Appendix A) leading to (i) discharge from home visits, (ii) return visit in 2 weeks, (iii) contacting a clinician at Tshepong Hospital via cellphone for further guidance, or (iv) calling for routine medical transport (ambulance service) to transport the participant to Tshepong Hospital for evaluation and likely admission.
(b) Medication reconciliation: review medication taking, medication availability, and prescribed medication plan. Counsel on appropriate dosing and address potential adherence barriers (e.g. lack of understanding, lack of medication availability, nausea or other side effects).
(c) Obtain laboratory specimens (whole blood or urine, as required based on the discharge officer assessments) for transport to the laboratory and provide medications dispensed for the patient from the Tshepong Hospital pharmacy as indicated for a given participant.
(d) Distribute any medications needed based on prescription from the discharge officer (based on a prior household visit assessment).

Primarily provided by counselor

(e) Household assessment: assess for food availability and home support; (involve social workers at Tshepong Hospital if indicated) (completed during medical assessment).
(f) Patient-centered counseling to address readiness for treatment engagement including readiness to accept treatment, readiness to face stigma and disclosure needs, building self-efficacy for care engagement, and providing counseling for symptoms of depression and/or alcohol abuse identified prior to hospital discharge or during home visits.
(g) Participants who have low food security identified prior to hospital discharge will be provided with a food supplement/parcel at the first home visit.

At the conclusion of the home visit, the team will contact (phone call or text message) the hospital-based PHRU research doctor, if indicated, based on the Patient Assessment Instrument or if the team desires specific guidance. The PHRU doctor will have access to the hospital file (all files pulled prior to the visit) and will provide guidance to the team. The guidance will fall into one of four general categories: 1) make no changes, 2) adjust medication taking, 3) obtain laboratory specimens, or 4) refer to discharge officer for further guidance and/or hospital for probable admission.

The total time of the Home Link visit is anticipated to be 1 hour. The review with the doctor prior to departing for household visits is expected to take about 15 minutes and the mobile phone contact with the PHRU research doctor to be <10 minutes per household visit.

2.6 Verification of hospital discharge date

Study staff will determine when study participants are discharged from the hospital in order to plan and schedule data collection follow-up to ascertain outcomes and to schedule the Home Link intervention home visits (for those in the Home Link arm).

2.7 Post-discharge follow-up

The primary outcome is mortality six months after hospital discharge. Secondary outcomes include mortality 12 months after hospital discharge, number of nights spent in a hospital,

number of ambulatory clinical encounters after the index hospitalization, and patient out-of-pocket costs for medical care. Outcomes will be assessed through scheduled contact and completion of a structured questionnaire with the participant or designated next of kin (either telephonic or in person if telephonic fails) at 8, 12, 26, and 52 weeks. Mortality will be further ascertained through a 26 and 52 week review of the Tshepong Hospital file (including the affiliated Klerksdorp hospital files) and matching of participant national identification numbers to the vital statistics register through consultation with the Department of Home Affairs . Repeat hospitalization will be ascertained using self-report / next of kin report and hospital records. Most subsequent hospitalizations can be expected to be at Tshepong Hospital due to the substantial distance to reach the next nearest hospital (>50 km to a lower level facility). In our prior experience we have observed rare use of alternative hospitals. Clinic visit data will be ascertained by self-report followed by verification through review of clinic paper or electronic (tier.net) records and National Health Laboratory Service electronic records (TrackCare).

Table 2. Scheduled visit windows

Visit name	Period	Primary goal
8 week follow-up	20 – 70 days	Maintain contact with participant
12 week follow-up	71-150 days	Assess care engagement, care satisfaction, mortality
26 week follow-up	151 – 245 days	Assess care engagement, , mortality; conduct psychosocial assessment
26 week hospital file review	>26 weeks post-hospital	Abstract care visits, re-admission, death
26 week Home Affairs vital status review	>26 weeks post-hospital	Match South African ID numbers
26 week care verification	>26 week post-hospital	Use electronic and paper files to verify self-reported clinic visits
52 week follow-up	365-455 days	Assess care engagement, mortality
52 week hospital file review	>365 days post-hospital	Abstract care visits, re-admission, death
52 week Home Affairs vital status review	>365 days post-hospital	Match South African ID numbers

2.7.1 Care verification

Clinical records will be accessed to determine linkage to care status, timing of linkage to care, ART continuation, retention in care, and relevant laboratory results. This will be done through reviewing paper clinic charts, electronic clinic data (tier.net), and electronic laboratory data (NHLS Trackcare system). Linkage between participants and records will be based on matching surname, first name, date of birth, sex, and appropriate date range.

2.7.2 Mortality

Mortality will be ascertained via:

(1) Telephonic contact with participant (alive) or next of kin, as provided by the participant, reporting a death
(2) Review of the Tshepong Hospital paper file
(3) South African Home Affairs vital statistics query using the participant national ID number

Mortality will be assessed after six months and again after twelve months.

2.7.3 Effectiveness of Home Link

Table 3. Effectiveness outcomes

Primary outcome	Mortality at six months by arm	Test of proportions (chi-square)
Secondary outcomes	Mortality at 12 months	Test of proportions (chi-square)
	Time to any non-acute follow-up	Cox proportional hazards
	Number of outpatient follow-up care encounters	Test of medians (Wilcoxon rank sum)
	Number of nights in hospital post-initial discharge	Test of medians (Wilcoxon rank sum)
	Self-reported cost of care	Test of medians (Wilcoxon rank sum)
Process outcomes	Acceptability of intervention	
	Feasibility of intervention	
	Feasibility of clinical trial	

2.7.4 Acceptability & Feasibility

2.7.4.1 Feasibility of Home Link

The goal of this assessment is to evaluate the feasibility of implementing the Home Link intervention and of endpoint ascertainment for the clinical trial of Home Link implementation.

Specific feasibility considerations are:

1) The proportion of participants in the Home Link arm who receive each scheduled/expected Home Link home visits
2) Success of the study team to ascertain six month mortality

We will assess the trial feasibility based on the proportion of eligible individuals who enroll and the proportion of participants that we are able to collect full outcome data on. We will assess the feasibility of implementing the intervention on the following measures: the proportion of planned home visits that are completed, the proportion of home medical assessments completed, the proportion of home medication reconciliation completed, the proportion of participants who receive patient-centered counseling, and the proportion of participants with identified food insecurity who receive food supplementation/parcels at the first home visit. The proportions will be considered individually and with a composite score to be interpreted in the context of the efficacy results with a general threshold that substantially more than half of components expected to be completed need to be completed for the intervention to be considered feasible.

Success will be based on *a priori* targets of ≥90% of planned home visits completed, successful follow-up of ≥75% of participants, and vital status ascertainment of >90% of participants.

Table 4. Feasibility Indicators

Numerator	Denominator	Measure

Number with first Home Link visit	Total in Home Link arm	Proportion
Number of completed Home Link visits	Number of planned/attempted Home Link visits	Proportion
Number of home medical assessments completed	Number of planned/attempted/completed Home Link visits	Proportion
Number of home medication reconciliation completed	Number of planned/attempted/completed Home Link visits	Proportion
Number of patient-centered counseling sessions completed	Number of planned/attempted/completed Home Link visits	Proportion
Number of participants who received food parcels	Number of Home Link participants with identified food insecurity pre-discharge	Proportion
Number of participants with 6 month vital status ascertainment	All study participants	Proportion
Number of participants with 6 month care engagement ascertainment For PWH: ≥1 HIV care visit For HIV-negative participants: ≥1 outpatient clinic visit	All study participants	Proportion
Number of participants with baseline laboratory and medical assessment completed	All study participants	Proportion

Acceptability

Acceptability will be assessed among participants in the intervention arm and health staff using an acceptability questionnaire and in-depth interviews. The (CRF F004) questionnaire based on the theoretical framework of acceptability developed by Sekhon et al. [41] that has seven core constructs: attitude (how an individual feels about the intervention with confidentiality and receipt of care and medical procedures such as phlebotomy occurring at home), burden (effort required for the intervention), ethics (concurrence with value system), coherence (how well the intervention is understood), opportunity costs, perceived effectiveness, and self-efficacy (confidence in performing or participating in the intervention). The acceptability scores will be interpreted in the context of the study efficacy results with a general threshold of the majority of participants scoring the constructs as acceptable (responses on Likert scale). Findings from the acceptability questionnaire will be further explored through in-depth interviews in a sequential explanatory mixed methods approach (described as follows).

Patient in-depth interviews: We will interview up to 40 patients recruited through a purposive sampling strategy to obtain a maximum variation sample by number of Home Link visits received and HIV status, timing of HIV diagnosis (during index hospitalization or prior, for those living with HIV), hospital readmission, sex, and age group. In-depth interviews will be conducted by trained research assistants in the participant's preferred language. Interviews will explore items identified in the quantitative survey for further exploration and: i) perceptions of and experiences with Home Link including participants perceptions of alignment of services with

needs (framed with the Andersen Behavioral Model), ii) confidentiality, impact of COVID-19 or other concerns with home visits, and iii) perceptions of quality of Home Link care.
Health care worker interviews: We will interview up to 10 health care workers (Home Link team) to understand their perspectives and experiences with delivering the intervention and to explore ways in which the model could be strengthened. We will also assess the perceived impact of COVID-19 on the homebased intervention. All audio-recorded interviews will be transcribed and translated into English (as necessary). Transcripts will be uploaded into qualitative coding software (e.g. Atlas.ti, MaxQDA) for the purposes of coding and analysis. Health care workers will be invited to participate by letter. Further study information and informed consent will be provided in private. The interviews will occur in a private space at a scheduled time convenient to the health care worker.

2.7.4.2 Bereaved Family members

Interviews with the bereaved family members: We will interview family members of up to 20 deceased participants to understand their experiences around the time of the passing of the participant, including what care the participant sought, how long they were ill for and what the family members think could have been done to assist the participant. In-depth interviews will be conducted by trained research assistants in the participant's preferred language. All audio-recorded interviews will be transcribed and translated into English (as necessary). Transcripts will be uploaded into qualitative coding software (e.g. Atlas.ti, MaxQDA) for the purposes of coding and analysis. Further study information and informed consent will be provided in private. The interviews will occur in a private space at a scheduled time convenient to the participant.

2.7.4.3 Effect of intervention on barriers to care engagement

We will compare, by study arm, constructs anticipated to be effected by the intervention: care access, burden of treatment including cost to the patient and time spent by the patient, patient satisfaction, correct medication administration, internalized and experienced HIV stigma, social support, and food security (Table 5).
Time spent and patient-level financial cost of care will be ascertained by participant self-report using a field team member administered questionnaire with questions focusing on the last clinical contact (clinic or household visit) since hospital discharge, the total number of contacts (visits), the cost of transport and incidental expenses with going to the clinic and lost wages. Specific cost characteristics (such as transport cost and date of clinical care visit) will be verified using objective measures such as local mini-bus fares and medical file abstraction (at 26 weeks after discharge).

Table 5. Measures and analysis for feasibility, acceptability, and effects on engagement in care

Assessment	Assessment methods	Timing	Statistical test
Feasibility and Acceptability			
Trial: Feasibility	Proportion of enrolled participants among approached and eligible patients Proportion of participants with complete follow-up	base-line 1 year	Proportion, total study

Intervention: Feasibility	Proportion of planned home visits successfully completed, patient-centered counseling sessions completed, medical assessments, medication reconciliations, and food security management	3 m	Proportion, Home Link Arm
Acceptability	Acceptability questionnaires with 7 acceptability domains for HCWs and participants	3 m	Proportion, Home Link arm
Acceptability	In depth interviews	3 m	Thematic analysis
Effects on care engagement barriers			
Patient cost	Structured questionnaire for participant self-report	3 m, 6m	Wilcoxon rank sum
Care satisfaction	Adapted South African care satisfaction survey[44]	3 m	Wilcoxon rank sum test
Medication reconciliation	Reconciling planned meds on discharged actual meds with patient & way that patient is taking	3 m	Proportion, Home Link arm
HIV stigma	Short form HIV stigma scale[45,46]	baseline, 6 months	Wilcoxon rank sum test
Social Support	MOS social support instrument[47]	baseline, 6 months	Wilcoxon rank sum test
Food security	Three question scale	baseline, 6 months	Wilcoxon rank sum test
Depression	CES-D (short)	Baseline, 6 months	Proportion
Alcohol use	Alcohol use disorder identification test (AUDIT), shortened version	Baseline, 6 months	Proportion

Medical conditions and psychosocial needs will be assessed prior to hospital discharge and post-hospital by using Home Link visit and other care contact records.

a. Medical assessment prior to hospital discharge: Clinical data will be abstracted or specifically obtained for the study, if not in the clinical record: HIV viral load, CD4 count, HIV drug resistance testing, Xpert Ultra for rapid TB diagnosis, discharge diagnoses, and discharge medications. Blood will be drawn from all participants living with HIV for drug resistance testing; however, we will only conduct the drug resistance test if the viral load result is >1000 copies/mL. We may use leftover specimen from the drug resistance test to repeat the viral load and drug resistance test using a plasma separation card in collaboration with the National Institute for Communicable Diseases (NICD).

b. Psychosocial assessment prior to hospital discharge: social support, depression, economic status, and HIV stigma will be measured. The 12-item HIV stigma scale[45] (including enacted, internalized, and anticipated stigma components), CES-D (short) depression scale, MOS social support instrument, food security, and AUDIT alcohol use instrument will be administered to participants prior to discharge (E002).

c. Post-hospital services delivered: All post-hospital assessments (Home Link visit clinical instrument (HL001), participant challenges identified during patient-centered counseling sessions (from structured counselor notes), triage decisions from the discharge officer, findings on laboratory testing, and clinical evaluation during inpatient or ambulatory care that Home Link arm participants receive will be abstracted from hospital or clinic paper or electronic records and

the electronic National Health Laboratory Service records. These data will be organized to describe the intensity of care, psychosocial needs, clinical decision making, and most common clinical scenarios.

Sampling: All participants will have in-hospital laboratory and psychosocial assessments. All participants in the Home Link arm will be included in the assessment of post-discharge needs and triage outcomes.

2.8 Analysis

2.8.1.1 Effectiveness analysis

Table 6. Effectiveness outcomes

Primary outcome	Mortality at six months by arm	Test of proportions (chi-square)
Secondary outcomes	Mortality at 12 months	Test of proportions (chi-square)
	Time to any non-acute follow-up	Cox proportional hazards
	Number of outpatient follow-up care encounters	Test of medians (Wilcoxon rank sum)
	Number of nights in hospital post-initial discharge	Test of medians (Wilcoxon rank sum)
	Self-reported cost of care	Test of medians (Wilcoxon rank sum)

2.8.1.2 Feasibility analysis

Table 7. Measures and analysis for feasibility, acceptability, and effects on engagement in care

Assessment	Assessment methods	Timing	Statistical test
Feasibility and Acceptability			
Trial: Feasibility	Proportion of enrolled participants among approached and eligible patients Proportion of participants with complete follow-up	base-line 1 year	Proportion, total study
Intervention: Feasibility	Proportion of planned home visits successfully completed, patient-centered counseling sessions completed, medical assessments, medication reconciliations, and food security management	3 m	Proportion, Home Link Arm
Acceptability	Acceptability questionnaires with 7 acceptability domains for HCWs and participants	6 m	Proportion, Home Link arm
Acceptability	In depth interviews	6 m	Thematic analysis
Effects on care engagement barriers			
Cost of care access	Structured questionnaire for participant self-report	3 m, 6m	Wilcoxon rank sum
Medication reconciliation	Reconciling planned meds on discharged actual meds with patient & way that patient is taking	3 m	Proportion, Home Link arm
HIV stigma	Short form HIV stigma scale[45,46]	baseline, 6 months	Wilcoxon rank sum test
Social Support	MOS social support instrument[47]	baseline, 6 months	Wilcoxon rank sum test
Food security	Three question scale	baseline, 6 months	Wilcoxon rank sum test
Depression	CES-D (short)	Baseline, 6 months	Proportion

Alcohol use	Alcohol use disorder identification test (AUDIT), shortened version	Baseline, 6 months	Proportion

2.8.1.3 Acceptability analysis

Our approach to the qualitative data will involve thematic analysis and employ both inductive and deductive coding techniques.[42,43] We will first develop an ***a priori*** code book that reflects key analytic concepts of ***predisposing***, ***enabling***, and ***need*** characteristics from the Andersen Behavioral Model. During the process of reading and coding of transcripts using this initial coding scheme, additional codes may be added to document emerging themes of interest.

Analysis will be led by co-I Kerrigan and will be assisted by the experienced qualitative PHRU team. Qualitative analysis will proceed by first exploring broad patterns and experiences of study participants, and then assessing possible similarities and differences in experiences between different types of patients (including different ages, gender, level and type of care engagement, etc.) and providers (different types). Given strong gender roles in South Africa, we will specifically explore potential differences in perceptions of and experiences with intervention services among patients based on gender of the participant.

2.8.1.4 Social and medical needs analysis

We will use descriptive analysis to describe the proportion of participants with specific findings (clinical or psychosocial) or triage decisions and outcomes following that decision path. Logistic regression will be used to assess for associations between post-hospital outcomes and in-hospital medical and psychosocial measures. A multivariable model will assess for specific associations and interactions between significant factors. Sex, age, and trial arm will be included, a priori, in logistic regression modeling. These findings will be used to refine the list of fields on the Home Link clinical instrument and clinical algorithm.

All post-hospital assessments (Home Link visit clinical instrument (Appendix)), participant challenges identified during patient-centered counseling sessions (from structured counselor notes), triage decisions from the discharge officer, findings on laboratory testing, and clinical evaluation during inpatient or ambulatory care that Home Link arm participants receive will be abstracted from hospital or clinic paper or electronic records and the electronic National Health Laboratory Service records. These data will be organized to describe the intensity of care, psychosocial needs, clinical decision making, and most common clinical scenarios.

3 Data Management

Data will be collected to review study associated outcomes in order to evaluate the extent to which the case management goals and objectives are being met. To achieve this, data will be collected in the Home Link and Care as Usual arms. In addition to this, data will also be collected to assess actual programme performance against planned activities.

3.1 Data collection tools

Table 8. List of data collection tools and intended use

Name of tool	Purpose	Schedule	Study arm
Screening Form (S001)	To document screening process and that participant meets enrollment criteria	In hospital	Home Link & CAU

Enrollment demographics and history form (E001)	To collect medical history prior to hospital admission, focused on HIV and TB	In hospital	Home Link & CAU
Psycho-social assessment (E002)	To assess depression, stigma, social support, and food security (CES-D (short), short-form HIV stigma, MOS social support, food security scale, AUDIT alcohol use instrument)	In hospital; post-hospital	Home Link & CAU
Locator form (L001)	To collect the participant's personal information important for identifying and contacting the participant for follow up after release.	In hospital	Home Link & CAU
Post release locator (L002)	To update the participant's personal information important for identifying and contacting the participant for follow up after release.	Post-hospital	Home Link & CAU
Hospital discharge or death documentation (D001)	Documentation of hospital outcome and date of in hospital death or hospital discharge	In hospital	Home Link & CAU
Off Study /Termination (T001)	To document discontinued participation in the study due to withdrawal, loss to follow up or end of the study procedures.	Post-hospital	Home Link & CAU
Follow-up participant or alternate contact (F001)	To collect medical history since last study contact	Post-hospital	Home Link & CAU
Post-hospital medical needs (F002)	Record medical interventions and services received post-hospitalization	Post-hospital	Home Link & CAU
Participant health related financial costs (F003)	Obtain self-report regarding health costs (transport to visits, medications, clinic costs)	Post-hospital	Home Link & CAU
Acceptability (F004)	Acceptability scale for subset of patient participants and health care works	Post-hospital	Home Link & HCWs
Care satisfaction (F005)	To collect information on care-satisfaction	Post-hospital	Home Link & CAU
Clinic Visit Verification (C001)	To collect details of self-reported participant clinic visits. Tier.net; NHLS Trackcare; clinic note abstraction	Post-hospital	Home Link & CAU
Home Link home visit assessment form (HL001)	Structured clinical and needs assessment form	Post-hospital	Home Link
Home Link fidelity (HL002)*	Document the Home Link home visit (arrival time, individuals present, services rendered, and departure time)	Post-hospital	Home Link
Home Link Counseling (HL003)	To document patient-centered counseling at Home Link home visits	Post-hospital	Home Link
Archive follow-up (A001)	To abstract re-admission, clinic visits, and documented death from the hospital paper file	Post-hospital	Home Link & CAU
Laboratory Testing (LT001)*	To document collection of lab specimens and results for HIV RNA, creatinine and CD4 counts.	Post-hospital	Home Link & CAU

Home Link Transition (TR001)*	To document discharge of participant from Home Link home services.	Post-hospital	Home Link
Interview Guide 1	Interview guide for patient participants	Post-hospital	Home Link
Interview Guide 2	Interview guide for health care workers	Post-hospital	HCWs

3.2 Study sample size justification

We propose to recruit a sample of 240 participants randomized 1:1 into care as usual and Care Link arms. The participants will be blocked to include 30 HIV-uninfected adults and 90 people living with HIV per arm. The sample size has been determined to be feasible given time and budget limitations while still providing insight into the efficacy. Using the base rate of mortality from our preliminary study of 26% and an alpha of 0.05 and a sample size of 120 split 1:1 in care as usual and Home Link arms we have represented power versus intervention arm mortality, with sub-group analysis limited to PWH, in Table 11. We note that the primary goal is feasibility and acceptability. We are appropriately powered only for a substantial decrease in mortality from 26% to 10%.

Table 9. Power by varying effect size on reducing post-hospital mortality

alpha	power	N	N1	N2	delta	p1	p2
.05	.1589	180	90	90	-.06	.26	.2
.05	.2527	180	90	90	-.08	.26	.18
.05	.3764	180	90	90	-.1	.26	.16
.05	.5212	180	90	90	-.12	.26	.14
.05	.6704	180	90	90	-.14	.26	.12
.05	.803	180	90	90	-.16	.26	.1
.05	.9019	180	90	90	-.18	.26	.08

3.3 Schedule of case report forms

Table 10. Scheduled study visit windows for all participants post-hospital

Case Report Form	Form Code	Visits:	Visit 0 Discharge	Visit 1 Post-discharge	Visit 2 Post-discharge	Visit 3 Post-discharge	Visit 4 Post-discharge
		Time since release:	Discharge	8 wk	12 wk	26 wk	52 wk
Hospital discharge form	D001		X				
Psychosocial assessment	E002					X	

Clinic Visit Verification	C001					X	X
Home Link home visit assessment form	HL001	At home visits					
Home Link fidelity	HL002	At home visits					
Home Link Counseling	HL003	At home visits					
Laboratory Testing (LT001)	LT001					X	X
Follow-up participant or alternate contact	F001			X	X	X	X
Post-hospital medical needs assessment	F002				X	X	
Post-hospital financial costs	F003				X	X	
Acceptability	F004				X		
Care satisfaction	F005				X		
Archive follow-up	A001					X	X
Home Link Transition	TR001	At home visits					
Off Study/Termination	T001		[X]	[X]	[X]	[X]	[X]

X required CRF, [X] may be required if updated or as necessary

3.4 Database

3.4.1 Structure of the database

This study will rely on two databases. One will be used to capture participant characteristics and outcomes (main database). The other database will be a study administrative database used for monitoring of Home Link visits (administrative database). Main study data will be captured into a secure web based REDCap™ (Research Electronic Data Capture) electronic database. The Redcap database provides; an intuitive interface for validated data entry; audit trails for tracking data manipulation and export procedures; automated export procedures for seamless data downloads to common statistical packages; and procedures for importing data from external sources. A separate database (administrative database) will be developed to assist with tracking of upcoming study follow-up visits. Data entry for the administrative database will be maintained on a daily basis for real-time use of data. On the day of enrolment, the identification and contact details will be entered into the paper locator CRF (L001) which will be stored in a locked cabinet in a secure office adjacent to Tshepong Hospital. The administrative database will be updated within three days of the participant's discharge date.

We will develop a separate database form within REDCap for each paper case report form (CRF). All fields will have appropriate range-checks for validation during data-entry. Field numbers and names in the database will correspond to numbers and names on the CRF. Data will be recorded either on paper CRFs or directly into REDCap. All paper data forms will be identified with the participant study identifier and will not include any personal identifier information (except for the screening and patient locator forms). Paper forms will be maintained in a locked cabinet in a secure office adjacent to Tshepong Hospital. For all data not captured directly into the database system during participant encounters, trained data capturers will enter data from paper forms into the database.

Data entry validation and automatic range checks will be incorporated in most data fields to reduce data entry errors. In addition, for data collected on paper CRFs and then entered into REDCap, a data monitor will compare approximately 10% of CRFs with data within the database. This will help to identify systematic errors. Such problems may lead to a review of a larger proportion of CRFs. In addition, bi-weekly electronic checks for inconsistencies within and across forms will be performed followed by CRF review of any data queries that are generated.

3.4.2 Database access

Access to the database (data entry, reporting, and extraction) is controlled by the Data Manager, Study Manager, and the REDCap Database Administrator. Study personnel requiring access to the database must complete required documentation and training prior to receiving the necessary username and password.

3.4.3 Locking of final database

The final study database is locked to changes after the clean file form has been signed. Final storage of the database is with the production folder structure together with all the Metadata, source data and the user written programs and the version of the system used to produce the database. The folder is given a special icon to show it is locked and the available choices are restricted to reading the data.

3.4.4 Data security

All paper study records (e.g. consent forms, screening logs) will be kept in a secure location accessible only to authorized study staff, investigators, and monitors. No personal identifiers will be captured on REDCap and all participants will be issued with a study specific number.

3.4.5 Study limitations

The proposed implementation research has the following limitations:

- Participant self-report regarding lapses in medications and entry into care may introduce bias as participants may favour the most socially acceptable responses. Verification of self-reported entry-into-care using clinic records will be conducted, where possible, for all participants. .
- Follow up and observation of participants in the care as usual arm (may result in modified or improved participant outcomes because of the fact that they are being contacted.

- **A low proportion participating would markedly reduce the generalizability of the results. Our experience is with an interest and willingness of hospitalized patients to participate in studies. Thus we do not anticipate this to be a significant limitation.**

4 Appropriate care in response to study-specific findings

During all evaluations including pre-discharge and post-discharge clinically relevant information may be collected. This information includes laboratory test results, health screening information, and assessments for depression (CES-D, short) and alcohol use disorder (AUDIT). Findings from all of these will be provided to the "discharge officer", a medical doctor, for determination of action. Post-hospital clinical assessments occurring in the Home Link arm are reviewed by the "discharge officer" as part of the intervention and the structured assessment checklist with specified triggers for action. Results from pre-discharge testing and psychometric tools for the care as usual participants will be provided to the "discharge officer" for review and sign-off. Results indicating clinical action will be appropriately referred (e.g. microbiologic test results indicating infection, CES-D (short) meeting a threshold for depression, AUDIT suggesting alcohol use disorder). Referrals will be made to the Tshepong specialty clinics, Tshepong-based clinical psychologists, Tshepong-based clinical social workers, or a primary care clinic at which a patient is receiving care will be contacted with clinical recommendations. These recommendations may include medical care (e.g. initiate TB treatment based on positive TB results) or psychological assessment at that clinic. For participants in the Home Link intervention arm with indications of depression and/or alcohol abuse, counselling will be provided during home-based visits.

5 Protection of human participants

5.1 Regulatory approvals

This study will be conducted according to Good Clinical Practice (GCP) guidelines and completed in compliance with international and local human subject research guidelines. Approvals will be sought from University of the Witwatersrand Human Research Ethics Committee, North West Province, and the Johns Hopkins University IRB.

5.2 Risks and benefits

- The nature of this research is focused on improving outcomes regarding a situation unique to hospitalized individuals. The majority of potential benefit from research results will inform care for this medically vulnerable population. The risk posed by the components of this study are equal to or less than that of daily life. The primary risk will be of inadvertent disclosure of HIV status through contact with study staff – risks present with obtaining public section HIV care in South Africa. While this risk is what is faced in public section care, it is of serious concern for the study and will be addressed through training of study staff and discretion during home visits including using unmarked vehicles.

1. **No excessive inducements for participation.**

Participants will not receive specific remuneration for overall study participation. Patient participants will receive R100 for time and or travel for in-depth interviews.

2. **The information is presented in language that is understandable to the subject population.**

The Participant Information Sheet (PIS) and other study related communication is at the participant level. Additionally, the PIS will be translated into the most common local languages spoken in the Matlosana area.

Written informed consent will be obtained from eligible participants or their next of kin while in the hospital for patient participants and from health worker participants at times convenient to them. The consent process will be done in a private area to ensure confidentiality. Informed written consent, using Ethics Committee/IRB-approved consent forms, will be obtained by trained study personnel prior to performing any study-specific procedures. Informed consent is a process that will be initiated prior to the individual's agreeing to participate in the study and will continue throughout the individual's study participation. Should informed consent initially be obtained from the potential participant's next of kin, we will additionally consent the participant if and when they're able to do so. Potential participants or their next of kin will receive information about risks and possible benefits of study participation, study objectives and procedures. Informed consent requires the legally effective signature or mark of the subject or their next of kin. A copy of the signed and dated informed consent document will be offered to each participant for his or her records. The rights and welfare of the subjects will be protected by emphasizing to subjects that the treatment by clinicians will not be adversely affected if they decline to participate in this study, and that they may withdraw consent at any time. The investigator will retain a copy of the signed consent forms, which may be inspected at the monitor's/auditor's request. The investigator will promptly report to the Ethics Committee/IRB of all changes in the research activity and all unanticipated problems involving risks to human subjects or others, and will not make changes in the research without Ethics Committee/IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

The informed consent process will include a verbal review of the study, provision on participant information sheets in relevant languages, review of the information sheets, and answering any questions. Participants or their next of kin who are unable to read or write will be asked to make a mark or thumbprint in the presence of a witness (verbal consent will not be obtained). Only written informed consent will allow for study participation.

3. Health care worker participation

Health service staff involved in the discharge process or Home Link intervention will be recruited for participation. Selected staff members will receive an invitation with follow-up by a study team member regarding interest in participation. Study information will be provided to the potential staff participant. Staff willing to participate will be asked to sign a written informed consent document in duplicate. One copy will be provided to the staff member and the other will be retained in study files.

The consent process and decision regarding participation will remain confidential from hospital officials, the study PI, and study co-investigators. Interviews among staff participants will be scheduled to take place in a private setting at a later time and date.

5.3 Clinical trials registration

The study will be registered with clinicaltrials.gov. Key study information and results will have open-access availability on the clinicaltrials.gov website. This is in accord with funder (NIH) regulations.

5.4 Confidentiality

All study records will be managed in a secure and confidential fashion. All records will be stored in research office space adjacent to the Tshepong Hospital in locked filing cabinets and access to the records will be restricted to specified study team members. Case report forms and case management documents will be identified using the participant's study number only, with locator information stored separately.

5.5 Data safety and monitoring

A data safety and monitoring board will be established to review of the protocol and monitoring plan prior to commencement of enrollment into the RCT and meet virtually prior to commencing enrollment and then every 6 months to review of RCT progress, enrollment and outcomes data, and any potential adverse outcomes. The meetings will review safety to suggest procedural changes and study modifications. There will be no criteria for study termination based on effectiveness because this is a pilot feasibility study with a total sample size that may not allow clear assessment of difference. The DSMB will include 3-5 members including individuals with experience with HIV care, clinical outcomes research, clinical trials, and good clinical practice.

6 Project Governance and Management

6.1 Research team

- **Dr. Christopher Hoffmann, MD, MPH, MSc** is a clinician scientist, Associate Professor at Johns Hopkins University. Dr. Hoffmann will provide overall leadership for study implementation.
- **Prof Neil Martinson MBBCh, MPH is a clinician scientist and Executive Director of the Perinatal HIV Research Unit. Prof Martinson is the South African PI and will provide oversight to the South African team.**

The study team (PI, South African PI, and co-Is) will meet biweekly to review study progress. The PI will meet weekly with the Research Manager to discuss operational aspects of the study implementation. Dr Kerrigan will meet as needed for qualitative analysis components. The PI will make 3 – 4 visits annually to study sites.

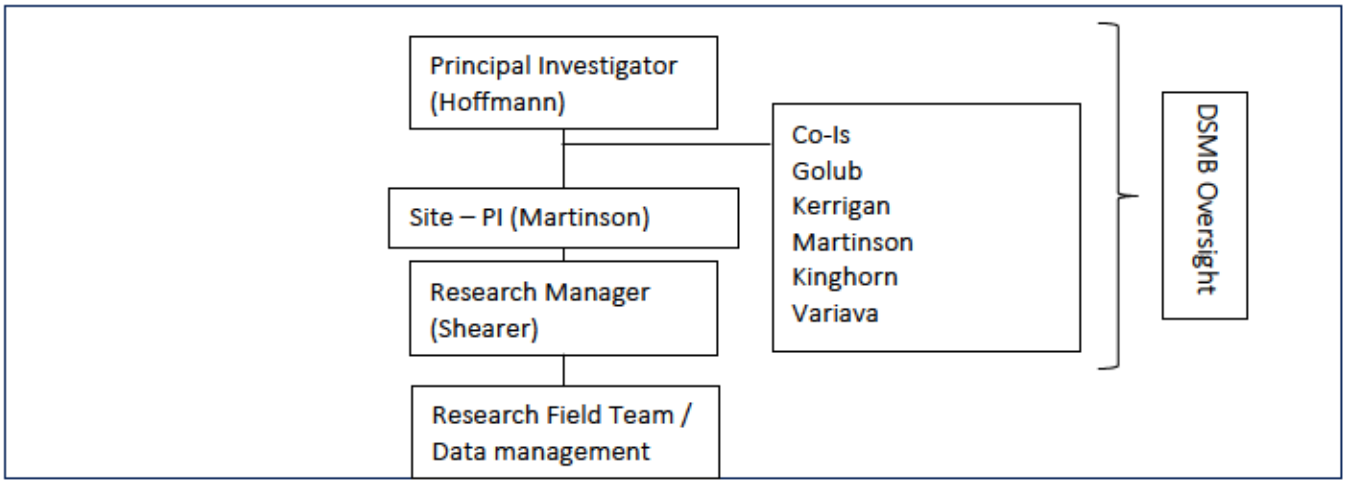

Figure 2: **Project Management Structure**

6.2 Publication policy

The research findings will be presented first to national stakeholders, and disseminated to stakeholders and participants in each province by means of local meetings. The results will be written up as one or more articles for submission to a suitable scientific journal.

6.3 Performance monitoring

The principal investigator will complete a monthly progress report that will facilitate monitoring of study progress and keeping the funders informed. These reports will capture vital information, such as IRB timelines, status of protocol development, enrolment figures, and any issues/delays that the PI may be experiencing.

7 Participant reimbursement

Participants will not receive payment for participation in the study. Patient participants will receive R100 for time and or travel for in-depth interviews.

8 Funding

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