STUDY PROTOCOL

The Sub-Saharan Africa Regional Partnership (SHARP) for Mental Health Capacity Building – A Clinic-Randomized Trial of Strategies to Integrate Depression Care in Malawi

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The Sub-Saharan Africa Regional Partnership (SHARP) for Mental Health Capacity Building – A Clinic-Randomized Trial of Strategies to Integrate Depression Care in Malawi

Sponsored by:

National Institute of Mental Health (NIMH) at the National Institutes of Health (NIH)

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ABSTRACT

Despite the heavy burden of mental illness, the mental health treatment capacity of most sub-Saharan African health systems is extremely limited. Although effective mental health treatment interventions are well defined in high-income countries, their deployment in low- and middle-income countries is limited due to lack of implementation science research that addresses the challenges of adapting evidence-based interventions to low-resource contexts and few researchers and policymakers adequately trained in implementation science. The Sub-Saharan Africa Regional Partnership (SHARP) for Mental Health Capacity Building seeks to make a meaningful impact on the mental health treatment gap in sub-Saharan Africa. The partnership brings together governmental, academic, and non-governmental partners invested in mental health research and treatment. SHARP will conduct critical implementation science research and build capacity among researchers and policy makers to facilitate scale-up of evidence-based mental health treatment in Malawi, Tanzania, and sub-Saharan Africa. This protocol covers the clinic-randomized trial planned for the second phase (Years 2-5) of the study, which will compare two different implementation strategies to facilitate scale-up of depression treatment within existing chronic disease clinics in Malawi.

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HISTORY OF PROTOCOL CHANGES

Version 1.0, 9 August 2018

- None to date.

Version 1.1, 07 November 2018

- Changed titled to: The Sub-Saharan Africa Regional Partnership (SHARP) for Mental Health Capacity Building – A Clinic-Randomized Trial of Strategies to Integrate Depression Care in Malawi
- Added sample size justification
- Revised objectives
- Updated list of sites
- Discussion of risks related to recording and to blood collection
- Removed “not” from “These recordings will NOT be identified with a code number” on pages 14 and 15

Version 1.3, 04 December 2019

- Changed patient interview follow-up schedule from 3 and 9 months to 3, 6 and 12 months

Version 1.4, 20 February, 2020

- Made follow-up schedule consistent across protocol (interviews during Year 3)
- Added to Year 3 qualitative interview population (added 6 Clinical Coordinators, 6 Friendship Bench counselors, and 6 SHARP research assistants to the existing population of 6 clinic directors, 6 providers, and 3 MOH administrators)
- Reduced sample size for patient qualitative interviews from 16 to 8

Version 1.5, 19 March, 2020

- Amended interview format to include phone calls

Version 1.6, 30 September, 2020

- Added to Year 3 qualitative interview population (added 6 more providers for a total of 12)

Version 1.7, 26 February, 2021

- Added to Year 3 cognitive interviews and structured surveys to evaluate providers’ perceptions of stigma and acceptance towards individuals with mental health disorders.

Version 1.8, 1 September, 2021

- Added Year 4 qualitative interviews with hospital workers and SHARP research assistants following results of Year 3 qualitative interviews

Version 1.9, 11 November 2022

- Removed Dignitas International personnel from protocol team roster
- Updated statistical analysis plan to replace generalized linear models with generalized estimated equation models.

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GLOSSARY OF TERMS/ACRONYMS

ABCD	Algorithm-Based Care for Depression
DALY	Disability-adjusted life year
EC	Ethics committee
IRB	Institutional Review Board
LMIC	Low- and middle-income country
MoH	Ministry of Health
NCD	Non-communicable disease
NHSRC	National Health Sciences Review Committee
RCT	Randomized controlled trial
SHARP	Sub-Saharan Africa Regional Partnership for Mental Health Capacity Building
YLD	Years lived with disability

1.0 INTRODUCTION

Despite the heavy burden of mental illness, the mental health treatment capacity of most sub- Saharan African health systems is extremely limited. Although effective mental health treatment interventions are well defined in high-income countries, their deployment in low- and middle-income countries is limited due to lack of implementation science research that addresses the challenges of adapting evidence-based interventions to low-resource contexts and few researchers and policymakers adequately trained in implementation science. The Sub-Saharan Africa Regional Partnership (SHARP) for Mental Health Capacity Building seeks to make a meaningful impact on the mental health treatment gap in sub-Saharan Africa. The partnership brings together governmental, academic, and non-governmental partners invested in mental health research and treatment. SHARP will conduct critical implementation science research and build capacity among researchers and policy makers to facilitate scale-up of evidence-based mental health treatment in Malawi, Tanzania, and sub-Saharan Africa.

1.1 Background and Literature Review

Mental health disorders, including depression, contribute substantially to global disease burden, disability and mortality. Mental health disorders are the leading cause of years lived with disability (YLD) (31.7%) and the fifth leading cause of global disability-adjusted life years (DALYs) (7.4%).[1, 2] Depression contributes more to this burden than any other mental health condition. A recent review indicates that mental disorders are associated with significantly increased mortality; a median of 10 years of potential life is lost due to mental disorders, and 14.3% of deaths worldwide (approximately 8 million) can be attributed to mental disorders.[3] Globally, more than 2.2 million excess deaths annually can be attributed to depression.[4] Across regions, sub-Saharan Africa suffers from the highest cost of years of life lost due to mental disorders.[1] At the same time, the capacity of many low- and middle-income countries (LMICs), and especially many sub-Saharan African countries, to respond to this mental health burden is severely limited.[5] The median number of mental health professionals per 100,000 population among sub-Saharan African nations is less than one-fiftieth of that found in the United States.[6, 7]

Given the limited human resources, most of the efforts to respond to the burden of mental health disorders in LMICs have focused on task-shifting strategies to expand treatment capacity. Such initiatives give community members or general medical providers the skills and support to deliver evidence-based depression treatment interventions.[8-10] Some efforts have trained lay health workers or non-specialist clinicians to deliver counseling interventions in, for example, Uganda, Tanzania, South Africa, Pakistan, and India.[11-18] Others have trained non-specialist clinicians, e.g. HIV clinicians or general care providers, to prescribe and manage antidepressant treatment in the context of regular medical care.[15, 19-21] [18] Both counseling and medication-based task-shifting approaches have demonstrated feasibility, acceptability, and efficacy in improving mental health outcomes in LMICs generally and sub-Saharan Africa specifically.

Despite the growing evidence base of task-shifting mental health interventions, rates of treatment for mental health disorders in LMICs are low. The proportion of individuals with a mental health disorder in LMICs who are not receiving treatment is estimated to be as high as 90%; the treatment gap for depression is even higher in many settings.[5] Several key factors are currently limiting the translation of this growing evidence base into actual health

system change. First, implementation science research is needed to close the knowledge gaps that policy makers face in trying to translate research to policy, for example what sorts of staffing and supervision structures are needed to sustain an evidence-based mental health intervention at scale? Relatedly, capacity to conduct implementation science research must be expanded among LMIC researchers. Finally, capacity among policy makers to interpret and apply implementation science research findings must be increased so that research can be efficiently used to inform health system redesign.

1.2 Study Rationale

Mental health disorders are among the leading causes of disease burden and disability worldwide. Globally, mental health disorders account for nearly a third of years lived with disability and are the fifth-leading cause of disability-adjusted life years.[1, 2] The global economic burden due to mental health conditions and related death and disability is expected to result in productivity losses of USD 16.1 trillion from 2010-2030.[22]

Both Malawi and Tanzania are currently in the process of revising their Mental Health Action Plans, and the potential for large impact from this project is high. In Malawi, the Non-Communicable Diseases and Mental Health Unit of the Ministry of Health was recently successful in expanding access to fluoxetine, a key antidepressant, across the country, based on the leadership of SHARP co-investigator Dr. Udedi. The unit has also recently expanded non-communicable diseases clinics to treat hypertension and diabetes across the country under the leadership of SHARP Malawi PI Dr. Masiye, and a current high priority is the integration and expansion of mental health services within those clinics. The leadership in both Ministries of Health is eager to see the proposed scale-up study and capacity-building activities take place. Given the Mental Health Action Plans in place in both countries and the demonstrated commitment by the Ministries of Health to using research to guide efficient and meaningful expansion of services, the proposed activities will have a large and sustainable impact on mental health care.

The aims and objective of SHARP are significant because they directly address the knowledge and capacity gaps that are currently hampering broader scale-up of mental health services in Malawi and Tanzania. SHARP will build critical bridges between governmental, academic, and non-governmental actors involved in mental health service delivery and planning, provide key evidence to guide expansion of mental health services, and expand capacity to conduct, interpret, and utilize mental health-related implementation science research to address the mental health treatment gap in Malawi, Tanzania, and the broader region.

2.0 HYPOTHESES AND STUDY OBJECTIVES

2.1 Hypotheses

Our primary objective is to compare two different implementation strategies to facilitate ongoing MOH efforts to scale up evidence-based depression treatment within NCD care. Specifically, we hypothesize that:

> **H1.** Compared to providers at clinics receiving the basic implementation package, providers at clinics receiving the enhanced implementation package will deliver depression treatment with greater fidelity.

H2. Compared to patients receiving care at clinics with the basic implementation package, patients receiving care at clinics with the enhanced implementation package will be more likely to achieve depression remission at 6 and 12 months.

H3. Compared to patients receiving care at clinics with the basic implementation package, patients receiving care at clinics with the enhanced implementation package will be more likely to have well controlled hypertension and diabetes at 6 and 12 months.

2.2 Study Objectives

Phase I (formative studies, not covered in this protocol)

Results from Phase I will inform the implementation of the Phase II research study comparing two different implementation strategies.

- We conducted in-depth interviews with providers, clinic directors, and Ministry of Health representatives to adapt the intervention to the NCD care context in Malawi.
- We conducted site visits to assess key contextual and structural characteristics of each clinic including organizational readiness for change, management support, patient panel size and demographics, number and training level of staff, staff-to-patient ratio, typical daily patient volume, hours of operation, and storage facilities for medications.

Phase II (Randomized Trial)

- Compare providers' fidelity of depression treatment between clinics receiving the basic implementation package vs. clinics receiving the enhanced implementation package.
- Compare patients' depression remission at 6 and 12 months between those receiving care at clinics with the basic implementation package vs. those receiving care at clinics with the enhanced implementation package.
- Compare patients' well controlled hypertension and diabetes at 6 and 12 months between those receiving care at clinics with the basic implementation package vs. those receiving care at clinics with the enhanced implementation package.

3.0 METHODOLOGY

We will conduct a clinic-randomized trial (RCT) to determine the best way to integrate evidence-based depression treatment into non-communicable disease (NCD) clinics in Malawi. We will compare implementation of depression treatment using (1) a basic implementation package vs. (2) an enhanced implementation package.

The basic implementation package will involve identifying an internal coordinator who is one of the full-time on-site providers at the clinic. The internal coordinator provides mentoring to peers and support to leadership in implementing the treatment program and aligning it with clinic priorities.

The enhanced implementation package will combine the internal coordinator with an external quality assurance committee. This committee will complete quarterly audits at the facility to evaluate compliance with the depression treatment protocol as well as providing

high-level support in implementing the treatment program through clinical expertise and limited on-site presence.

Clinics will be randomized 1:1 to receive either the basic or the enhanced implementation package. Clinics will then implement depression treatment as part of standard care at their NCD clinics. All patients at each clinic will receive that clinic's standard care.

To evaluate patient health outcomes, we will enroll a cohort of patients from each NCD clinic. (Sample size and inclusion criteria are below.) Participants will complete assessments at baseline and 6 and 12 months. Assessments will measure sociodemographics, depressive severity, self-reported health, and key medical, structural, and psychosocial factors including trauma history, intimate partner violence, other violence in the home, socioeconomic measures, coping, social support, self-efficacy, experiences of stigma related to mental health, medical and psychiatric comorbidity, and risk factors for hypertension and diabetes. Medical appointment attendance data will be abstracted from clinic records.

We will conduct qualitative interviews to provide context for the primary study findings. In year 3, we will interview a subsample of 8 patients (4 in each arm: 2 with depression remission and 2 who remained depressed) to understand their experiences with each intervention. We will ask about satisfaction with and engagement in each intervention component and barriers and facilitators to retention in care. At 3 higher and 3 lower performing clinics (6 clinics total), we will interview clinic directors (District Medical Officers), Clinical Coordinators, NCD providers, Friendship Bench counselors, and SHARP research assistants (n = 6 clinic directors, 6 Clinical Coordinators, 12 NCD providers, 6 Friendship Bench counselors, and 6 SHARP research assistants) to contextualize implementation strategy and intervention acceptability and fidelity. We will also assess implementation climate and intervention-values fit. Finally, we will interview key MOH representatives (n=3) to understand the facilitators and barriers to future scale up. In year 4, we will interview 3 hospital staff and 1 SHARP research assistant from each of the 10 study sites (n=40). These interviews expand upon the findings of the year 3 qualitative interviews and will add further depth to the study's primary findings.

3.1 Study Sites

Study activities will take place at 11 non-communicable disease clinics distributed across the three regions of Malawi. These clinics include:

1) Bwaila Hospital (Lilongwe District)
2) Chilumba Rural Hospital
3) Karonga District Hospital
4) Kasungu District Hospital
5) Machinga District Hospital
6) Mchinji District Hospital
7) Mulanje District Hospital
8) Phalombe Rural Hospital
9) Salima District Hospital
10) Zomba Central Hospital

3.2 Population

Patients at the participating NCD clinics who meet the following eligibility criteria will be invited to participate.

Inclusion criteria

1. Ages 18-65 years (antidepressant treatment considerations differ for those <18 or >65 years, and these age groups are expected to be very rare in the target clinics),
2. Current or new patient receiving care for either hypertension or diabetes from the NCD clinic at a study site listed in Section 3.1, and
3. Elevated depressive symptoms (PHQ-9 score ≥5).

Exclusion criteria

Patients will be excluded if they have a history of bipolar or psychotic disorder, or show emergent threat of self-harm.

3.3 Duration

The Phase II RCT will occur during project years 2-4 (November 2018-October 2021). We will complete training for providers and staff in the two arms. We will initiate the two implementation strategies at all clinics and spend 24 months recruiting participants. Follow-up monitoring will extend an additional 12 months, through year 4.

3.4 Sample Size

A total of 116 patients will be enrolled from each clinic to measure clinical outcomes over time, for a total sample of 1,160 patients recruited over a two-year period.

Sample size and power: Assumptions. Statistical power analyses are based on these assumptions: (1) two-sided statistical significance tests; (2) Type I error $\alpha=0.05$; (3) power $(1-\beta)$ of 80%; (4) intraclass correlation coefficient (ICC) of 0.02 for the mental health outcome. For behavioral interventions, clinic-level ICCs normally range from <<0.01 to 0.04. For effect size, up to 30% of depressive episodes may remit without treatment. We assume that the basic implementation package may improve depression treatment, so we assume the incidence of depression remission to be 40% with the basic package. A difference of 15 percentage points or more in depression remission in the enhanced arm relative to the basic arm would be clinically meaningful and worth detecting. Therefore the study is powered to detect this difference. Based on extremely high retention success in prior studies and the short time frame of the primary outcome (3 months), 90% retention is assumed. Given these assumptions, we will enroll 116 participants per clinic from 10 clinics, or 1,160 participants overall. Fewer clinics would require a prohibitive sample size

We will also complete qualitative interviews with 8 patients, 6 clinic directors, 6 Clinical Coordinators, 12 providers, 6 Friendship Bench counselors, 6 SHARP research assistants, and 3 MOH officials. These interviews will take place in Year 3 of the study. Given standard sample size guidelines for qualitative data collection, this sample size is expected to be sufficient for theme saturation in each group.

We will additionally conduct of 16 cognitive interviews and 200 structured surveys with nurses, clinicians and peer friendship bench counsellors to evaluate providers' perceptions of stigma and acceptance towards individuals with mental health disorders. These

interviews and surveys will take place in Year 3 of the study. The desired sample size for cognitive interviewing, while adequate for the inclusion of variety of staff, reflects the expectation that data saturation will be reached with a relatively small number of participants. The desired sample size for structure interview is reflective of the expectation that approximately 10 participants are needed for every survey item in the measure.

We will also complete Year 4 end point qualitative interviews with a similar group of health workers and SHARP staff interviewed during Year 3. In Year 4, these interviews will take place at each of SHARP's 10 study sites, specifically: 10 clinic directors, 10 Clinical Coordinators, 10 providers, and 10 SHARP research assistants (n=40).

3.5 Data Sources

Data will come from the following sources:

1. Patient participants: The 1,160 patients will complete structured interviews, either in-person or via phone, with trained interviewers at baseline, 3, 6 and 12 months. Research interviewers will also measure blood pressure, blood glucose, height, and weight.
2. Qualitative interviews with patients: Additional information on acceptability of the depression treatment program will be gathered via in-depth interviews with a subset of patients (n=8).
3. Clinical records: Information on depression treatment delivery and fidelity will be abstracted from clinical records.
4. Clinic director, Clinical Coordinator, provider, Friendship Bench counselor, SHARP research assistant, and MOH interviews: Information about implementation strategy and intervention acceptability and fidelity from in-depth interviews with clinic directors (n=6), Clinical Coordinators (n=6), providers (n=12), Friendship Bench counselors (n=6), SHARP research assistants (n=6), and MOH officials (n=3). Cognitive interviews will be conducted with providers (n=8) and Friendship Bench counselors (n=4). Structured surveys will be conducted with providers, friendship bench counselors, and clinic leadership (n=200).
5. End point qualitative interviews at each of SHARP's study sites will focus on additional factors affecting implementation strategy fidelity like organization climate, organizational change, and barriers and facilitators to strategy implementation. Specifically, this information will be gathered from clinic directors (n=10), Clinical Coordinators (n=10), providers (n=10), and SHARP research assistants (n=10).

3.5.1 Record Availability

The site investigator will make all data abstraction documents and records readily available for inspection by the local IRB and the Office for Human Research Protections (OHRP) as requested.

4.0 STATISTICAL ANALYSIS PLAN

Analysis of implementation and effectiveness outcomes will be intent-to-treat comparisons between arms. Comparisons will be made using generalized estimating equation models with a log link and binomial error distribution to compare proportions. The design effect introduced by clinic-level randomization will be addressed using the bias-corrected robust variance estimate for GEE models recommended given the small number of clusters. A secondary, as-treated analysis will restrict the analysis to those who received a minimum

dose of the depression treatment program (e.g., at least three depression care management appointments).

5.0 ETHICAL CONCERNS

5.1 Human Subjects

5.1.1 Institutional Review Board

Prior to implementation of this RCT, all protocol materials will be approved, as appropriate, by local institutional review boards (IRB) / ethics committees (EC) responsible for oversight of the evaluation including the National Health Sciences Research Committee of Malawi (NHSRC) and the Biomedical Institutional Review Board of the University of North Carolina at Chapel Hill. All research will adhere to Malawian and US ethical standards for research in human subjects.

5.1.2 Confidentiality, Risks, and Risk Minimization

Breach of confidentiality: There is always the possibility of a breach of confidentiality when conducting research. Disclosure of medical or other personal information about participants, particularly mental health status may result in negative stigma being associated with the individual and/or family. Our research team is very aware of the need for absolute confidentiality and has extensive experience in dealing with highly sensitive personal medical and family information. While we acknowledge that a breach of confidentiality is possible, we anticipate that the likelihood is very low because of the precautions that will be taken to protect confidentiality. Research data will be coded (with identifiers removed). The linking file that connects the codes to individual identities will be securely stored by the study team. Research data will be stored securely on password-protected machines or servers or in locked cabinets, with access restricted to study staff.

Mental health counseling sessions may be recorded so that supervisors can provide feedback to the counselors about the quality of their counseling. These recordings will be identified with a code number only and will not be shared with anyone outside the research team. If participants do not want their counseling sessions recorded, they can choose not to participate in the study. This information is included in the informed consent form.

Qualitative and cognitive interviews will also be recorded. These recordings will be identified with a code number only and will not be shared with anyone outside the research team. If participants do not want to be recorded, they can choose not to participate in the qualitative component of the study. This information is included in the informed consent form.

Psychological distress from interview questions pertaining to mental health: To expose participants to as little psychological distress as possible and to ensure protection of participant identities and confidentiality, all questions will be asked in a private place at the health facility or a private place of the participant's choosing. Interviews will be conducted by trained interviewers in a language in which the participant is comfortable responding.

Discomfort: Patients may experience discomfort from the collection of a small amount of blood for blood glucose monitoring. This risk will be minimized by using trained clinical staff for blood collection.

Indication of threat of harm to self or others reported in response to interview questions: Patients indicating such threat of harm during interviews will be referred to existing clinical

response pathways as defined by each clinic. For participants with indication of acute risk of self harm, research staff will ensure handoff to a clinical team member.

Protection from COVID-19: As of March 2020 the likelihood of Malawi experiencing initial cases and rapid escalation of COVID-19 is high, therefor we are adding the option of phone interviews in case there is a need to minimize exposure to the novel coronavirus to participants and staff.

5.1.3 Benefits to Participants

Participants will not receive any direct benefit from participating in the study. Whether or not they participate in the research component, all patients at the participating sites will receive that site's standard care.

The study will raise awareness about the diagnosis of depression, a condition that has received little research attention in sub-Saharan Africa. The study will also provide essential information about the potential reciprocal relationships between depression and NCD infection. This information will inform an appropriate intervention for depression in the future.

While this study has some risks associated with participation, we anticipate that few participants will experience negative events as a result of taking part in the study. The risk to individual participants is small and the potential benefit to society is substantial. Therefore, the risk/benefit ratio is favorable.

5.1.4 Costs and Compensation

Patients, providers, directors, and MOH officials invited to participate will received a travel reimbursement equivalent to 10 USD for each research interview in which they participate. Participants will not assume any extra costs as part of this study.

5.1.5 Informed Consent

This protocol and the informed consent documents and any subsequent modifications will be reviewed and approved by the IRB and ethics committees responsible for oversight of the study: the Biomedical Institutional Review Board of the University of North Carolina at Chapel Hill and the National Health Sciences Research Committee of Malawi (NHSRC). All procedures conform to US and Malawian ethical standards regarding research involving human subjects.

Written informed consent will be obtained. Informed consent will clearly explain the purpose of the research, what will be required of the individual, and the risks and benefits of participation. For providers and clinic directors, the informed consent process will emphasize that the provider is free to participate or not; a decision not to participate will have no negative impact on his or her employment, evaluation, or anything else related to the workplace; and the provider is free to end participation at any time. For patients, the informed consent process will emphasize that the patient is free to participate or not; a decision not to participate will have no negative impact on any aspect of his or her clinical care; and the patient is free to end participation at any time. The informed consent process and all documents will be in the provider's or patient's preferred language (likely English for providers and Chichewa or Chitumbuka for patients). Participants will be presented an informed consent form with the above information and contact information for the PI, study personnel, and IRB. Illiterate participants will be asked to put their mark (in lieu of a signature) as a written sign of consent.

The investigators have experience obtaining informed consent for trials in Malawi and thus the informed consent process has been designed to maximize understanding of potential risks.

5.2 Adverse Event Reporting

We do not anticipate any adverse events occurring given the nature of the minimal risks associated with this research. However, in the case that a breach of confidentiality does occur, the study team will immediately inform the IRBs.

- Deaths related to study participation shall be reported by the PI to the NIMH and IRBs immediately and no later than within 5 business days of the PI first learning of the death
- Unexpected Serious Adverse Events related to study participation shall be reported by the PI to the NIMH and IRBs within 10 business days of the study team becoming aware of the SAE
- Unanticipated Problems Involving Risks to Subjects or Others shall be reported by the PI to the NIMH and IRBs within 10 business days of the study team becoming aware of the problem
- Adverse events and SAEs, including deaths, that are deemed expected and/or unrelated to the study shall be submitted in summary form to the NIMH and IRBs with the annual progress report
- Protocol violations shall be submitted in summary form to the NIMH and IRBs with the annual progress report

5.3 Study Discontinuation

The study may be discontinued at any time by the UNC IRB, the NHSRC, the Office for Human Research Protections (OHRP), or other government agencies as part of their duties to ensure that research participants are protected.

6.0 PUBLICATION AND DISSEMINATION OF RESEARCH FINDINGS

Local dissemination of evaluation results is critical to the success of this project. We will conduct a data interpretation workshop during which we will work with stakeholders to present preliminary findings. This workshop will serve as a platform for discussion of involved staff, stakeholders, and ministry officials through which we will frame the implications of the evaluation results. Subsequent dissemination meetings after the data are fully analyzed will emphasize development of a data use plan from which stakeholders, staff, and ministry officials will help to guide the local dissemination agenda and target audiences. Given the scope of this proposal and its intended audience, we have identified some venues that are likely to be a suitable target for dissemination. A venue of particular interest is the Annual Malawi Mental Health Research and Practice Conference sponsored by the Department of Mental Health at the College of Medicine. Where possible we will also submit abstracts to regional and international venues. Publication of the findings is expected in peer reviewed scientific journals. The results of this evaluation will be published and will be integral to understanding the role of depression treatment in NCD clinics in Malawi. However, any presentation, abstract, or manuscript will be made available for review to the NCDs and Mental Health unit at the Ministry of Health and the NHSRC.

In addition to presentation at local and regional conferences, all involved clinics will receive a formal presentation regarding program outcomes and proposed next steps. In coordination with our stakeholders and partners in the Ministry of Health, we will also develop presentations that are geared specifically to local clinics that were not involved in the program, transferring relevant information and “lessons learned” from on-the-ground healthcare workers. Our goal of result dissemination is directly relevant to our capacity building objectives with stakeholders – stakeholders, including clinical staff involved in the implementation of the proposed intervention, will be actively involved in the framing and contextualization of results prior to presentation or publication.

7.0 WORKPLAN

Table 1. Timeline and activities				
	August 2018 – July 2019	**August 2019 – July 2020**	**August 2020 – July 2021**	**Aug-Oct 2021**
Activity				
Creation of protocol and consent forms				
IRB approval				
Training (both arms)				
Intervention: Recruitment				
Intervention: Follow-up				
Fidelity monitoring				
Assessment of satisfaction				
Cost measurement and analysis				

7.1 Project Management

The overall direction of the project will be provided by Jones Masiye, Mina Hosseinipour, and Brian Pence, the PIs for this study, in collaboration with the other co-investigators. Dr. Hosseinipour will provide training and on-site supervision of the evaluation data abstraction and management activities. Vivian Go, co-investigator and qualitative analysis expert, will oversee the analysis of any qualitative data. Jones Masiye will oversee dissemination activities.

8.0 BUDGET

9.0 REFERENCES

1. Murray, C.J., et al., *Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.* Lancet, 2012. **380**(9859): p. 2197-223.
2. Whiteford, H.A., et al., *The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010.* PLoS One, 2015. **10**(2): p. e0116820.
3. Walker, E.R., R.E. McGee, and B.G. Druss, *Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis.* JAMA Psychiatry, 2015. **72**(4): p. 334-41.
4. Charlson, F.J., et al., *Excess mortality from mental, neurological and substance use disorders in the Global Burden of Disease Study 2010.* Epidemiol Psychiatr Sci, 2015. **24**(2): p. 121-40.
5. World Health Organization, *mhGAP : Mental Health Gap Action Programme : scaling up care for mental, neurological and substance use disorders.* 2008, World Health Organization: Geneva, Switzerland.
6. World Health Organization, *Mental Health Atlas 2011*. 2011, World Health Organization: Geneva, Switzerland.
7. World Health Organization, *Mental Health Atlas : 2005*. 2005, Geneva, Switzerland: World Health Organization.
8. Murray, L.K., et al., *Building capacity in mental health interventions in low resource countries: an apprenticeship model for training local providers.* Int J Ment Health Syst, 2011. **5**(1): p. 30.
9. Lancet Global Mental Health, G., et al., *Scale up services for mental disorders: a call for action.* Lancet, 2007. **370**(9594): p. 1241-52.
10. Collins, P.Y., et al., *Grand challenges in global mental health.* Nature, 2011. **475**(7354): p. 27-30.
11. Bolton, P., et al., *Group interpersonal psychotherapy for depression in rural Uganda: a randomized controlled trial.* Jama, 2003. **289**(23): p. 3117-24.
12. Thurman, T.R., R. Kidman, and T.M. Taylor, *Does investment in home visitors lead to better psychological health for HIV-affected families? Results from a quasi-experimental evaluation in South Africa.* AIDS Care, 2014. **26 Suppl 1**: p. S2-10.
13. Kaaya, S.F., et al., *Randomized controlled trial evaluating the effect of an interactive group counseling intervention for HIV-positive women on prenatal depression and disclosure of HIV status.* AIDS Care, 2013. **25**(7): p. 854-62.
14. Rahman, A., et al., *Cognitive behaviour therapy-based intervention by community health workers for mothers with depression and their infants in rural Pakistan: a cluster-randomised controlled trial.* Lancet, 2008. **372**(9642): p. 902-9.
15. Patel, V., et al., *Effectiveness of an intervention led by lay health counsellors for depressive and anxiety disorders in primary care in Goa, India (MANAS): a cluster randomised controlled trial.* Lancet, 2010. **376**(9758): p. 2086-95.
16. Safren, S.A., et al., *A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals.* Health Psychol, 2009. **28**(1): p. 1-10.
17. Chibanda, D., et al., *Problem-solving therapy for depression and common mental disorders in Zimbabwe: piloting a task-shifting primary mental health care intervention in a population with a high prevalence of people living with HIV.* BMC Public Health, 2011. **11**: p. 828.

18. Chibanda, D., et al., *Group problem-solving therapy for postnatal depression among HIV-positive and HIV-negative mothers in Zimbabwe.* J Int Assoc Provid AIDS Care, 2014. **13**(4): p. 335-41.
19. Pence, B.W., et al., *Feasibility, Safety, Acceptability, and Preliminary Efficacy of Measurement-Based Care Depression Treatment for HIV Patients in Bamenda, Cameroon.* AIDS Behav, 2014.
20. Wagner, G.J., et al., *A Structured Protocol Model of Depression Care versus Clinical Acumen: A Cluster Randomized Trial of the Effects on Depression Screening, Diagnostic Evaluation, and Treatment Uptake in Ugandan HIV Clinics.* PLoS One, 2016. **11**(5): p. e0153132.
21. Adams, J.L., et al., *Feasibility of nurse-led antidepressant medication management of depression in an HIV clinic in Tanzania.* Int J Psychiatry Med, 2012. **43**(2): p. 105-17.
22. *World Economic Forum. 2011. The global economic burden of non-communicable diseases. A report by the World Economic Forum and the Harvard School of Public Health.* *http://www3.weforum.org/docs/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf Accessed July 10, 2016.*
23. Bernard, H.R., *Research Methods in Anthropology. 2nd ed.* 1995, Walnut Creek: Altamira Press.