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The sub-Saharan Africa Regional Partnership for Mental Health Capacity Building (SHARP) Scale-up Trial: Study Design and Protocol

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Abstract

Objective: Depression is a leading cause of death and disability worldwide, including in low- and middle-income countries (LMIC). Depression often co-exists with chronic medical conditions, where it is associated with worse clinical outcomes. This confluence has led to calls to integrate mental health treatment with chronic disease care systems in LMIC. This paper describes the protocol and rationale for a trial comparing the effectiveness and cost-effectiveness of two different multifaceted implementation packages to support integration of evidence-based antidepressant management and psychotherapy into chronic non-communicable diseases (NCD) clinics in Malawi.

Methods: Using constrained randomization, the sub-Saharan Africa Regional Partnership for Mental Health Capacity Building (SHARP) will randomly assign 10 NCD clinics 1:1 to a basic implementation strategy of an Internal Coordinator (IC), a provider within the chronic care clinic who champions depression services by providing training, supervision, operations, and reporting, vs. IC plus an External Quality Assurance Committee (EQAC), which additionally provides a quarterly audit of intervention component delivery with feedback to providers and the health management team.

Results: We will compare key implementation outcomes (fidelity to intervention), effectiveness outcomes (patient health), and cost-effectiveness. We will assess clinic characteristics that may influence uptake and fidelity.

Next Steps: This trial will provide key information to guide the Malawi Ministry of Health in scaling up depression management in existing NCD settings. The SHARP trial will make a substantial contribution toward enhancing both mental health treatment and implementation science research capacity in Malawi and the region.

Introduction:

Background

Depression is a leading cause of death and disability worldwide, including in low- and middle-income countries (LMICs) (1-3), with mortality rates twice the general population that are not limited to severe cases or to suicide.(4) Despite these high societal, economic, and quality-of-life costs, those with depressive illness do not receive the same quality of physical health care as the general population.(4) Depression often co-exists with increasingly prevalent chronic medical conditions in LMICs, such as hypertension and diabetes, and is associated with worse clinical outcomes for those comorbid conditions. (5) This confluence has led to calls for integrating mental health treatment with expanding chronic disease care systems in LMICs. (6, 7)

Despite depression's high prevalence and negative consequences, the depression treatment capacity of most sub-Saharan African health systems is severely limited. The median number of mental health professionals/ 100,000 population among Sub-Saharan African nations is less than one-fiftieth of that found in the United States, (8, 9) and over three-quarters of those needing mental health treatment there have no such access to care .(10) This enormous mental health treatment gap demands a focus on task-sharing models that

equip non-specialists, such as primary care providers or community workers, to address common mental health problems. (10)

A strong evidence base exists for both psychosocial counseling and antidepressant treatment and for their effectiveness when delivered by general practitioners and community workers in LMICs in research trials. For example, with psychosocial counseling, the Friendship Bench – a culturally adapted, manualized intervention-- utilizes lay health-workers or community members to deliver structured problem solving therapy and effectively manage common mental disorders in primary healthcare settings (11, 12)

Similarly, Algorithm-Based Care for Depression (ABCD), a task-sharing depression treatment model that utilizes antidepressants, has a strong evidence base and high potential for scale-up and impact in low-resource settings. ABCD enables non-psychiatric staff to manage depression effectively in clinical settings through prescribing antidepressants using algorithms that guide dose titration depending on systematically assessed depression symptom severity and antidepressant side effects. The availability and demonstrated efficacy of low-cost antidepressants in low-resource settings makes an approach like ABCD a highly promising strategy for efficient integration of depression treatment into existing clinical care systems. We have conducted research for over 10 years on the effectiveness of ABCD in primary care(13, 14) and in HIV care, (15) and more recently have demonstrated the safety, feasibility, and acceptability of ABCD in Africa. (16) Other research has demonstrated the effectiveness of integration of ABCD into HIV care in Uganda(17) and its integration into chronic disease care in high-income countries.(18, 19)

Despite this strong evidence base, a key knowledge gap impeding the scale-up of such services in low-resource settings is the level of resource investment required to achieve acceptable fidelity and effectiveness in real-world practice. Implementation science research to identify optimal implementation strategies is critical to advance scale-up efforts. The Sub-Saharan Africa Regional Partnership (SHARP) for Mental Health Capacity Building aims to address this gap. Our objective is to expand mental health treatment in the region through high-quality implementation science research; development of research and implementation capacity among governmental, academic, and non-governmental partners; and enhancement of dialogue between those partners.

One part of SHARP is the Scale-Up Study, whose goal is to compare the implementation and effectiveness outcomes of two implementation packages to support the integration of depression screening and treatment into standard care in non-communicable disease (NCD) clinics in Malawi. The environment is ripe for scaling up. The Malawi Ministry of Health has identified expansion of depression treatment in its chronic diseases clinics as a high current priority.(20, 21) However, in a setting with limited resources and few mental health professionals, and where the country's first psychiatrist in a generation completed medical training two years ago, the most efficient way to implement such a treatment model is unclear. A key knowledge gap impeding the scale-up of Friendship Bench and ABCD is the level of resource investment required to achieve acceptable fidelity and effectiveness in real-world clinics.

Accordingly, we will conduct a clinic-randomized controlled trial (RCT) to determine the best way to integrate evidence-based depression treatment into NCD clinics in Malawi. We will compare implementation of depression treatment using (1) a basic implementation package vs. (2) an enhanced implementation package. These two implementation packages were informed by prior implementation science strategies involving external and internal facilitation to implement evidence-based mental health treatment programs in clinical care(22-24) and were adapted through consultation with the Malawi Ministry of Health to be most relevant to the clinical context in Malawi. The basic implementation package will involve identifying an internal coordinator who is one of the full-time on-site providers at the clinic, reflecting an approach often used by the Malawian public health system. 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, a scalable and feasible package based on prior work in Malawi with HIV patients. 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.

Key challenges informed our selection of study design elements; we list these in Table 1.

Hypotheses:

Our hypotheses are as follows:

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.

This paper will describe in detail a protocol for a scale-up study that compares the implementation effectiveness and cost-effectiveness of two different implementation packages in achieving integration of depression management into NCD clinics in Malawi: a basic implementation package (Internal Coordinator only, or IC) vs. an Internal Coordinator plus External Quality Assurance (IC + EQAC).

Methods

Overall study design

Our goal is to compare the success of two approaches to integration of depression screening and treatment into 10 NCD clinics in Malawi by implementing a clinical trial with 1:1

constrained randomization by clinic, such that 5 clinics receive a basic implementation package (IC) and 5 clinics receive an enhanced implementation package (IC + EQAC). This constrained design will ensure balance of group-level prognostic factors across the comparison arms, allowing us to avoid imbalance in region, number of providers, number of patients per month, quality of engagement in NCD service delivery, quality of engagement in initial study site visit, and quality of recordkeeping. We will compare outcomes for those receiving care at clinics with basic vs. enhanced implementation packages, as measured by (1) providers' fidelity of depression treatment; (2) patients' depression remission at 3, 6, and 12 months; and (3) patients' well controlled hypertension and diabetes at 3, 6 and 12 months. We will also compare the cost-effectiveness of the two packages in achieving depression remission and NCD control.

Settings and site selection

Following a site assessment of key contextual and structural characteristics of each clinic including organizational readiness for change, management support, patient panel size and demographics, and storage facilities for medications among potential clinics in Northern, Central and Southern Malawi, we selected 10 hospital-based NCD clinics representing the three regions of Malawi: Northern (2), Central (4), and Southern (4). The trial focuses on secondary level district hospitals, the setting for the recent establishment of NCD clinics nationwide. We will enroll 116 patients from each of 10, clinics throughout Malawi (total sample = 1160).

Target population/selection criteria

We will enroll patients meeting the following criteria in the research outcome interview component of the trial:

Inclusion criteria—Eligible participants will be between 18-65 years, be a current or new patient receiving care for either hypertension or diabetes or both from a participating NCD clinic, and have elevated depressive symptoms (PHQ-9 score ≥5). Patients will be excluded if they have a history of bipolar or psychotic disorder, or show emergent threat of self-harm.

The Research Assistant will evaluate all NCD patients for potential eligibility. All patients, regardless of whether they are enrolled in the research outcome interviews component, will contribute data to the primary fidelity outcomes since those data come from de-identified aggregation of clinical records on all patients.

Study procedures and design of implementation strategy

Depression screening and treatment program provided at both sites: In both arms, a depression screening and treatment program is being integrated into routine NCD care. In half the clinics, this integration is being supported by the IC model; in the other half, the integration is being supported by the IC model in combination with the EQAC model. The depression screening and treatment program at all sites consists of the following components:

Training: Given empirical support for a "train the trainers" model,(25) we trained three clinicians from each site as ICs, a role that includes training their colleagues. These trainers then trained all NCD care providers (clinical officers and nurses) at their facility in administration and scoring of the Patient Health questionnaire 9 (PHQ-9) (a tool that screens for and monitors severity of depressive symptoms(26) and which we have validated in Malawi,(27)), response to suicidal thoughts, antidepressant management, and follow-up treatment decisions using the ABCD. NCD care providers at participating sites include nurses who handle vital signs monitoring, weight assessment, and health talks while one or more clinical officers handle patient consultation and have prescribing authority. Both groups have received a brief orientation to mental health issues, primarily serious mental illness, as part of their nursing or medical training but have generally received no specialized mental health training.

In addition, 5-6 peer NCD patients at each site have been trained in a problem-solving therapy-focused counseling intervention packaged as the "Friendship Bench" by Chibanda and colleagues in Zimbabwe(11), an intervention designed for low resource settings that we have previously adapted for use in Malawi.(28) Dr. Chibanda's team trained a group of Malawian trainers who have now trained these peer patients as counselors. The top performing 1-2 counselors from each site during training were identified as local peer supervisors.

Clinical care: All patients presenting for care at participating NCD clinics will be given a PHQ-9 at registration along with their NCD medical chart ("mastercard"). Patients will take the PHQ-9 into the consultation room with the health care worker (either a clinician or nurse), who will complete and score the PHQ-9. Patients with a PHQ-9 score of 0-4 are recommended for no mental health treatment. Patients with a positive screen for the core depression symptoms of low mood or anhedonia (i.e a score of >0 on the first two items of the PHQ 9, also known as a PHQ-2 score) and with a score of 5-9 are recommended for the Friendship Bench intervention while patients with a score of ≥10 are recommended for antidepressant initiation. The actual treatment plan is at the clinician's discretion (patients can both be initiated on antidepressants and referred for counseling).

The treatment plan is recorded on a "mental health mastercard" medical chart which is then filed with the PHQ-9 and the NCD mastercard to be retrieved at the next visit, when the treatment plan is re-assessed and adjusted if needed.

Basic implementation package (IC) (5 sites) The IC package consists of identifying a Clinical Coordinator (internal champion) at each site. This Coordinator is an existing on-site NCD clinician and facility NCD coordinator who is responsible for ensuring the smooth integration of the treatment program. One Coordinator and two Alternates from each site were identified and trained as the clinician trainers identified above under the depression treatment program. These coordinators have the following responsibilities: train all health care workers at the health facility in the depression treatment program (both initial training and as-needed additional training based on new arrivals); maintain a log of current health care workers and training status; ensure accurate recordkeeping to track number screened, number with depression, number receiving treatment, and to permit follow-up of patients

previously started on treatment; lead depression care supervision monthly; supervise Friendship Bench supervisor monthly; ensure NCD clinic coverage; ensure stable antidepressant medication supply; raise implementation challenges with facility leadership; and compile monthly reports to submit to MOH.

This basic implementation strategy, with its identification of a local Coordinator with these responsibilities, reflects an approach often used in the Malawian public health system by which new programs are rolled out.

Enhanced implementation package (IC+EQAC) (5 sites) The IC+EQAC package includes all the elements of the IC package, with the addition of an EQAC that visits each facility on a quarterly basis to audit paperwork, review service delivery, and provide feedback and recommendations to the Coordinator, the facility leadership, and the MOH. Each external quality assurance committee will consist of 2-3 Ministry of Health officials, one Friendship Bench master trainer, and 1-2 additional staff members for administrative and logistical support. The site visit will last 2 days and will include: an initial meeting with the Coordinator and facility leadership to discuss successes and challenges; review of recordkeeping; training, supervision, and duty logs of clinicians and counselors; service delivery indicators; completeness of medical charts; and the appropriateness of treatment decisions as recorded on the medical charts; direct observation of clinic flow and the delivery of care, including depression screening and treatment plan discussion; a meeting with all Friendship Bench counselors that will include listening to at least one recorded counseling session and a discussion of successes and challenges; a debrief meeting with the Coordinator and facility leadership to discuss findings and recommendations; and a written report submitted to the facility's Director for Health and Social Welfare and the NCDs and Mental Health Unit of the Ministry of Health.

Measures

Our key measures (Tables 2 and 3) allow us to address our hypotheses regarding fidelity, depression remission, and control of hypertension and/or diabetes. As fidelity measures for ABCD, we will monitor via periodic chart review (1) percent of new patients completing the PHQ-2 (target ≥80%); (2) percent of PHQ-2-positive screens with a PHQ-9 (target ≥90%); (3) percent of PHQ-9-positive screens with assessment for depression (target ≥90%); (4) percent of patients with confirmed depression and enrolled in the study who start antidepressant treatment or Friendship Bench counseling (target ≥80%); (5) percent of follow-up encounters at which the clinical decision follows the algorithm (target ≥80%); (6) percent of algorithm divergences for which the reason for divergence is documented (target ≥90%); (7) number of completed supervision sessions.

Friendship Bench fidelity will be assessed through the domains of dose delivered, dose received, and adherence. We will measure dose delivered by process data showing the number of sessions made available to participants by their counselors. Similarly, we will measure dose received by the number of sessions participants actually attend. Adherence will be measured using the Friendship Bench fidelity checklist, which rates a counselor's adherence to core Friendship Bench counseling components while listening to an audio recording of a counselor's session. All sessions for which the client consents to recording

will be recorded, and a random 10% per counselor will be reviewed and rated for fidelity during the course of the trial.

Depression remission will be defined as a PHQ-9 score <5, a score widely used and validated.(29) Depression response, a common secondary indicator of treatment effectiveness, will be defined as a ≥50% decrease in PHQ-9 score from baseline.(29) Depression-free days is a cumulative measure of burden of depression over time calculated by translating depressive severity measures at the beginning and end of each time interval into a proportion of days spent depressed according to a previously published algorithm.(30-32)

Hypertension and diabetes outcomes will be measured at 0, 6, and 12 months by properly trained study data collectors recording the data on a tablet and submitted electronically for data storage and later analysis.

Analysis strategy

Analysis of primary and secondary outcomes will be intent-to-treat comparisons between arms (Table 2). Comparisons will be made using generalized linear regression models with a log link and binomial error distribution to compare individual-level or appointment-level probabilities. Our outcomes will be measured at baseline, 3 months, 6 months, and 12 months.

Primary outcomes: Implementation Outcomes (fidelity to intervention): We have three primary outcomes (Table 3). Our first outcome is the probability that each patient eligible for depression screening completes depression screening. We define completion of depression screening as completing the PHQ-2, and, if the PHQ-2 score is >0, also completing the PHQ-9. Our second outcome is the probability that each patient eligible for depression treatment actually starts treatment within 30 days of identification. We define eligibility for depression treatment as a PHQ-9 total score of 5 or above and a final determination from the treating clinician that the patient is appropriate for depression treatment. Our third primary outcome is the probability at each follow-up appointment in the first three months of depression treatment that the clinical treatment decision follows the depression treatment guidelines.

For these three primary fidelity outcomes, where depression screening and treatment actions are clustered within provider and clinic, the analysis will use a robust variance estimate clustered by provider and clinic.

Secondary outcomes: Effectiveness Outcomes (patient health): We have two secondary outcomes. The first is the probability that each patient achieves depression remission at 3 months. The second outcome is the probability that each NCD patient's NCD is well controlled at 3 months.

For the secondary patient-level effectiveness outcomes, the design effect introduced by clinic-level randomization will be addressed using a robust variance estimate clustered by clinic.

Supplemental analyses: Planned supplemental analyses will (a) consider hypertension and diabetes patients separately and (b) consider patients with uncontrolled vs. well-controlled baseline NCD separately. Subgroup analyses will be conducted with regression models fit with and without an interaction term(s) between intervention arm and the stratifying variable.

Sample size calculations are based on two-tailed statistical significance tests, a Type I error probability (α) of 0.05, and desired power ($1-\beta$) of 0.80. The fidelity outcomes are event-specific probabilities. Events (depression screening, treatment initiation, follow-up action) are nested within providers who are nested within clinics, the unit of randomization. Assuming a moderately high within-provider correlation (ICC=0.5) and a lower across-provider-within-clinic correlation (ICC=0.1), and given the large number of providers per clinic, the combination of provider-level and clinic-level design effects will yield an effective sample size of n=92 for the primary outcomes. This effective sample size will confer 80% power to detect absolute improvements (risk differences) of between 18-27 percentage points in the fidelity outcomes, depending on the outcome frequency (risk) in the comparison arm.

Patient-level outcomes (e.g., depression remission) are patient-specific probabilities that are nested within clinics but not within providers (patients frequently do not see the same provider across visits). Assuming low intra-cluster correlation in this patient outcome (ICC=0.02), as seen in similar studies(33-36), our sample of 1,160 patients across 10 clinics is equivalent, after accounting for the clinic-level design effect, to an effective sample size of n=352. Assuming 90% retention at 3 months (in line with very high retention rates achieved in many previous large multi-site trials by UNC Project-Malawi)(37, 38), this sample confers 80% power to detect an absolute improvement (risk difference) of between 11-15 percentage points in the patient-level outcomes, depending on the outcome frequency (risk) in the comparison arm.

The need for adjusted analyses will be evaluated by comparing the characteristics of participants enrolled in the two arms. Although constrained randomization is expected to yield clinics with approximately balanced characteristics between the two arms, clinics in one arm may have more effective screening and therefore identify different types of patients with depression; thus patient characteristics may not be balanced between arms. We will evaluate balance between arms in demographic (age, sex), NCD (hypertension vs. diabetes, controlled vs. uncontrolled) and mental health characteristics (depressive symptom severity, anxiety symptoms, PTSD symptoms, alcohol use). We will assess potential confounding by comparing the unadjusted primary analysis to an analysis controlling for potential confounders. Both unadjusted and adjusted results will be presented.

Cost-effectiveness analyses: We will estimate the average and total costs of an IC vs. IC plus EQAC, and the incremental cost per additional case of remitted depression at 3 months of IC + EQAC relative to IC alone. These health and economic impact data will inform stakeholders about sustainability, value-for-money, and opportunities for efficiency gains. We will measure non-research costs of the intervention using globally accepted best practices. Costs will be captured throughout the trial. We will measure total costs for

delivery of each approach deterministically.(39) We will use probabilistic sensitivity analysis to account for stochastic uncertainty and use league tables to display results. (40)

Trial status/timeline

We launched our trial in May 2019. We are planning for 24 months of recruitment (through spring 2021), with 12 months of follow-up (through spring 2022).

Results

The trial will generate critical knowledge to inform policymakers, administrators, and clinicians on which strategies may be more effective at implementing and sustaining standard evidence-based depression screening and management approaches in busy, real world NCD clinics with limited resources. With fidelity, depression remission, and good control of hypertension and/or diabetes as the main outcomes, along with an assessment of cost-effectiveness, stakeholders will be able to use evidence to inform strategy selection for implementing depression management packages. Various scenarios exist. For example, should each strategy implement and sustain the depression screening and management package with fidelity, and with little difference in clinical outcomes, stakeholders would likely opt for the basic package. Should both be implemented with fidelity, but the enhanced version produces better clinical outcomes, stakeholders could discuss whether the increased benefit is worth the increased cost. In any case, meaningful information will be created to help stakeholders make the best informed decision they can.

Other key results will evolve from the project's capacity-building efforts. As part of the overall SHARP project, which involves trainees in both Malawi and Tanzania, we will train young researchers to design, implement, and analyze studies researching how to implement evidence-based mental health interventions in low resource settings. Small grant opportunities will allow them to propose their own pilot projects as well as participate in the current study. Further, we are partnering with another global mental health hub, Scaling up Partnerships in Research to Implement and Disseminate Sustainable and Scalable Evidence Based Practices in Mozambique (PRIDE)(41), to jointly mentor other young investigators from their hub for related projects occurring within Malawi and Tanzania.

Next Steps

The Malawi and Tanzania MOHs strongly support the design of the proposed scale-up study because of the perceived high value and relevance of the proposed depression treatment approach to the mental health agendas in both countries and the importance of identifying the most effective and cost-effective strategy for integrating depression screening and management into NCD care. Integration of antidepressants and psychosocial counseling into existing NCD care is viewed as an important component of an overall mental health response because the high prevalence of depression and the limitations in human resources necessitate an efficient, low-cost approach. The Malawi MOH supports our design and views it as scalable and sustainable within the Malawi health care system. The study is seen as a logical next step of ongoing MOH efforts to expand access to depression management and as an important complement to other efforts to expand counseling capacity. Should these

findings show benefit in such a resource-limited setting as Malawi, we believe these findings will be generalizable to other countries in sub-Saharan Africa.

Upon its completion, this Scale-Up Study will provide key information to guide the Malawi MOH in furthering its intention of scaling up ABCD in existing chronic disease care settings. We will use study results as the basis for drafting a detailed revision to the national Mental Health Action Plans in Malawi and Tanzania, in collaboration with the MOHs and other SHARP partners. Further, the execution of the study will provide SHARP mentees the opportunity to gain invaluable experience in mental health-related implementation science research by participating in the design and conduct of specific aspects of the study under the mentorship of more senior investigators. Overall, this component of the SHARP U19 application will make a substantial contribution toward the SHARP goal of enhancing both mental health treatment and implementation science research capacity in Malawi and Tanzania.

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References

1. Lopez AD, Mathers CD, Ezzati M, et al.: Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 367:1747–57, 2006 [PubMed: 16731270]
2. Kessler RC, Aguilar-Gaxiola S, Alonso J, et al.: The global burden of mental disorders: an update from the WHO World Mental Health (WMH) surveys. Epidemiol Psichiatr Soc 18:23–33, 2009 [PubMed: 19378696]
3. Demyttenaere K, Bruffaerts R, Posada-Villa J, et al.: Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. JAMA 291:2581–90, 2004 [PubMed: 15173149]
4. World Health Organization: Meeting Report on Excess Mortality in Persons with Severe Mental Disorders. Geneva, Switzerland: WHO, 2015
5. Moussavi S, Chatterji S, Verdes E, et al.: Depression, chronic diseases, and decrements in health: results from the World Health Surveys. Lancet 370:851–8, 2007 [PubMed: 17826170]
6. Prince M, Patel V, Saxena S, et al.: No health without mental health. Lancet 370:859–77, 2007 [PubMed: 17804063]
7. Raviola G, Becker AE, Farmer P: A global scope for global health--including mental health. Lancet 378:1613–5, 2011 [PubMed: 22008421]
8. World Health Organization: Mental Health Atlas 2011. Geneva, Switzerland: World Health Organization, 2011
9. World Health Organization: Mental Health Atlas 2005. Geneva, Switzerland: World Health Organization, 2005
10. World Health Organization: mhGAP : Mental Health Gap Action Programme : scaling up care for mental, neurological and substance use disorders. Geneva, Switzerland, 2008
11. Chibanda D, Weiss HA, Verhey R, et al.: Effect of a Primary Care-Based Psychological Intervention on Symptoms of Common Mental Disorders in Zimbabwe: A Randomized Clinical Trial. JAMA 316:2618–26, 2016 [PubMed: 28027368]
12. Chibanda D, Mesu P, Kajawu L, 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 [Internet] 11, 2011

13. Gaynes BN, Rush AJ, Trivedi MH, et al.: Primary versus specialty care outcomes for depressed outpatients managed with measurement-based care: results from STAR*D. J Gen Intern Med 23:551–60, 2008 [PubMed: 18247097]
14. Landis SE, Gaynes BN, Morrissey JP, et al.: Generalist care managers for the treatment of depressed medicaid patients in North Carolina: a pilot study. BMC family practice 8:7, 2007 [PubMed: 17338822]
15. Adams JL, Gaynes BN, McGuinness T, et al.: Treating depression within the HIV "medical home": a guided algorithm for antidepressant management by HIV clinicians. AIDS Patient Care STDS 26:647–54, 2012 [PubMed: 23134559]
16. Pence BW, Gaynes BN, Atashili J, et al.: Feasibility, Safety, Acceptability, and Preliminary Efficacy of Measurement-Based Care Depression Treatment for HIV Patients in Bamenda, Cameroon. AIDS and behavior, 2014
17. Wagner GJ, Ngo V, Goutam P, 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 11:e0153132, 2016 [PubMed: 27167852]
18. Katon W, Guico-Pabia CJ: Improving quality of depression care using organized systems of care: a review of the literature. Prim Care Companion CNS Disord 13, 2011
19. Katon WJ, Lin EH, Von Korff M, et al.: Collaborative care for patients with depression and chronic illnesses. N Engl J Med 363:2611–20, 2010 [PubMed: 21190455]
20. Government of Malawi Ministry of Health: Malawi Health Sector Strategic Plan II 2017–2022: towards Universal Health Coverage. Lilongwe, Malawi, 2017
21. Government of Malawi Ministry of Health: National Mental Health Policy (Draft):. Lilongwe, Malawi, 2019
22. Kilbourne AM, Abraham KM, Goodrich DE, et al.: Cluster randomized adaptive implementation trial comparing a standard versus enhanced implementation intervention to improve uptake of an effective re-engagement program for patients with serious mental illness. Implement Sci 8:136, 2013 [PubMed: 24252648]
23. Kilbourne AM, Goodrich DE, Lai Z, et al.: Reengaging veterans with serious mental illness into care: preliminary results from a national randomized trial. Psychiatr Serv 66:90–3, 2015 [PubMed: 25554233]
24. Kilbourne AM, Goodrich DE, Nord KM, et al.: Long-Term Clinical Outcomes from a Randomized Controlled Trial of Two Implementation Strategies to Promote Collaborative Care Attendance in Community Practices. Adm Policy Ment Health 42:642–53, 2015 [PubMed: 25315181]
25. Martino S, Ball SA, Nich C, et al.: Teaching community program clinicians motivational interviewing using expert and train-the-trainer strategies. Addiction 106:428–41, 2011 [PubMed: 20925684]
26. Spitzer RL, Kroenke K, Williams JB: Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. Jama 282:1737–44, 1999 [PubMed: 10568646]
27. Udedi M, Muula AS, Stewart RC, et al.: The validity of the patient health Questionnaire-9 to screen for depression in patients with type-2 diabetes mellitus in non-communicable diseases clinics in Malawi. BMC psychiatry 19:81, 2019 [PubMed: 30813922]
28. Stockton MA, Udedi M, Kulisewa K, et al.: The impact of an integrated depression and HIV treatment program on mental health and HIV care outcomes among people newly initiating antiretroviral therapy in Malawi. PloS one 15:e0231872, 2020 [PubMed: 32374724]
29. Lowe B, Unutzer J, Callahan CM, et al.: Monitoring depression treatment outcomes with the patient health questionnaire-9. Medical care 42:1194–201, 2004 [PubMed: 15550799]
30. Pyne JM, Tripathi S, Williams DK, et al.: Depression-free day to utility-weighted score: is it valid? Medical care 45:357–62, 2007 [PubMed: 17496720]
31. Lave JR, Frank RG, Schulberg HC, et al.: Cost-effectiveness of treatments for major depression in primary care practice. Arch Gen Psychiatry 55:645–51, 1998 [PubMed: 9672056]
32. Pence BW, Gaynes BN, Adams JL, et al.: The effect of antidepressant treatment on HIV and depression outcomes: results from a randomized trial. AIDS (London, England) 29:1975–86, 2015

33. Pals SL, Beaty BL, Posner SF, et al.: Estimates of Intraclass Correlation for Variables Related to Behavioral HIV/STD Prevention in a Predominantly African American and Hispanic Sample of Young Women. Health Education & Behavior 36:182–94, 2009 [PubMed: 19188372]

34. Parker DR, Evangelou E, Eaton CB: Intraclass correlation coefficients for cluster randomized trials in primary care: The Cholesterol Education and Research Trial (CEART). Controlled Clinical Trials 26:260–7, 2005

35. Smeeth L, Ng ES: Intraclass correlation coefficients for cluster randomized trials in primary care: data from the MRC Trial of the Assessment and Management of Older People in the Community. Control Clin Trials 23:409–21, 2002 [PubMed: 12161083]

36. Eldridge SM, Ashby D, Feder GS, et al.: Lessons for cluster randomized trials in the twenty-first century: a systematic review of trials in primary care. Clin Trials 1:80–90, 2004 [PubMed: 16281464]

37. Cohen MS, Chen YQ, McCauley M, et al.: Antiretroviral Therapy for the Prevention of HIV-1 Transmission. New England Journal of Medicine 375:830–9, 2016

38. Campbell TB, Smeaton LM, Kumarasamy N, et al.: Efficacy and Safety of Three Antiretroviral Regimens for Initial Treatment of HIV-1: A Randomized Clinical Trial in Diverse Multinational Settings. PLoS medicine 9:e1001290, 2012 [PubMed: 22936892]

39. Drummond MF, Sculpher MJ, Torrance GW, et al.: Methods for the Economic Evaluation of Health Care Programmes. Oxford: Oxford University Press, 2005

40. Tan-Torres Edejer T, Baltussen R, Adam T, et al.: Making choices in health: WHO guide to cost-effectiveness analysis. Geneva, Switzerland: WHO, 2003

41. Wainberg M: Scaling up PRIDE Mozambique - Scaling up Partnerships in Research to Implement and Disseminate Sustainable and Scalable Evidence Based Practices in Mozambique, 2017

Highlights

- Given the substantial burden of depression in low-and middle-income countries (LMIC), and the limited mental health resources, effective strategies integrating mental health treatment into chronic disease care systems are crucial.
- The SHARP clinical trial project, based in Malawi, will compare a basic implementation strategy of an Internal Coordinator (IC) vs. IC plus an External Quality Assurance committee, which additionally provides a quarterly audit of intervention component delivery with feedback to providers and the health management team.
- Implementation and cost-effectiveness outcomes will make a substantial contribution toward enhancing both mental health treatment and implementation science research capacity in Malawi and the region.

Table 1:

Key Challenges, Design Solutions, and Advantages

Design Solutions	Advantages (conferred by that design solution)
Challenge: Engagement of policy makers	
Inclusion of a policy maker as a principal investigator (in Malawi) and as co-investigators (Malawi, Tanzania)	Immediate feedback and input to make study questions and outcomes relevant to policy decision making
Challenge: implementation of Friendship Bench counseling	
Weighed options of lay health workers, peers, other options. Opted for to train peer patients for Friendship Bench.	Involvement of peers more sustainable and consistent with original Friendship Bench model
Trained trainers within Malawi	Have built a cadre of trainers who can continue to train counsellors throughout the country after completion of study
Challenge: Ensuring consistent medication supply	
Tasking Internal Coordinator; monthly reporting; intervention with Central Medical Stores by policy makers; intervention with DHMTs to prioritize stocking antidepressants; Friendship Bench as alternative	More consistent supply of amitriptyline and fluoxetine
Challenge: Lack of trained personnel and increased clinical workload	
Tasking the Internal Coordinator with training other clinicians, nurses, data clerks, and other relevant clinical staff at their NCD clinics (strategy of “training everyone”)	Ensures coverage for screening and treatment of depression across clinicians, which can improve sustainability; builds training capacity of Internal Coordinator; builds clinical capacity of other clinicians
Challenge: Ensure policy relevance of findings	
Ministry of Health official a principal investigator; engage multiple stakeholders	Findings more likely to be actionable for Ministry of Health and relevant to policy goals
Challenge: Ensure findings are generalizable to all of Malawi	
Selected non-communicable diseases clinics housed in 10 hospitals distributed across the country in each of the three regions in Malawi (Northern, Central, and Southern regions).	Provides information relevant to each region
Constrained 1:1 Randomization	Avoids imbalance in region, number of providers, number of patients per month, quality of engagement in NCD service delivery, quality of engagement in initial study site visit, and quality of recordkeeping.
Challenge: Create allocation concealment mechanism	
Randomization will be masked until 3 months after trial launch.	Avoids initial startup support being affected by knowledge of study arm. At 3 months, the first external quality assurance committee visits will occur, revealing allocation
Challenge: Feasibility	
Use of a mental health mastercard that mirrors their already used NCD medical chart mastercard (each of which will be available for each clinic visit).	Familiarity of card will increase likelihood of implementation
The *basic Implementation strategy*, with its identification of a local Coordinator with these responsibilities, was designed to reflect an approach often used in the Malawian public health system by which new programs are rolled out.	Familiarity of approach will increase likelihood of implementation.

Design Solutions	Advantages (conferred by that design solution)
The *enhanced Implementation package* includes all the elements of the basic implementation package, with the addition of an external quality assurance committee based on a successful approach used in Malawi for HIV care dissemination that visits each facility on a quarterly basis to audit paperwork, review service delivery, and provide feedback and recommendations to the Coordinator, the facility leadership, and the MOH.	Basing package on a previously successful implementation strategy in Malawi will increase likelihood of implementation.
Challenge: Blinding in clinic-level interventions precludes personnel from being masked to allocation*	
To assess fidelity, we will use de-identified aggregation of clinical records on all patients	Data analysis will be conducted in blinded fashion.
To assess remission, we will use PHQ-9 self-report measures by patients, who will not be told the allocation by research staff and are unlikely to be aware of the allocation.	Data analysis will be conducted in blinded fashion.
To assess hypertension and diabetes outcomes, we will use objective measures unaffected by blinding	Data analysis will be conducted in blinded fashion.

* In a clinic-level intervention, most personnel may not be masked to allocation. The Clinical Coordinator, Friendship Bench counselors, and facility leadership cannot be masked to allocation once the external quality assurance committee site visits have started, because all of these individuals will meet with and/or receive reports from the external committee. Patients cannot be explicitly blinded to allocation. Research Assistants (the research outcome assessors) are each permanently based in one site and are present in clinic daily; it is likely not feasible to coordinate or conduct the external committee site visits without the local research assistant's awareness.

DHMT = District Health Management Team; MOH = Ministry of Health; NCD = Non-communicable disease

Table 2:

Table of Measures

Construct	Measure	Source	Time point
Screening			
Depression screening coverage	Completion of screening with PHQ-2 and PHQ-9	Clinical logs	Ongoing throughout study period
Treatment initiation			
Initiation of counseling or antidepressants	Initiation of counseling or antidepressants within 30 days of depression identification	Clinical logs	Ongoing throughout study period
Fidelity			
Friendship Bench counseling fidelity	Number of sessions attended. Counselor fidelity to problem-solving therapy core components.	Clinical logs Review of audio-recorded sessions	Ongoing throughout study period
Antidepressant dosing algorithm fidelity	Initial antidepressant dose Re-assessment at follow-up appointments. Treatment adjustment per algorithm at follow-up	Clinical logs	Ongoing throughout study period
Patient outcomes			
Depression remission	PHQ-9	Research interview	3, 6, 12 months
Hypertension control	Blood pressure	Research interview	3, 6, 12 months
Diabetes control	Fasting blood glucose	Clinical records	6 months

Table 3:

Study Outcomes

	Definition	Type
Primary Outcome		
Fidelity in depression screening	Probability that each patient eligible for depression screening completes depression screening.	Binary
Fidelity in depression treatment initiation	Probability that each patient eligible for depression treatment actually starts treatment within 30 days of identification. *	Binary
Fidelity in follow-up depression treatment monitoring and adjustment	Probability at each follow-up appointment in the first three months of depression treatment that the clinical treatment decision follows the depression treatment guidelines.	Binary
Secondary Outcomes		
Probability that each patient achieves depression remission at 3 months.	Depression remission is defined as a Patient Health Questionnaire-9 score <5 at 3 months	Binary
Probability that each NCD patient's NCD is well controlled at 3 months. **	Well-controlled NCD will be defined for hypertension patients as systolic blood pressure <140 mmHg AND diastolic blood pressure <90 mmHg, and for diabetes patients as fasting blood glucose <130 mg/dl, following the Malawi Clinical Guidelines for the Management of NCDs	Binary

* Eligibility for depression treatment is defined as having a PHQ-9 total score of 5 or above and having a final determination from the treating clinician that the patient is appropriate for depression treatment.

** Hypertension is measured by research assistants at each study visit while fasting blood glucose is measured as part of routine clinical care and will be abstracted.