College of Medicine

IMPACT OF DEPRESSION AND OTHER COMMON MENTAL DISORDERS ON ANTIRETROVIRAL TREATMENT OUTCOMES AMONG MALAWIAN WOMEN IN THE PEPFAR-PROMOTE STUDY

BY

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DECLARATION

I, Dingase Elizabeth Dula, hereby declare that this thesis is my original work and has not been presented for any other awards at the University of Malawi or any other University.

Signature: 

Date: 23 March 2022

CERTIFICATE OF APPROVAL

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DEDICATION

This dissertation is dedicated first and foremost to God my Father, and to my amazing family that is a true definition of resilience in hard times and hope for a better future. My friends Fumbani, Mels, Patrick that pushed me beyond my limits and literally pulled me up, Professor Johnstone Kumwenda for always having faith in his students. Everything does have a beginning and an end!

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ABSTRACT

Common mental disorders (CMDs) are highly prevalent among people living with HIV(PLWHIV). If left untreated, they negatively affect HIV treatment outcomes. Low cost, low intensity interventions for CMDs such as Friendship Bench problem solving therapy (FB-PST) are being adopted in various clinical care settings. There is need to test effectiveness of these interventions in randomized controlled trials. The objectives of this study was to determine the prevalence of Common Mental Disorders (CMDs) among Women living with HIV (WLHIV) on lifelong antiretroviral therapy (ART) and efficacy of Friendship Bench Problem Solving Therapy (FB-PST) on CMD symptoms and viral load (a composite marker of ART adherence). A randomized FB-PST intervention among WLHIV at the Blantyre, Malawi site co-enrolled in the multi-country PEPFAR PROMOTE cohort study was conducted, with 18 months follow-up for HIV-ART outcomes. Standardized Self Reporting Questionnaire (SRQ)-20 was used to screen for CMDs (March 2018- Dec 2018).

Eligible women with a CMD without suicidality were randomized to receive FB-PST (trained study peer-counselors) or referred for standard-of-care (SOC) treatment. Prevalence of SRQ-20 based CMD was high, 65/326 (19.9%); of these, 52 eligible women were randomized to FB-PST or SOC (1:1 ratio). Pre-intervention, 48 (90.6%) participants diagnosed with CMD had VL<1000 copies/ml and 160 (89.4%) without CMD had VL<1000 copies/ml (p=0.804). 14(21.5%) CMD sufferers reported suicidality. At 6 months postintervention, 26(100%) FB-PST treated women had VL <1000 copies/ml versus 18(69.2%) women in SOC arm (p= 0.005). At 12 months post-intervention, 26(100%) in the FB-PST arm maintained VL <1000 copies/ml versus

18(69.2%) in the SOC-treated arm. 18 months post-intervention, 18 (69.2%) women in the FB-PST arm had VL<1000copies/ml compared to 8 (30.7%) in the SOC arm (p=0.062). 14 (53.8%) treated with FB-PST had CMD resolution (SRQ score <8) 6 months post- intervention versus 16(61.5%) in the SOC arm (p=0.804). In conclusion, there was high prevalence of CMDs among WLHIV. Task shifting models of CMD treatment such as Friendship Bench PST are potentially as effective as standard of care in improving CMD symptoms and HIV treatment outcomes if they are delivered in their entirety as intended.

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ABBREVIATIONS AND ACRONYMS

PEPFAR	The President's Emergency Plan for AIDS Relief
PROMOTE	The PEPFAR PROMise Ongoing Treatment Evaluation study
PROMISE	The Promoting Maternal and Infant Survival Everywhere study
CMDs	Common Mental Disorders
PST`	Problem Solving Therapy
SRQ-20	Self-Reporting Questionnaire-20
PMTCT	prevention of mother to child transmission
MTCT	Mother to child transmission
MINI	Mini-International Neuropsychiatric Interview
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
ICD-10	International Classification of Diseases, Tenth Revision
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
CCR5	C-C chemokine receptor type 5

CHAPTER ONE: INTRODUCTION AND REVIEW OF THE LITERATURE

1.1 Introduction

Depression, anxiety, and somatic symptoms, collectively called common mental disorders (CMDs) are some of the leading causes of mental disorders worldwide, with more than 264 million people affected (1). CMDs differ from temporary mood swings and short-lived emotional responses to stressful events in everyday life. Typically, CMDs are chronic, display high rates of lifetime incidence and early age onset (2). Symptoms of CMDs include fatigue, irritability, sadness, worry, panic, forgetfulness, sleep problems, phobias, compulsions and obsessions (2).When, long lasting and with moderate or severe intensity, CMDs may become serious health conditions. They can cause the affected person to suffer greatly and function poorly at home, at school and work (2). In particular, depression is associated with suicide which is the second leading cause of death in 15-29-year-olds (1). Close to 800, 000 people die due to suicide every year globally (1).

There is a complex relationship between HIV and neuropsychiatric disease. Many of these associations go both ways, i.e., psychiatric disorders place people at increased risk of being infected with HIV, and HIV seems to increase the risk of developing several neuropsychiatric conditions (3). Compared to the general population and comparable HIV seronegative individuals, evidence suggests that the prevalence of CMDs is two- to four-fold higher in persons living with HIV (PLWHIV) (4). Depression is the most common neuropsychiatric complication of HIV infection and can occur in all phases of

the infection (4). Mixed depressive, anxiety and somatic symptoms are frequently seen as a comorbidity in people living with HIV/AIDS (5-8).

The aetiology of CMDs in PLWHIV is multifactorial and can be attributed to the virus, the immune system, or antiretroviral therapy (3). HIV itself can cause HIV associated neurocognitive disorders (HAND) a spectrum of illnesses including psychosis, peripheral neuropathy, encephalopathy and AIDS dementia (3). Some antiviral agents can cause neuropsychiatric disease, either by direct neuronal toxicity, immune activation or ongoing viral replication because of inadequate antiviral penetration into the CNS (9). Several drugs among the six classes of antiretroviral drugs are associated with neuropsychiatric illness. Efavirenz, a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), has been linked with disturbances of sleep, distressing or vivid dreams including nightmares, dizziness, light headedness, nervousness, and irritability. These symptoms may occur soon after the drug is started and were originally thought to resolve with continued use (10-11). More ominous clinical symptoms may occur later, including the development of depression, headaches, and cognitive impairment (10). Integrase Strand Inhibitors (INST) such as raltegravir and dolutegravir have been associated with insomnia, headache, depression and suicidality (12-13). Other ART classes (Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Protease Inhibitors, Fusion inhibitors and C motif Chemokine Receptor 5 (CCR5) blockers) are less implicated. The Malawi National antiretroviral (ART) program has adopted the World Health Organization's recommendations currently also recommends Dolutegravir (DTG)-based regimens as first line treatment for adults living with HIV (13).

Efavirenz (EFV) –based regimens preceded DTG and are being phased out because of increasing resistance and troublesome side effects including neuropsychiatric diseases.

Over the past 20 years, numerous studies have been conducted in various settings, with widely varying sample sizes and measures to determine the prevalence of CMDs in various PLWHIV populations such as pregnant and postpartum women and adolescents. These studies have estimated the prevalence of CMDs to range from 11 to 42 % in these populations (2-5, 7-8, 14-15). Possible reasons for this wide variability of prevalence include samples consisting of patients selected from different specific subpopulations at risk of HIV infection, different diagnostic techniques, varying assessment tools for CMDs or different cutoff scores, small sample sizes, and inadequate control groups of the studies (4).

The prevalence of CMDs among PLWHIV in Malawi has been reported to range between 1–19% (14-15). Women in Malawi are disproportionally affected by both HIV and CMDs (15). Women that were motivated to engage in HIV care during pregnancy may not be keen to remain in care after the postpartum and breastfeeding period when the risk of mother to child transmission of HIV has been removed. CMDs are one of the contributors of reduced engagement of women in HIV care (15). Suggested reasons for this include: loss of interest, poor concentration, poor motivation, reduced self-efficacy, fatigue, hopelessness, and suicidality; key characteristics of CMDs (15). Incorporating CMD screening and treatment into HIV women's care may be key to improving engagement and retention in care across the HIV care continuum.

1.2 Rationale

There are limited resources for mental health care in Malawi, and a scarcity of mental health infrastructure and specialists. There are only five qualified psychiatrists and three functioning psychiatric hospitals in the country for a population of nearing 20 million (1618). Because it is unlikely that the number of specialists and infrastructure could grow rapidly enough to meet the urgent demands of the population, task-shifting models of care that shift specialized services to non-specialists are a popular and cost effective strategy for providing mental health services particularly for mild to moderate conditions (19-21). Of the few depression treatment interventions developed for the sub-Saharan region, most employ a task-shifting approach (21).

One notable task-shifting intervention is the Friendship Bench (FB) behavioral activation and problem-solving therapy (22). Developed over many years of research in Zimbabwe, FB is patient-centered counselling that utilizes principals of cognitive behavioral therapy (CBT) for the treatment of CMD (22). The hallmark of FB is Problem Solving Therapy (PST) that teaches patients how to identify triggers and effectively manage stressful life events by learning or reactivating problem solving skills (22). Lay Health Workers (LHWs) are trained for two weeks by certified PST providers to deliver the intervention. The intervention consists of an average of six sessions of 30–45 min of structured PST, delivered in a discrete area outside of the clinic building on a bench (The Friendship Bench). The PST components consist of problem listing and identification, problem exploration, developing an action plan, implementation, and follow up (22). The program has proven efficacy in improving

CMD outcomes (22-23). In a cohort (n = 320) of patients recruited at primary health care facilities in Zimbabwe, the mean CMD score based on a locally validated screening tool for CMD, the Shona Symptom Questionnaire (SSQ) fell from 11.3 (SD 1.4) before treatment to 6.5 (SD 2.4) after 3–6 sessions on the Friendship Bench(22-23). Nonetheless, data regarding the effect of FB PST on HIV care outcomes has been mixed (22,23). Therefore, there is need to understand the feasibility of task-shifting program implementation and the effectiveness of these models of depression care to meet the mental health care needs of PLHIV.

The Lay Health workers that deliver FB-PST are peer counsellors called mentor mothers. A mentor mother is a mother living with HIV who is trained and employed by a health care facility or other healthcare institution (24). The mentor mother is responsible for giving oneon-one support to pregnant or postpartum women living with HIV; encourage enrollment, adherence and retention in HIV care, perform tracing for women who miss clinic visits; and educate on PMTCT and health-related topics. Facility-based mentor mothers have assisted nearly 2.5 million women living with HIV (WLHIV) in Sub Saharan Africa (24). Programs in countries with mentor mothers such as Uganda, South Africa, Nigeria, Ethiopia, and Malawi report lower MTCT rates, improved ART adherence, increased uptake of early infant HIV diagnosis, and reduced workload on skilled health workers (24).

This paper describes the CMD prevalence in a cohort of Malawian WLHIV on lifelong ART and the effect of Friendship Bench problem solving therapy intervention for on symptom improvement, ART adherence and viral load.

CHAPTER TWO: OBJECTIVES

2.1 Broad objective

The broad objective of the study was to assess prevalence of CMDs among WLHIV and assess the performance of Friendship Bench problem solving technology in the treatment of CMDs in this population.

2.2 Specific Objectives

1. To determine rates of CMDs among women in PROMOTE study at the Blantyre site and their impact on adherence to treatment and the antiretroviral treatment outcomes specifically:

a) To determine the proportion of WLHIV with a score of ≥ 8 on the Chichewa version of the Self Reporting Questionnaire-20 and confirmed to have a CMD on a MINI psychiatric interview,

b) To compare adherence to ART between women with CMDs and women without CMDs,

c) To compare rates of HIV viral load suppression between women with CMDs and those without CMDs.

2. To test efficacy of Friendship Bench PST intervention for CMD delivered by mentor mothers in improving symptoms of CMD, adherence and viral load in cases and compare with controls, specifically:

a) Describe changes in SRQ-20 scores from baseline and at months 6, 12 and 18 study visits post intervention

b) Describe changes in reported adherence to antiretroviral therapy from baseline to months 6, 12 and 18 study visits post intervention

c) Determine changes in viral load over time at months 6, 12 and 18 study visits post intervention

2.3 Hypotheses

1. The null hypothesis is that the Prevalence of CMDs among women in the PROMOTE study, denoted p1, will be higher than that in the general population, denoted p2, (i.e. p1-p2>0). Assuming a prevalence between 1-19% as seen in previous studies conducted in Malawi (7-10). The alternative hypothesis will be the Prevalence of CMDs in women in the PROMOTE study, denoted p1, will not be higher than that in the general population, denoted p2, (i.e. p1-p2=0.)

2. The null hypothesis is that the women in the PROMOTE study with a diagnosis of CMDs (m1) will have the same reported adherence and same rates of HIV viral suppression compared to women that do not have these conditions (m2). So Ho: m1=m2. The alternative hypothesis will be that the women in the PROMOTE study with a diagnosis of CMDs (m1) will have poorer reported adherence and higher viral loads compared to women that do have these conditions (m2).

The hypothesis is that a CMD treatment program integrated into routine HIV care will improve adherence, ART and depression treatment outcomes more than a standard referral program.

CHAPTER THREE: METHODS

3.1 Introduction

The study consisted of three stages: 1) Administration of a screening tool for Common Mental disorders (CMDs) 2) Clinical diagnosis of CMD using a psychiatric interview 3) Randomization of participants with CMD to either receive Friendship Bench PST (FB-PST) or referral for standard-of-care (SOC).

3.2 Study design

This was a randomized intervention study of brief, lay health worker-delivered Friendship Bench Problem Solving Therapy (FB-PST) among WLHIV with common mental disorder.

3.3 Study population

This Friendship Bench (FB) study was a randomized intervention study of WLHIV enrolled (March 2018- Dec 2018) in Blantyre, Malawi nested in the US PEPFAR-PROMOTE study. The PROMOTE study is a five-year observational cohort of sub-Saharan African WLHIV (n=1987) enrolled between December 2016 and October 2017 across four countries (Malawi, South Africa, Uganda and Zimbabwe) and their children previously enrolled in the PROMISE mother-to-child HIV prevention ART trial (25). The PROMOTE study is ongoing at eight research sites in four African countries: Malawi, South Africa, Uganda and South Africa. One thousand, nine hundred and eighty seven (1987) mothers and their children were recruited from September 2016 to August 2017 into the PROMOTE study (25). The PROMOTE study aims to measure

long-term antiretroviral treatment (ART) safety and adherence; compare HIV disease progression; assess subsequent adverse pregnancy outcomes; evaluate effect of ART exposure on growth and development in HIV-exposed uninfected children; and assess long-term survival of mothers and children (25). At baseline, 97.8% of Malawian women reported currently using ART; 96.4% were in WHO clinical class 1 or 2; median CD4 cell count was 825 cells per microliter; and viral load was undetectable in 85% of the women (25). The nested study was conducted at the Blantyre Malawi site only and began one year after the commencement of the PROMOTE study.

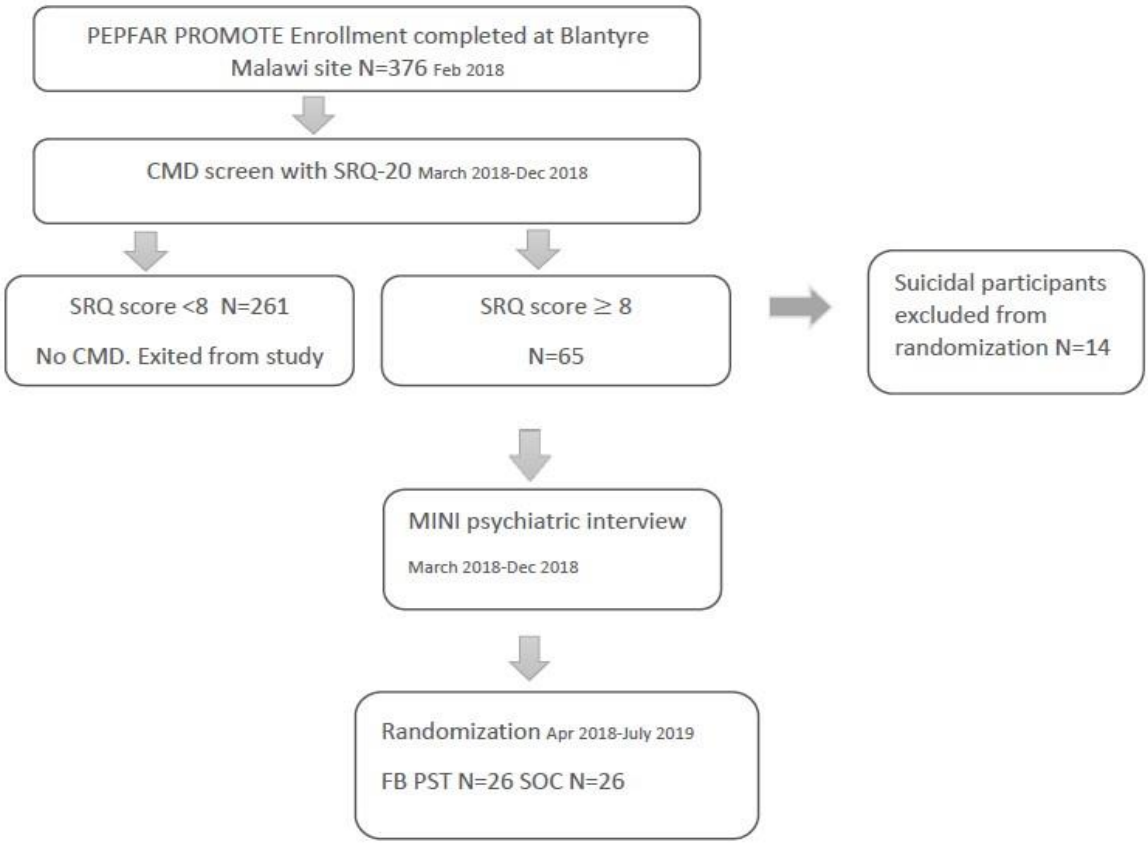

Figure 1: Participant recruitment

3.4 Sample size calculation

A sample size of 392 participants was sufficient to detect a statistically important difference between groups using a two-tailed z-test of proportions between two groups with 80% power and a 5% level of significance. However the Blantyre site projected to enroll approximately 390 women in the PROMOTE study and about 350 in the substudy. The rate of common mental disorder among HIV/AIDS patients in Malawi of >1% <19% was used to determine the sample size using Stata software (”sampsi .08 .18, alpha(.05) power(.80)”.

3.5 Data collection

Screening for CMDs was performed using a Self Reporting Questionnaire (SRQ)-20. Screening was conducted by study nurses that underwent a seven-day training on how to administer the screening tool. The SRQ-20 is a brief measure of psychiatric symptomatology designed by the World Health Organization (WHO) to be used across cultures as a screening tool for common mental disorder (26). It consists of 20 questions with yes/no answers exploring symptoms of depression, anxiety, and somatic complaints such as headache and non-specific gastrointestinal symptoms. It has been translated and validated in several African countries and has been widely used in studies of perinatal depression in developing countries. It has been translated to Chichewa and validated for use in the Malawian setting (26). Chichewa is the most widely spoken language in Malawi and in the area where the study was conducted. A Chichewa translation of the SRQ was used in one previous study amongst women in a rural setting in Malawi (26). A score ≥8 was set as the cut-off for diagnosing depression

as recommended by the WHO (26). Item 17 in the self-reporting questionnaire assess for suicidality by asking "*has the thought of ending your life been on your mind*?".

Clinical diagnosis of Common Mental Disorder was done using the Mini-International Neuropsychiatric Interview (M.I.N.I.). This was administered by a clinical psychologist and trained clinicians. The M.I.N.I is a short structured diagnostic interview, developed jointly by psychiatrists and clinicians in the United States and Europe, for DSM-IV and ICD-10 psychiatric disorders (27). With an administration time of approximately 15 minutes, it was designed to meet the need for a short but accurate structured psychiatric interview for multicenter clinical trials and epidemiology studies. The M.I.N.I used in this study is based on the DSM-IV-TR and has been translated to Chichewa for use in clinical practice (27). Following the clinical diagnostic assessment, diagnoses assigned included major depressive episode, dysthymia, mood disorder with psychotic features, mild depression, current suicide risk, post-traumatic stress disorder, manic episode, panic disorder, current agoraphobia, generalized social phobia and others.

For this study, three mentor mothers were employed full time. They were trained for seven days on depressive disorders and how to administer Friendship bench problem solving therapy by a team of certified Friendship bench providers using original Friendship bench material. The team of trainers comprised of one doctor, two nurses and one clinical psychologist all who are certified PST providers trained by the original FB-PST developers. Participants in the standard of care arm were sent to a mental health clinic which is a fiveminute walk from the study clinic. The clinic is manned by

psychiatry nurses, clinical psychologists, and psychiatrists. Participants were given a form, which was completed at the standard of care clinic by a provider and returned to the study clinic. This form collected information such as diagnosis, therapy initiated (counselling or drugs), plans for follow up, among others. To mitigate contamination between the intervention and control arms, mentor mothers were employed specifically for the study and were not involved in administering SOC treatments and the participants in different arms had appointments separated spatially and temporally.

3.5.1 Viral load and adherence data

Viral load and adherence information was transcribed from the parent PEPFAR-PROMOTE study. HIV viral load in the parent study was conducted using nucleic acid amplification tests (NAAT) on plasma. These evaluations are conducted every 6 months in the parent study. Adherence is assessed using the AIDS Clinical Trials Group Adherence Questionnaire (ACTG-AQ). This is a questionnaire that explores adherence to antiretroviral treatment, including items measuring adherence to medications yesterday, 2, 3, and 4 days ago, adherence to schedule during the last weekend and when any medication was last skipped.

The questionnaire's responses are weighted to calculate an adherence level from 0-100 (25).

3.6 Data analysis

Data collected in the sub-study was digitized and merged with the data from the parent study in order to perform the analyses. SRQ data was merged with selected data from

the PROMOTE dataset. Due to the implementation science nature of this study, we only abstracted routinely collected study data from the parent study.

For aim 1 prevalence data, T-test was used to check for statistical significance for variables where the mean was the statistic of interest. The Fischer's exact test to assess the association of factors between participants with CMD and those without. For aim 2 (changes in CMD symptomatology, differences in ART adherence and viral load between those treated with FB-PST compared to SOC), we used the paired T-test to compare changes in these variables before and after the intervention.

3.7 Ethical review

Regulatory approvals were obtained from Johns Hopkins School of Medicine IRB (JHPSOM IRB Study Number TR00006520) and College of Medicine Research and Ethics Committee (COMREC) COMREC Study Number P.09/17/2270. All participants gave written informed consent to join the study and allow the abstraction of their data from the parent study. The evaluation only used de-identified data to ensure the protection of participants' identities and confidentiality. Patients with CMD received care regardless of whether or not they provided consent for their data to be abstracted.

CHAPTER FOUR: RESULTS

4.1 Introduction

Of 376 PROMOTE participants approached, 326 agreed to join the study. Of the 326 participants recruited, 65 (19.9%) scored ≥8 on the SRQ-20. Sixty five (65) participants subsequently had a MINI clinical interview by a clinical psychologist or clinician to characterize the nature of their depressive disorder. Following administration of the MINI, participants were subsequently randomized to into one of two arms; arm A (n=26) where they received Friendship Bench problem-solving therapy in the study or arm B (n=26) where they were referred to receive standard of care treatment at Queen Elizabeth Central Hospital (QECH) mental health outpatient clinic. Participants that screened positive for suicidality on the SRQ-20 (n=14, 21.5%) were not randomized, but were referred for psychiatric evaluation at the Queen Elizabeth Central Hospital mental health clinic right away. Two hundred and sixty one (261) participants (80.1%) scored <8 on the SRQ-20 and therefore did not require any intervention. 38/65 (58.5%) cases had the SRQ-20 re-administered post-intervention.

4.2 Participant baseline characteristics

The mean age among CMD sufferers was 31 years (SD 4.2) and 33 years among those without CMD (SD 5.4). Participants had been on ART for an average of 2.9 years (SD 0.7 with CMD, without CMD SD 0.9 respectively) at the time of depression screen. Fourteen (21.5%) of the CMD cases were suicidal on screening. Over 96% of participants were on EFV-based regimens. The majority of participants were unemployed (53.8% with CMD and

52.5% of without CMD, respectively). 43 (64.5%) with CMD had access to electricity and 139 (53.5%) without CMD had access to electricity. Access to electricity as used as a proxy for socio-economic status. Fifty one (78.5%) of those with CMD were married or had a primary regular partner and 213(81.6%) CMD- were married or had a primary regular partner (P=0.989).There was no difference in age, duration on ART, type of ART regimen, employment status, marital status and economic status between cases identified to have CMD and those without CMD. Table 1 below summarizes these variables.

Table 1: Participant baseline characteristics

Variables	**CMD present (SRQ score ≥8 n=65)**	**No CMD (SRQ score <8 n=261)**	**p-value**
Age (years)	31.3 (SD 4.2)	32.9 (SD 5.4)	P=0.541
Years on ART	2.9 (SD 0.7)	2.9 (SD 0.9)	P=0.950
Baseline suicidality	14	-	
ART regimen EFV-based regimen Non-EFV based regimen	 63 (96.9%) 2 (3.1%)	 213(96.9%) 8(3.1%)	P=0.839
Employment status Employed Not employed	 30 (46.2%) 35 (53.8%)	 124 (47.5) 137 (52.5%)	P=0.913
Access to electricity access electricity No access	 43 (66.1%) 22 (33.8%)	 139 (53.3%) 122 (46.7%)	P=0.130
Marital stat partner/married No regular partner	 51 (78.50%) 14 (21.5%)	 213 (81.6%) 48 (18.40%)	P=0.989
HIV viral load <1000 copies/ml ≥1000 copies/ml	 48 (90.6%) 5 (9.4%)	 160 (89.4%) 19 (10.6%)	P=0.804

At baseline, 48 (90.6%) of those with CMD had VL 1000copies/ml versus 160 (89.4%) among those without CMD p= (0.0804) (*Table 1*).

All participants randomized to the study arm received Friendship Bench problem solving therapy. In the standard of care arm, four participants (15.4%) also received Friendship bench problem solving therapy because some mental health providers were trained to provide the service, while 21 (80.8%) received another form of counselling. Three participants (11.6%) in the standard of care arm received a combination of counselling therapy plus medication (*Table 2*).

The most frequently occurring diagnoses were major depressive episode, dysthymia, mood disorder with psychotic features, manic episode and current suicide risk (*Figure 2*). The majority of participants had two or more diagnoses (*Figure 2*).

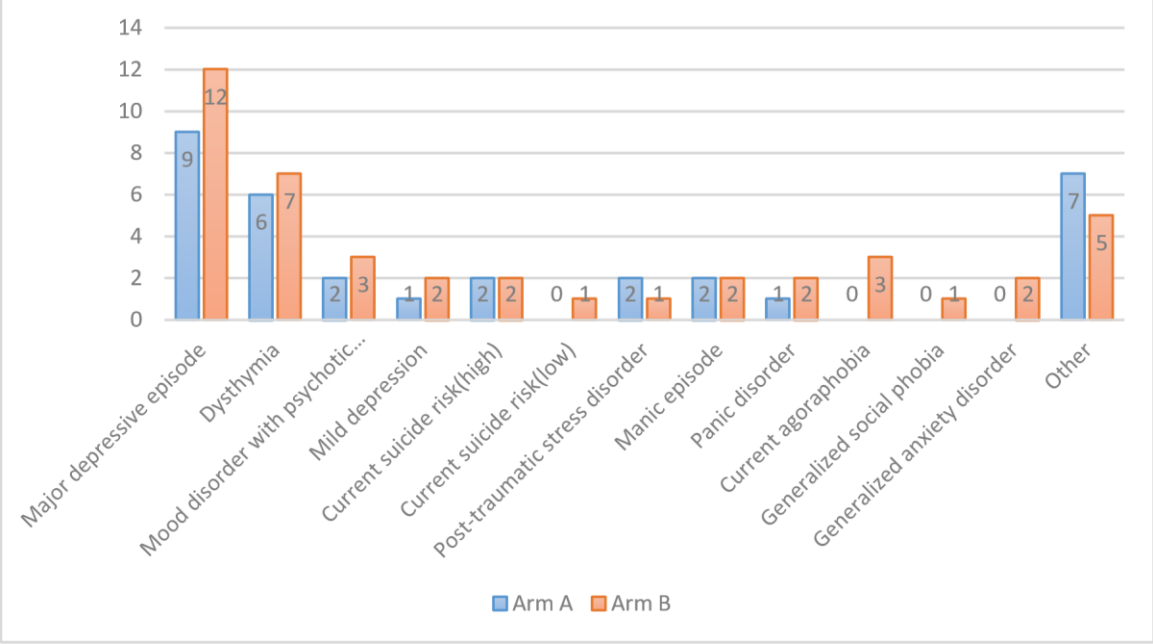

Figure 2: Diagnoses on MINI

Table 2: CMD treatment exposure among randomized

	Arm A (FB-PST) n=26	**Arm B (SOC) n=26**
Friendship bench problem solving therapy therapy	26(100%)	4(15.4%)
Other form of counselling by mental health professional	-	21 (80.8%)
Counselling by mental health professional plus medication	-	3[++] (11.6%)

[++]*1 participant received amitriptyline 25 milligrams once a day for 9 weeks, 1 participant received amitriptyline 25 milligrams once a day for 6 weeks, one participant received fluoxetine 20 milligrams once a day for 4 weeks.*

More than 50% (57.7%) of participants randomized to the FB-PST arm received 6 or more sessions of therapy. The rest received five or less sessions. A small number (4=15%) of participants in the SOC arm also received six or more Friendship Bench Problem Solving therapy sessions and 81% received 5 or less sessions. In the FB-PST, the majority of participants (57.7%) received six or more Friendship Bench problem solving therapy sessions. The rest (42.3%) received five or less FB problem solving therapy sessions. In contrast, 4(15.4%) in the SOC arm received six or more sessions and 21(80.8%) received five or less counselling sessions (*Table 3*).

Table 3: CMD treatment over time

	Arm A (FB-PST) n=26	**Arm B (SOC) n=26**
Number of Friendship bench therapy sessions attended 1-5 6-10	11(42.3%) 15(57.7%)	0(0.0%) 4(15.4%)
# of Counselling sessions by mental health professional 1-5 6-10	-	21(80.8%) 4(15.4%)

At 6 months post-intervention, 26(100%) FB-PST treated women had VL <1000 copies/ml versus 18(69.2%) women in SOC arm (p= 0.005). At 12 months post-intervention, 26(100%) in the FB-PST arm maintained VL <1000 versus 18(69.2%) in the SOC-treated arm. 18 months post-intervention, 18 (69.2%) women in the FB-PST arm had viral suppression compared to 8 (30.7%) in the SOC arm (p=0.062). 14 (53.8%) treated with FB-PST had CMD resolution 6 months post- intervention versus 16(61.5%) in the SOC arm (p=0.804) (*Table 4*).

Table 4: Impact of intervention on treatment outcome

	Arm A (FB-PST) n=26	**Arm B (SOC) n=26**	**P value**
Adherence: never >5 days without ART through 6 months	24(96.0%)	26(100%)	0.852
VL < 1,000 copies/mL			
6 months after intervention	26(100.0%)	18(69. 2%)	0.005
12 months after intervention	26(100.0%)	18(69. 2%))	0.063
18 months after intervention	18(69. 2%)	8(30.7 %%)	0.062

Of the 26 participants who received FB-PST (arm A), 14 (53.8%) had SRQ-20 readministered post-intervention versus 16 (61.5%) who received SOC treatment (p=0.804). Seven out of the fourteen (50%) participants who were previously suicidal had SRQ score of <8 post intervention. There was no statistically significant difference in CMD symptom resolution between those who underwent friendship bench intervention and those who underwent standard of care (*Table 5*).

Table 5: Impact of intervention on CMD symptoms

Total	**Arm (FB-PST)**	**SRQ score < 8 postintervention**	**Arm (SOC)**	**SRQ score < 8 postintervention**	**P -value**	**Suicidal**	**SRQ score < 8 postintervention**
Total # of that had SRQ-readministered post intervention	14 of 26	14 (53.8%)	16	16(61.5 %)	0.8 04	8/14	7 (50.0%)
Total number that did not have SRQ administered due to study closure	12	-	10	-		5	-

CHAPTER FIVE: DISCUSSION

5.1 Introduction

We investigated the prevalence of common mental disorders in a cohort of women living with HIV on life-long antiretroviral therapy and the impact of CMD on treatment outcomes including viral load. We also studied the impact of Friendship Bench problem solving therapy on CMD symptoms and treatment outcomes.

5.2 Prevalence of CMD

Our results reveal that there is a high prevalence of CMD among women living with HIV- on lifelong ART in Blantyre, Malawi. Almost one third of the women in this study had a CMD. This is in keeping with existing data that CMDs are highly prevalent in various subpopulations of people living with HIV in Malawi including newly diagnosed adults, adolescents, antennal and postnatal mothers (28). One previous study in Malawi sighted problematic alcohol use as a risk factor for severe depressive symptoms in adults living with HIV, but we did not investigate for this association in this population. Unemployment and low socio-economic status (as indicated by no access to electricity) were not associated with presence of CMD symptoms, although these are common triggers for common mental disorders in existing literature (29). The suicidality rate in this study (21.5%) was higher than that found in other studies of PLWHIV, which was 7-8 %(7, 8, 9). One of the reasons for this high suicidality rate could be that the study team had known the participants for over five years and had established a good relationship with them, which made it easier for the participants to be forthcoming about sensitive matters such as suicidal ideation.

5.3 CMDs and ART treatment outcomes

CMDs are known to affect adherence to long term treatment. Previous data from sub Saharan Africa has suggested that PLWHIV who also have CMD symptoms are less likely to be adherent to ART (30). In contrast, we found no difference in adherence to ART between those with and without CMD. Both groups had good treatment outcomes as evidenced by good virologic suppression (>90% with viral loads <1000 copies/ml at the time of diagnosis of depression). However, it should be noted that this particular group of women have been in longitudinal follow up in a study for over 5 years where viral loads are measured every 6 months and adherence and motivational counselling is done routinely. This is in contrast to real standard of care stings in Malawi here viral loads are measured very 1-2 years and client tailored counselling is not always possible.

All CMD cases in this study received intended care, regardless of study arm. Previous implementation science studies that have tried to integrate mental health care in HIV care settings in Malawi have sighted major challenges such as unavailability of community health workers to provide counselling, low retention rates in FB PST and stock-outs of antidepressant drugs in primary care facilities (19). In the study, these challenges were not encountered because we employed mentor mothers that were always available to provide problem solving therapy sessions. In addition, we actively followed up participants either by phone or home visits if they missed a scheduled problem solving therapy session. All CMD suferers that were randomized to receive standard of care received an appropriate intervention (counselling or drugs). The mental health care facility utilized in the study is a tertiary level facility which may have contributed to good quality of care. Nevertheless, it is clear that adequate resources (human, financial,

supervision, mentoring) are needed after screening has taken place to ensure that people with CMDs receive the care they require.

The original Friendship Bench protocol called for a minimum of 6 weeks of weekly therapy session, but only about half of participants in the study arm required that duration. The other half received five or less sessions.

Some participants that were referred to standard of care also received Friendship Bench problem solving therapy. It is expected that FB problem therapy will become widely used in mental health care settings in a lot of African settings because of its low cost and low intensity.

While majority of participants sent for standard of care reported optimal adherence 6 months after receiving an intervention for CMD, their outcomes following CMD care were suboptimal compared to those that received Friendship Bench problem solving therapy.
Fewer had suppressed viral loads and CMD remission.

5.4 Limitations

Our results should be considered in light of several limitations. Firstly, there was contamination as some participants in the control arm also received the study intervention (Friendship Bench Problem Solving Therapy) at the standard of care clinic. As a result, the treatment effect estimate may have been reduced. We had relatively low numbers in both the study and control arms, which may have affected the results. Secondly, we did not manage to assess CMD symptomatology and ART adherence at 12 and 18 months post-intervention due to time and

resource constraints. We were however able to transcribe viral load at these time-points from the parent study. Thirdly study resources influenced the conditions in the study and as such, it may not be possible to immediately apply the findings to low-resource settings. In addition, it is difficult to compare outcomes between those that received drugs and those that did not receive any antidepressants.

Finally, we found the SRQ-20 (administration time 5-10 minutes) more practical to use compared to the MINI clinical interview tool (administration time 15 minutes). Administration of the latter re also depended on availability of a clinical psychologist or clinician at the time the participant as in the clinic. As such, most participants had to be rescheduled for another day. It is unlikely that participants would have returned for the MINI evaluation had the visit not been incentivized by transport reimbursement. MINI psychiatric interview may be more suitable for specialized psychiatric settings in working out complex or treatment refractory CMD cases.

CHAPTER SIX: CONCLUSION

This study demonstrated that CMDs are highly prevalent in this cohort of Malawian WLHIV on ART. Major depressive disorder, dysthymia and mood disorder with psychotic features were the most frequently encountered subtypes of CMDs in this population. Simple screening tools such as the SRQ-20 can be used alongside other widely used tools with comparable results. One-layered screening is more feasible than inclusion of a second diagnostic interview tool. Considerable resources need to be invested in HIV care clinics (e.g. government employed lay health workers dedicated to mental health, active follow up of participants that miss appointments, community based mental health programs) in order to administer full courses of CMD treatment that can meaningfully affect HIV treatment outcomes.

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APPENDIX

Table 6: Other diagnoses

Non generalized social phobia	0	1
History of depression in the past two years	1	0
Current hypomanic episode	1	0
Psychiatric disorder	0	1
Loss of interest in most things enjoyed before	0	1
Past episode of mania	1	0
Past suicide attempt	0	1
No diagnosis	1	0
Inconclusive diagnosis	3	3

** In addition, we also re-administered the SRQ-20 to the participants that did not have CMD in the beginning to screen if some had developed CMD symptoms since the first round of screening. A total of 259 participants were re-screened for CMD. A total of 17 participants had SRQ-20 scores of ≥8 in the second round of screening. These underwent MINI psychiatric evaluation before being randomized again to receive counselling in the study or referral to standard of care. All randomized participants completed treatment in their assigned arms.