UNIVERSITY OF CAPE TOWN

MENTAL HEALTH AND ANTIRETROVIRAL THERAPY ADHERENCE AMONG PEOPLE LIVING WITH HIV ATTENDING AN HIV CLINIC IN BLANTYRE, MALAWI

By

DENNIS CHASWEKA

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DEPARTMENT OF PSYCHIATRY AND MENTAL HEALTH

FACULTY OF HEALTH SCIENCES

SUPERVISORS

PROFESSOR KATHERINE SORSDAHL

DR. CLAIRE VAN DER WESTHUIZEN

DECLARATION

I, Dennis Chasweka, hereby declare that this thesis is based on my original work and no part of it has been submitted elsewhere for research of for purpose of obtaining a degree. Acknowledgements have been made where other sources have been used.

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ABSTRACT

Background: Tremendous progress has been achieved in the treatment for HIV/AIDS since the 1980s. This significant improvement and progress in HIV treatment has largely been attributed to antiretroviral therapy (ART). Non-adherence to ART commonly causes ART treatment failure and the development of drug-resistant strains of HIV, resulting in increased mortality. Common mental disorders have been found to be strongly associated with non-adherence. In Malawi, where HIV is prevalent, there is a paucity of studies on how common mental disorders are associated with non-adherence. The present study aimed at examining the association between depression, anxiety and alcohol use disorder symptoms and ART adherence among people living with HIV/AIDS (PLWHA) attending an HIV clinic in Blantyre, Malawi.

Methods: This was a facility-based quantitative study with a cross-sectional descriptive design with 213 PLWHA attending an HIV clinic. The participants completed a survey consisting of demographics and mental health disorders symptoms screening tools, namely the 9-item Patient Health Questionnaire (PHQ-9) for depression symptoms, the Generalized Anxiety Disorder 7-item scale (GAD-7) for anxiety symptoms and the Alcohol Use Disorders Identification Test (AUDIT) for alcohol use and related harms. ART adherence was assessed using pill count, a self-report measure and a combined measure of both pill count and self-report adherence.

Results: The prevalence of depressive symptoms among the participants was 32%, 26% for anxiety symptoms and 16% of participants reported any life-time alcohol use. The majority of participants (75.6%) were found to have good pill count-based adherence while only 41.7% and 33.2% of participants reported good adherence on the self-report and combined measures respectively. The results showed that older participants were more likely to self-report good adherence than younger participants (OR=1.03; 95%CI=1.01-1.06, p-value=0.050). The participants who scored higher on the AUDIT were less likely to self-report good adherence to ART (OR=0.88; 95% CI=0.78-1.00, p-value=0.050). Side-effects were statistically significantly associated with both pill-count and combined adherence. The participants that experienced side effects from the treatment were less likely to be adherent on pill count (OR=0.19; 95% CI=0.07-0.53, p-value=0.001) and the combined adherence measure (OR=0.45; 95% CI=0.24-0.83, p-value=0.011). Alcohol use was again significantly associated with combined adherence. The participants who reported ever having used alcohol were less likely to be adherent to ART on the combined adherence measure (OR=0.51; 95% CI=0.29-0.93, p-value=0.026). No statistically significant association between depressive and anxiety symptoms and ART adherence was found.

Conclusion: The findings show that symptoms of common mental disorders were highly prevalent among PLWHA. Alcohol use, younger age group and experiencing side-effects from ART were significantly associated with ART non-adherence. Further research is required to investigate how depression and anxiety is associated with ART adherence among PLWHA in a Malawian population using larger sample sizes. The current study also highlights the need to routinely screen PLWHA for mental health problems. Further research using advanced designs, such as randomized clinical trials incorporating implementation science approaches, is also needed to evaluate the feasibility and effectiveness of integrating mental health services into HIV care in Malawi.

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LIST OF ABBREVIATIONS

AE	Adverse events
AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
AUDIT	Alcohol use disorder identification test
CES-D	Centre for epidemiological studies depression scale
COPD	Chronic obstructive pulmonary disease
DALY's	Disability-adjusted life years
GAD-7	Generalized anxiety disorder-7
GBD	Global burden of disease
GDP	Gross domestic product
HAND	HIV- associated neurocognitive disorder
HIV	Human immunodeficiency virus
ICD	International classification of disease
MEMS	Medication event monitoring system
MOH	Ministry of Health
MPHIA	Malawi Population-based HIV Impact Assessment
MSPSS	Multi-dimensional scale of perceived social support
PHQ-9	Patient health questionnaire-9
PLWHA	People living with HIV/AIDS
QECH	Queen Elizabeth central hospital
UNAIDS	United Nations Programme on HIV/AIDS
VAS	Visual analog scale
WHO	World health organization
YLL	Years lost to life

CHAPTER 1: INTRODUCTION

1.1 Background

The HIV/AIDS pandemic still remains a top public health threat in many countries since its discovery in the early 1980s. Current reports indicate that approximately 37.7 million people were living with the virus by the end of 2020 (UNAIDS, 2021a). Sub-Saharan Africa is the worst affected region, harboring 70% of HIV-infected people (WHO, 2016). According to data from the 2019 Global Burden of Disease Study (GBD), HIV/AIDS is still one of the leading causes of DALYs globally, ranking second after road injuries among adults of ages 25-49 years (Vos et al., 2020). HIV/AIDS was also the eleventh leading cause of death out of the 369 diseases and injuries in the 2019 GBD study. Malawi, a southern African country of 18 million people, has one of the highest prevalence of HIV in the region, estimated to be 10% of the population (UNAIDS, 2021b). HIV prevalence also varies by regions within Malawi. Southern Malawi has a higher prevalence (18.2 %) compared to central and northern Malawi, estimated to be 11.8 % and 7.3 % respectively (MPHIA, 2016).

Tremendous progress has been achieved in the treatment for HIV/AIDS since the first cases emerged in the early 1980s. HIV/AIDS is currently regarded as a chronic disease which differs from the early days when it was considered a terminal disease. This significant improvement and progress in HIV treatment has largely been attributed to antiretroviral therapy (ART). ART has been shown to be effective to halt disease progression, and reduce mortality and morbidity (Glaubius et al., 2021; Johnson et al., 2017). A study conducted in Kwazulu Natal, South Africa evaluating the impact of ART on life expectancy showed an increase of 11.5 years in life expectancy by 2011, compared to 2003 before ART was scaled up (Bor, Herbst, Newell, & Bärnighausen, 2013). In northern Malawi, the HIV/AIDS mortality rate reduced from 6.4 to 2.7 per 1000 persons four years after rolling out ART in the Karonga district (Floyd et al., 2010). Additionally, in higher HIV prevalence settings, ART has also been shown to decrease the risk of transmitting the virus (Johnson et al., 2013). A study by Tanser et al. (2013) in Kwazulu Natal, South Africa showed that the risk of transmitting HIV is 38% lower when 40% of HIV positive people in a community are on ART compared to when 10% of the HIV-positive population is on ART (Tanser, Bärnighausen, Grapsa, Zaidi, & Newell, 2013).

Studies examining predictors of optimal viral suppression among HIV-infected people have shown adherence to medication to be a strong predictor compared to other biological factors such as drug resistance, duration on ART and drug potency (Cobb et al., 2020; Ford et al., 2010; Achappa et al., 2013). For optimal adherence, at least 95% adherence to medication is recommended (WHO, 2015). Sub-optimal adherence has been strongly linked to ART treatment failure and development of drug-resistant strains of HIV, resulting in increased mortality (Redd et al., 2020; Ekstrand et al., 2011; Mannheimer et al., 2005). Treatment failure due to non-adherence poses a great threat to future HIV care in resource-constrained countries such as Malawi where there is limited access to second-line regimens (Ekstrand et al., 2011) (See table 1, ART regimens used in Malawi). Therefore, adherence is a vital component of delivering HIV care to ensure favorable outcomes.

REGIMEN	**Paediatric Formulation**	**Adult Formulation**
0	**0P=** **ABC** 60mg/**3TC** 30mg+ **MVP** 50mg	**0A=** **ABC** 600mg/**3TC** 300mg + **NVP** 200mg
1	**1P=** **d4T** 6mg/**3TC** 30mg/**NVP** 50mg	**1A=** **d4T** 30mg/**3TC** 150mg/**NVP** 200mg
2	**2P=** **AZT** 60mg/**3TC** 30 mg/**NVP** 50mg	**2A=** **AZT** 300mg+**3TC** 150mg/**NVP** 200mg
3	**3P=** **d4T** 6mg/**3TC** 30mg + **EFV** 200mg	**3A=** **d4T** 30mg+**3TC** 150mg+ **EFV** 600mg
4	**4P=** **AZT** 60mg/**3TC** 30mg + **EFV** 200mg	**4A=** **AZT** 300mg/**3TC** 150mg+ **EFV** 600mg
5		**5A=** **TDF** 300mg/**3TC** 300mg/**EFV** 600mg
6		**6A=** **TDF** 300mg/**3TC** 300 mg +**NVP** 200mg
7		**7A=** **TDF** 300mg/**3TC** 300mg + **ATV/r** 300/100
8		**8A=** **AZT** 300mg/**3TC** 150mg+**ATV/r** 300/100
9	**9P=**	

	ABC 60mg/**3TC** 30mg+**LPV/r** 100/25	
3TC=Lamivudine **ABC**=Abacavir **ATV/r**=Atazanavir/Ritonavir **AZT**=Zidovudine **d4T**=Stavudine **EFV**=Efavirenz **LPV/r**= Lopinavir/Ritonavir **NVP**=Nevirapine **TDF**=Tenofovir		
Standard ART 1st line(Regimen 0-6), 2nd Line (Regimen 7-9)		

Table 1. Standard paediatric and adult regimens used in Malawi (Health, 2014)

A number of factors have been found to be associated with adherence to ART. Studies in Sub-Saharan Africa have reported the following factors to be associated with non-adherence: longer duration on ART, side effects experienced, HIV-associated stigma, lack of social support, longer distance to clinic, non-disclosure of HIV status, single marital status, poverty and low patient knowledge regarding ART (Madiba & Josiah, 2019; Mesic et al., 2019; Chigova, 2016; Katz et al., 2013; Nel & Kagee, 2011). However, mental health problems have also been consistently found to influence adherence to ART among people living with HIV/AIDS (PLWHAs).

A number of mental disorders have been found to be associated with non-adherence. For example, depression has been reported as a major risk factor for non-adherence to ART both in high-resource and resource-constrained settings such as Sub-Saharan Africa (Sin & DiMatteo, 2013). Anxiety disorder is another mental disorder that has been associated with non-adherence (Nel & Kagee, 2011). Alcohol use disorder is also associated with sub-optimal adherence to ART (Velloza et al., 2020; Tran et al., 2014; Hendershot et al., 2009). Other mental health problems that have been shown to be correlated with sub-optimal adherence to ART are psychological distress and neurocognitive impairment (Nakimuli-Mpungu et al., 2012; Nyamayaro et al., 2020).

At the present time, a very few studies have been conducted in Malawi specifically investigating the association between mental health problems and adherence to ART. The few studies that have been conducted in Malawi only focused on depressive symptoms (Stockton et al., 2021; Spielman et al., 2021). At the present, it is not known how other common mental health problems, anxiety and alcohol use disorder, impact ART adherence. The present study aimed at addressing this gap.

1.2 AIM & OBJECTIVES

1.2.1 Aim

To assess symptoms of common mental disorders and ART adherence among HIV-positive people attending an HIV clinic in Blantyre, Malawi.

1.2.2 Objectives

a) To estimate the prevalence of probable common mental disorders and ART adherence among HIV-positive people attending an HIV clinic in Blantyre, Malawi.

b) To examine the association between depression, anxiety and alcohol use disorder symptoms and ART adherence among HIV-positive people attending an HIV clinic in Blantyre, Malawi.

CHAPTER 2: LITERATURE REVIEW

This chapter begins with a brief overview of HIV disease and then outlines the global health burden due to the virus by looking at HIV-associated mortality and disability adjusted life years. The chapter further outlines the HIV burden in Malawi, and presents a summary of barriers to ART adherence. The chapter then reviews published literature predominantly from African settings examining association between three common mental disorders (depression, anxiety and alcohol use disorders) and ART adherence.

2.1 Human Immunodeficiency Virus

The human immunodeficiency virus (HIV) is primarily transmitted through exchange of body fluids e.g. blood, vaginal fluids, and semen and breast milk. HIV attacks and weakens the body's immune system, specifically targeting the CD4 cells which defend the body against infections. If untreated, HIV makes the body susceptible to cancers and opportunistic diseases such as cryptococcal meningitis and tuberculosis (TB); thereby, progressing to the severe phase of Acquired Immune Deficiency Syndrome (AIDS) (WHO, 2018a). Symptoms and signs of early HIV infection include fever, rash, headache and sore throat. As the disease progresses signs and symptoms include weight loss, swollen lymph nodes, diarrhea, neurocognitive impairment and other symptoms associated with HIV disease and opportunistic infections (WHO, 2018a).

Globally, 79.3 million people have been infected with the virus since its outbreak (UNAIDS, 2021). Sub-Saharan Africa is the worst affected region, harboring about 70% of the HIV-infected people by the end of 2019 (WHO, 2020). According to UNAIDS HIV country profiles, Eswatini has the highest HIV prevalence in the world estimated to be 26.8 %, followed by Lesotho at 21.1 % as of 2018. There were 4 800 new infections in Eswatini and 7700 new infections in Lesotho in 2020 (UNAIDS, 2021). HIV/AIDS is one of the leading causes of global disease burden, as measured by HIV/AIDS-related mortality and disability-adjusted life years (DALYs).

2.2 Global Burden of HIV

HIV/AIDS remains a significant cause of death globally. Globally, HIV/AIDS is the sixth-leading cause of death. It is estimated that since its outbreak, 36.3 million people have died from HIV/AIDS-related conditions (UNAIDS, 2020). The peak of global and regional HIV/AIDS – related deaths per year was between 2004 and 2005 with two million deaths globally (UNAIDS,

2016). Global and regional HIV/AIDS mortality trends have significantly changed since the introduction of ART (ART). From 1990 to 2015 there has been a 45% reduction in HIV/AIDS-related deaths. Despite this reduction and an increase in ART coverage in sub-Saharan Africa, HIV/AIDS still is the leading cause of death in this region. The Eastern and Southern Africa region has the highest mortality rates among all the other regions in sub-Saharan Africa (see figure 1).

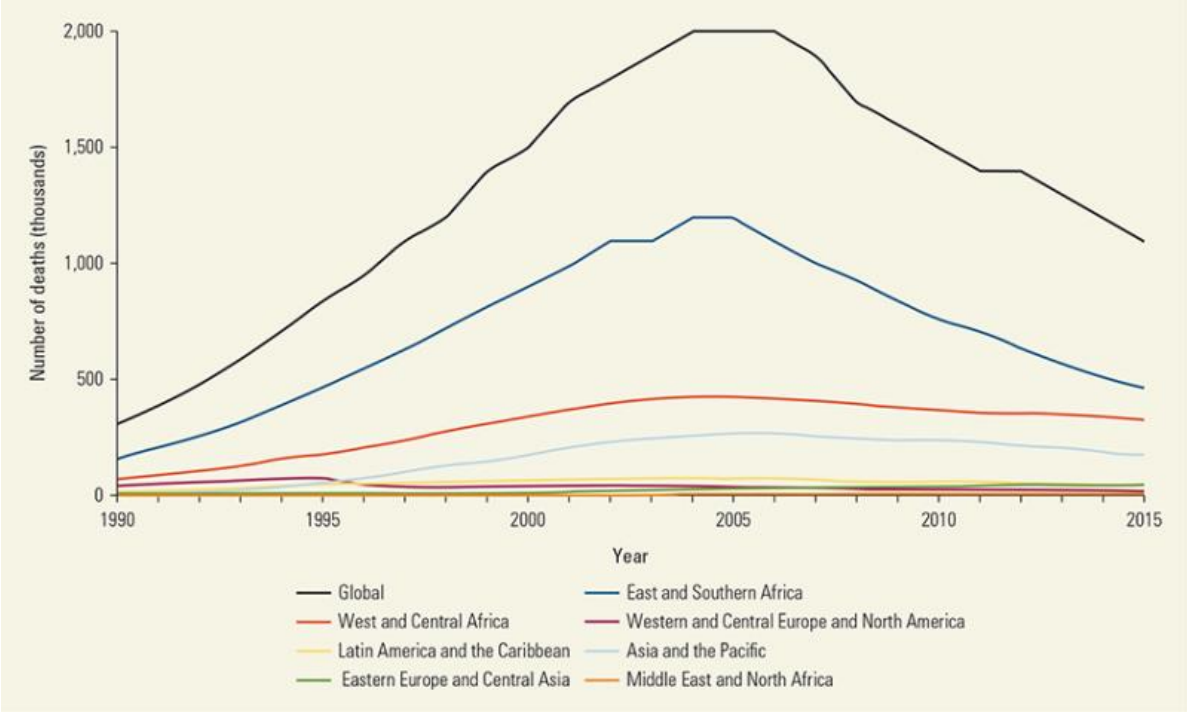

Figure 1. Trend of HIV/AIDS-related deaths from1990 to 2015 (UNAIDS, 2016.)

According to the World Health Organization (WHO), the HIV/AIDS mortality trend is declining significantly. It is estimated that by year 2030, annual HIV/AIDS-related deaths will be less than 400 000 (WHO, 2017). These estimates depend on an increase in ART treatment coverage for PLWHA.

While mortality rates provide some insight into the impact of HIV/AIDs, DALYs further outline the burden by combining years of life lost (YLLs) and years lived with disability (YLDs) (YLLs + YLDs = DALYs). In their study, Kyu et al. (2018) evaluated the global-level disease burden of HIV/AIDS as measured by DALYs compared to other 359 diseases from 1990 to 2017 from 195 countries under the GBD study. The findings showed that in 2017, HIV/AIDS was the twelfth

major cause of DALYS globally among females and thirteenth leading cause among males. This represents a 53.9 % decline for females and a 44.8 % decline for males (among all global causes of DALYs) from the 2007 GBD study which indicated HIV/AIDS as third and seventh leading cause of DALYs lost among female and males respectively. Despite this significant global decline in DALYs due to HIV/AIDS, HIV still remains a leading cause of DALYs. According to the recent 2019 GBD study, HIV/AIDS was the eleventh leading cause of DALYs in 2019 representing a 1.9% increase from 2017 (Vos et al., 2020). Africa, especially southern sub-Saharan region, had the highest DALYs rate among all the regions between 1990 and 2019 (Wu et al., 2021). In 2019, southern sub-Saharan region had the highest age-standardized DALYs rate at 12776.70 per 100000 people (Wu et al., 2021).

HIV/AIDS has also had a negative impact on regional economies, especially in the sub-Saharan Africa region where a high prevalence of HIV is reported. Early growth trajectories of 30 sub-Saharan African countries indicated that from 1990 to 2025, economic growth rates would be 1.47% lower due to the impact of HIV/AIDS (Veenstra & Whiteside, 2005). Similarly in 2000 at the peak of the pandemic, using cross-country regressions, the World Bank economists estimated that Africa's rate of growth per capita in gross domestic product (GDP) from 1990-1997, was reduced by 0.7% due to impact of HIV in those peak years (Bonnel, 2000).

2.3 HIV/AIDS in Malawi

Malawi's estimated population stands at 18.6 million as measured in the 2018 population and housing census (World Bank, 2019). Malawi's economy largely depends on agriculture, which accounts for more than one-third of its gross domestic product (GDP) and close to 90% of exports (NSO, 2018). Malawi has one of the highest prevalence estimates of HIV in the region, at 10% of the population (UNAIDS, 2017b). HIV prevalence also varies by regions within Malawi. According to the last Malawi HIV population-based impact assessment (MPHIA), southern Malawi had a higher prevalence (18.2 %) compared to central and northern Malawi estimated to be 11.8 % and 7.3 % respectively by 2016 (MPHIA, 2016). The annual incidence of HIV among adults was 18000 by the end of 2019 with more newly-infected females (12000) compared to males (5800) (UNAIDS, 2020).

Since the first cases in the mid-1980s, HIV/AIDS has had a devastating impact on individuals' livelihoods and the economy of Malawi. It is estimated that 990 000 people have died due to HIV/AIDS since its outbreak (UNAIDS, 2021). An economic model analysis on the impact of HIV/AIDS on Malawi's projected GDP per capita from 2000 to 2015 showed a 4.5 % reduction compared to an HIV/AIDS-free scenario. It is estimated that between 1990 to early 2000s, Malawi lost 20 percent of economically active people to HIV/AIDS (Arrehag, De Vylder, Durevall, & Sjöblom, 2006). However, the negative consequences for the Malawian economy are not only due to the loss of human capital, but also to HIV/AIDS-related morbidity. At its peak and during the 2001 hunger crisis, HIV/AIDS epidemic in Malawi was also linked to food insecurity and declining agricultural productivity especially for poor HIV-affected households as labor and capital was diverted to HIV care (Shah, 2002). Treatment for HIV/AIDS is, therefore, vital; not only to improve morbidity and mortality associated with the disease, but to also to improve its negative impact on general livelihoods and economy of the country.

2.4 Global response and 90:90:90 targets

In a drive to control and reduce global HIV/AIDS morbidity, mortality, incidence and prevalence, the UNAIDS set the 90:90:90 targets (UNAIDS, 2014). The 90:90:90 targets stipulate that 90% of HIV positive people should know their status, 90% of people tested positive should be linked to care and 90% of HIV positive people linked to care should be retained in care and virally suppressed. By the end of 2020, 84% of all HIV-positive people knew their status, 87% of the people with known status were on treatment and 90% of HIV-positive people were virally suppressed globally (UNAIDS, 2021). Significant resources have been allocated to assist in treatment and prevention of the epidemic. It is estimated that 21.3 billion US dollars was spent on the HIV/AIDS response in low- and middle-income countries (LMIC) in 2017 (UNAIDS, 2018).

2. 5 Adherence to ART

The introduction of ART has greatly improved HIV-related morbidity and mortality (Tesfaye et al., 2021; Floyd et al., 2010; Barak et al., 2019). Consequently, the scaling up of ART services has been a top public health priority in most LMIC, often aided by external donor funding (Shiffman, 2006). By the end of 2020, 27.5 million HIV-infected people were estimated to be on ART globally

(UNAIDS, 2021a). However, to ensure the optimal benefits of ART, lifelong adherence to the prescribed treatment regimen is crucial (WHO, 2015) .

Adherence to ART varies across different populations and settings. Few studies have evaluated global adherence estimates together with regional adherence differences. A meta-analysis by Mills et al. (2006) evaluated adherence estimates utilizing data from 31 North American and 27 sub-Saharan Africa studies. Twelve countries were represented in the sub-Saharan African studies. The majority of the studies (70%) used self-report measures to assess adherence. North American studies showed a pooled adherence estimate of 55 % compared to 77% for those conducted in sub-Saharan Africa (Mills, Nachega, Buchan, & et al., 2006). In Malawi, different studies have indicated favorable levels of ART adherence. A study by Bell et al. (2007) including 80 patients at Queen Elizabeth Hospital, Blantyre compared adherence measured by pill count and medication event monitoring system (MEMS) which uses an electronic sensor to track times and dates when the bottle cap opens. MEMS and pill count adherence were 88% and 98.6% respectively (Bell, Kapitao, Sikwese, van Oosterhout, & Lalloo, 2007). Another study by Ferradini et al. (2006) exploring adherence and viral failure among 1308 patients receiving ART at Chiradzulu hospital in Southern Malawi, indicated a 91% adherence by pill count and 92% adherence by self-report measure (Ferradini et al., 2006).

One of the main reasons for these varying rates of adherence to ART is the different methods that are employed to assess ART adherence. Assessing ART adherence levels is essential in identifying high-risk patients who could benefit from extra adherence support and counseling. The WHO classifies medication adherence measurement as objective and subjective (WHO, 2003). Objective adherence measures such as Electronic Data Monitoring (EDM) and pharmacy refill data are mostly employed in high-resource settings (Simoni et al., 2006). However, these approaches are resource-intensive, requiring advanced technology or comprehensive record keeping, which is not always feasible in sub-Saharan Africa (Bova et al., 2005). Pill count and self-report measures are strategies that are widely employed in low-resource settings (Minzi OM, 2008). Self-report measures are cheap and less complex to use, making this strategy accessible for these settings. Moreover, such measures have been demonstrated to accurately predict viral load (Bangsberg et al., 2001; Finitsis et al., 2016). However, despite the evidence of the link to viral load results, both pill count and self-report measures have shown to overestimate adherence (Minzi OM, 2008). Lam

and Fresco (2015) reviewed both objective and subjective medication adherence measures to highlight their advantages and disadvantages. The table below provides an overview of different types of adherence measures and their associated advantages and shortcomings as reviewed by Lam & Fresco (2015) (see table 2).

Adherence Measure	Description	Advantages	Disadvantages
OBJECTIVE MEASURES			
Direct measure - Biological markers (urine, blood etc.) -Biochemical measures	Drug concentration or metabolites in body fluids	- Most accurate Can provide physical evidence	-Intrusive -Varied drug metabolism -No quantifiable biomarkers/drug metabolites -Drug-drug interactions and drug-food interactions -Expensive -Require qualified staff and techniques to perform -Bias occurs if patients know the schedule of the tests (white coat adherence)
Secondary data analysis -Medication possession ratio - Multiple interval measure of medication acquisition	Adherence patterns derived from patient data e.g. pharmacy refills, electronic prescription, insurance claims	-Able to assess multi-drug adherence -Ideal for research (can be used to analyze data for larger population using centralized data systems) - Can identify patients at risk for treatment failure -Provide medication-refilling pattern	-Doesn't provide clues on barriers to adherence -Difficult to track prescriptions obtained elsewhere -Possible overestimation of adherence - Fail to identify partial adherence
Electronic medication packaging devices -Medication Events Monitoring Systems (MEMS)	A microprocessor records time and date every time drug container is opened	-Highly accurate -Identifies medication-taking patterns - Identify partial adherence	-It is expensive -Possible overestimation of adherence(patients might create false impression of adherence without taking the drugs) -Difficult to coordinate with outpatient refills

			-Incorrect use can lead to categorization of patients as nonadherent - Pressure to patients
Pill count	Amount of dosages taken between scheduled clinic visits vs dosages received (adherence ratio)	-Simple -Low cost -Considered more accurate that subjective measures e.g. self-report	- Not for nondiscrete dosages -Potential adherence underestimation for patients who refill before running out -Unable to characterize medication-taking or adherence pattern
SUBJECTIVE MEASURES			
Self-report and Clinician Assessment -Patient-kept diaries -Scales and questionnaires -Patient interviews	Provider or patients' evaluation of their medication –taking behaviour	-Low cost and simple to use -Practical and flexible in resource-constrained setting -Real time feedback -Able to identify individual concerns and potential interventions	- Least reliable -Poor sensitivity and specificity attributed to false input, poor communication skills -Bias as patients might fear being blamed for missed doses - Affected by communication skills of interviewers and questions in the questionnaire

Table 2. Advantages and disadvantages of different adherence measures (adapted from Lam & Fresco, 2015)

In Malawi, routine ART adherence assessment is done by pill count as stipulated in the national ART guidelines (Health, 2014). Patients are required to bring their medication bottles to each ART clinic visit and the healthcare providers count remaining pills to determine adherence percentage. Adherence percentage of 95% or more is regarded as being adherent. Pill count adherence percentage is calculated using the following formula (Lam & Fresco, 2015):

Pill count %= (Number of dosage units dispensed − number of dosage units remained)/ (prescribed number of dosage unit per day × number of days between 2 visits) x 100

2.6 A social-ecological approach to ART adherence

A number of factors are associated with adherence to ART. Factors influencing ART adherence may be categorized using a socio-ecological framework which explores the factors at multiple levels. The ecological perspective was first proposed by Bronfenbrenner (1977) as a new approach of broadening research on human development by focusing on relationships between a person and their environment at multiple levels. The model not only focuses on an individual's immediate setting but also on larger social, cultural and structural contexts, and the complex interactions between these contexts (Bronfenbrenner, 1977). The model has been used in different fields. For instance, the socio-ecological model has been used to analyze individual, cultural and structural factors that can be modified to promote health (Golden & Earp, 2012). The model has also been used to understand social and structural factors of HIV risks to implement multiple-level prevention strategies (Baral et al., 2013).

The social-ecological framework has been recommended for assessing medication adherence as an individual's behavior, such as poor adherence, is facilitated by multiple systems, including individual, family and structural risk factors which if identified could lead to interventions addressing adherence (Kazak, 1989). On the other hand, the socio-ecological model does not provide adequate understanding of the complex relationships between different factors for effective intervention. However, the socio-ecological model has an advantage of providing an adequate foundation for behavioural interventions as it assesses multi-level factors outside individualistic factors (Kazak, 1989). Using a social-ecological framework, Musheke et al. (2009) categorized multiple factors into personal or individual, social, health service and structural factors adapted from Roura et al., 2009. The investigators utilized the framework to indicate the dynamic and complex interaction between factors that influence ART adherence, especially in a resource-limited setting. Barriers to ART adherence identified in the literature are presented below according to this framework.

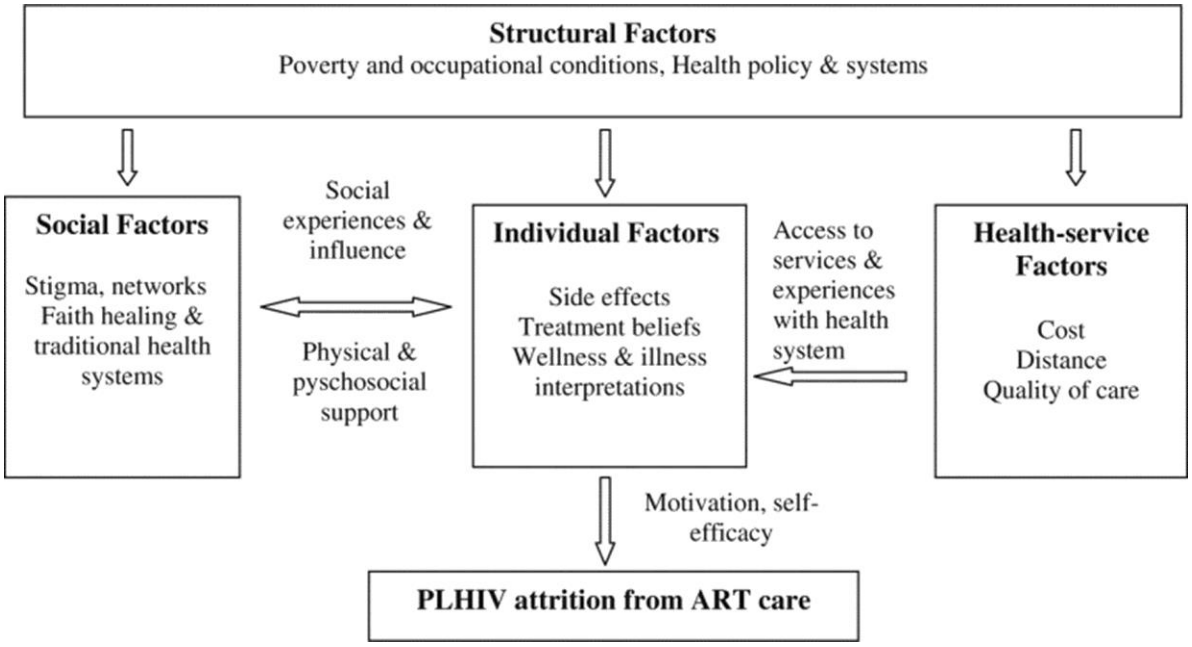

Figure 2: Socio-ecological framework of ART adherence barriers as designed by Musheke et al., 2012 in Zambia, adapted from Roura et al., 2009.

2.7 Barriers to ART Adherence

2.7.1 Structural and Health Service Factors

Health system structure and services are also key determinants of ART adherence. The setup, delivery of services, quality of care, providers' attitude, cost of care and distance to health facilities are some of the factors that impact on medication-taking behavior (Musheke, 2014). Colvin et al. (2014) conducted a systematic review to investigate health service barriers to ART initiation and adherence among HIV-positive pregnant and postpartum women. Forty two studies were included in the final analysis. The findings found the following key service delivery barriers to ART initiation and adherence: poor communication skills and lack of coordination skills among health service workers, substandard clinical practices, and gaps in providers' training. In a related structural review on barriers to ART adherence among pregnant and postpartum women, Hodgson et al. (2014) found breach of confidentiality by health workers, high cost of services, long queues at clinic, negative health workers' attitudes and inadequate dispensing of medication as key barriers.

Structural barriers to ART adherence are mainly common in low-resource settings like sub-Saharan Africa. According to Kagee et al. (2011), structural barriers to ART are defined as "economic, institutional, political and cultural factors that collectively impact the extent to which persons living with HIV follow their medication regimen." Kagee et al. (2011) reviewed notable structural barriers to ART adherence in southern Africa. The barriers were categorized into three sets: poverty-related, institutional, and cultural barriers. Key poverty-related barriers included difficulties with access to transport, food insecurity, and lost wages. Key institutional and cultural barriers salient in southern Africa included: inadequate medical care services, inadequate training of lay workers, and low levels of health literacy, stigma, and gender inequalities (Nel & Kagee, 2011).

2.7.2 Social factors

Social factors have also been found to influence medication-taking behavior. Social factors pertain to interpersonal relationships with family members and peers as well as links to social or community institutions that influence and shape people's norms, such as churches (Musheke et al., 2014). In a systematic review of barriers to ART adherence among pregnant and postpartum women, Hodgson et al. (2014) found that non-disclosure of HIV status, fear of violence from partner after disclosure, stigma and no family support were key social factors influencing non-adherence.

Disclosure of HIV status has been shown to be a key social barrier that is associated with ART adherence. In a recent structured review and meta-analysis, Dessi et al. (2019) examined the role of status disclosure on ART adherence among people living with HIV in Ethiopia. Seven studies conducted between 2010 and 2015 were included in the analysis. Results showed that patients who disclosed their status were 1.64 times more likely to have optimal adherence to ART compared with those who did not disclose their status (OR: 1.64, 95% CI: 1.11, 2.42).

HIV-related stigma is also another key social barrier that has been associated with ART non-adherence. In another review of 75 studies conducted among 26 715 PLWHA in 32 countries, Katz et al. (2013) investigated the impact of HIV-related stigma on adherence. The results showed that there was a positive association between stigma and ART non-adherence among 71% of all 41 quantitative studies included in the review.

Social support may also exert a strong influence on ART adherence. Heestermans et al. (2016) conducted a systematic review to examine key determinants of ART adherence among adults receiving treatment in sub-Saharan Africa. The 146 studies included in the final analysis represented 161 922 PLWHA across Africa. The results showed that the main determinants of ART non-adherence were stigmatization and lack of social support. Another meta-analysis by Dimatteo (2004) of 122 studies evaluating correlation between social support and adherence, found the odds of being adherent were 1.74 greater in patients from stable families and 1.53 less in patients from unstable families. Additionally, married or cohabitating couples showed higher adherence levels compared to people living alone (DiMatteo, 2004).

2.7.3 Individual factors

Individual factors are personal characteristics that influence medication-taking behavior. Examples include self-efficacy, side effects experienced, treatment beliefs, knowledge and attitude towards illness and motivation, among others (Musheke et al., 2014). Hodgson et al. (2014) conducted a systematic review of 34 studies examining barriers to ART adherence among pregnant and postpartum women. The results showed that key individual factors influencing ART non-adherence among pregnant and post-partum women were lower education levels, younger ages, denial of HIV, forgetfulness, concerns over child safety, drug/alcohol usage and lack of food. Additionally, Langebeek et al. (2014) conducted a meta-analysis of 207 global studies on predictors and correlates of adherence to ART and found that the following individual-level barriers were significantly associated with non-adherence: concerns about ART, beliefs about the necessity of ART and being prescribed a protease-inhibitor based ART regimen.

Experiencing side effects from HIV medication has also been linked with suboptimal adherence (Zhang et al., 2016; Li et al., 2017; Fonsah et al., 2017). HIV drugs have different reported adverse effects (AE). For instance, nucleotide reverse transcriptase inhibitors drugs are associated with lipodystrophy, lactic acidosis, and hyperlipidemia while non-nucleotide reverse transcriptase inhibitors drugs are associated with rash, liver toxicity and neuropsychiatric symptoms (Reust, 2011). In their systematic review of 33 studies examining impact of AE on ART adherence, Li et al. (2017) found that side-effects from Efavirenz-containing regimens were associated with lower adherence rates. In a study by Kim et al. (2016) exploring barriers to ART adherence among mothers on Option B+ (lifelong ART treatment for pregnant and breastfeeding women) in

Lilongwe, Malawi the investigators found that the main barrier was side effects (rash and fatigue) of ART experienced.

Having HIV-associated neurological conditions has also been linked to lower ART adherence (Ettenhofer et al., 2010). For instance, in a Swiss longitudinal study of 59 patients diagnosed with HIV associated neurocognitive disorder (HAND) at ART initiation showed a 50% decline in adherence after three years compared to patients with normal neuropsychological status (Kumal et al., 2017). Furthermore, mental disorders have also been associated with suboptimal adherence. The following sections reviews studies that have examined association between common mental disorders and ART adherence.

2.8 Mental Health among PLWHA

The mental well-being of PLWHA is considered essential to HIV care as evidence has linked psychological problems to poor adherence levels and treatment outcomes (Baingana, Thomas, & Comblain, 2005). Moreover, mental health problems have shown to be highly prevalent among people living with HIV (Olashore et al., 2021; Brandt, 2009). Thus, the high prevalence of mental disorders among HIV-infected populations increases the risk of not meeting the UNAIDS 90% ART adherence target at global and country levels. The relationship between mental disorders and HIV/AIDS is described as bi-directional, with one aggravating the other (Kim et al., 2015). While other mental disorders like psychotic and personality disorders have been found to increase ART non-adherence, the main research focus has been on three common mental disorders, namely depression, alcohol use and anxiety disorders (Blashill et., 2015; Chibanda, Benjamin, Weiss, & Abas, 2014; Kelly et al., 2014). There are no clear established mechanisms on how mental health problems impact adherence. However, mood disorders like anxiety and depression are hypothesized to compromise cognitive function, energy and motivation which might impact patients' disposition and ability to comply with the treatment (Dimatteo, Lepper & Croghan, 2000). Alcohol consumption is also hypothesized to amplify ART toxicity; such that, patients may opt to omit ART doses after alcohol consumption due to fear of toxic symptoms (Braithwaite & Bryant, 2010). Data from sub-Saharan Africa on the association between depression, anxiety and alcohol use disorder and ART adherence is presented below.

2.8.1 Depression and ART adherence

Depression has been widely studied compared to other mental disorders with regard to the link with ART adherence. Many studies have shown that depressive symptoms are highly prevalent and that being at-risk for a depressive disorder is a strong predictor of ART non-adherence among people living with the virus (Nakimuli-Mpungu, 2012). Similar studies have been conducted in sub-Saharan African countries, including South Africa (Nel & Kagee, 2013), Tanzania (Belenky et al., 2014) Uganda (Wagner et al., 2017), Ethiopia (Letta et al., 2015) and Nigeria (Farley et al., 2010.).

In the Western Cape, South Africa, Nel and Kagee (2013) examined the association of depressive symptoms with ART adherence among 101 patients attending an ART clinic. The Beck Depression Inventory-II was used to screen for depression and a six-item self-report adherence survey was used to assess adherence levels. The self-report survey assessed HIV medication taking behavior over the previous 2-week period and 40.4% participants were found to have moderate to severe depressive symptoms. The results indicated that compared to those reporting optimal adherence, those with non-perfect adherence were three times more likely to have moderate to severe depressive symptoms (OR=2.73; CI=1.09-6.82).

In another recent longitudinal study, Wagner et al. (2017) examined the association between depression and ART adherence at baseline, 6 months and 12 months among 1021 patients enrolled in three different studies in Uganda. The participants were recruited at ART initiation and assessed up to 12 months. For depression, the Patient Health Questionnaire (PHQ-9) was used and ART adherence levels were assessed using a self-report questionnaire on how well participants took medication previous seven days. Out of the 1021 participants, 9% were assessed as being at risk for major depression and 29% for moderate depression. Using bivariate comparisons, results showed both at 6 months and 12 months that participants who reported good adherence levels had lower depressive symptoms (mean=3.58) at baseline and lower severe depressive symptoms rate compared to those with reported suboptimal adherence levels (mean=5.32 ; $p < 0.001$), (severe depressive symptoms rates =5.9% versus 15.5%; $p<0.001$). In a similar retrospective observational study conducted in Tanzania, Belenky et al. (2014) investigated the relationship between depressive symptoms and ART adherence among 402 participants at baseline and 12 months later. The relationship between ART adherence and clinical outcomes, namely virologic failure (, was

assessed using viral load tests, and immune system suppression, measured by CD4 count, was also examined. WHO defines virologic failure as back to back viral load measurements of 1000 copies/ml or more within three months of adherence support (WHO, 2016). Depressive symptoms were measured using the PHQ-9 and ART adherence was assessed using a four-item self-report survey assessing missing doses over the previous month. Ten percent of the participants were identified as being at risk for moderate to severe depression. The results indicated that both at baseline (OR = 1.18, 95% CI [1.12, 1.24]) and 12 months (OR = 1.08, 95% CI [1.03, 1.14]), participants with depressive symptoms were at greater odds of being non adherent. However, there was an inverse relationship between the severity of depressive symptoms and virologic failure, as well as immunosuppression, such that an increase in depressive symptoms score corresponded to lower odds of virologic failure (OR = 0.93, 95% CI [0.87,1.00]) and immune suppression (OR = 0.88, 95% CI [0.79, 0.99]).

Letta et al. (2015) conducted a cross-sectional study to examine factors associated with ART adherence among 626 patients attending an ART clinic in Eastern Ethiopia. Depression was assessed using the Centre for Epidemiological Studies Depression scale (CES-D) and ART adherence was measured using a self-report questionnaire assessing whether medication doses were either delayed or missed by 90 minutes or more during the previous seven days. In the results, depression emerged as being significantly associated with ART non-adherence as patients with depression were more likely to be non-adherent compared to non-depressed patients (AOR = 0.36; 95 % CI = 0.21–0.61). Another factor found to be associated with nonadherence was nondisclosure of HIV status as patients who did not disclose their HIV status were less likely to be adherent than those with disclosed their sero-status (AOR = 0.45;95 % CI = 0.21–0.97). In a similar cross-sectional observational study conducted in Nigeria, Farley et al. (2010) examined the association between depressive symptoms and ART adherence among 222 patients attending HIV clinic. Depression was measured using the CES-D and ART adherence was assessed by pharmacy refill rates. A pharmacy refill rate of less than 95% indicated nonadherence. CES-D scores were categorized as moderate depressive symptoms if score was greater or equal to 16 and severe depressive symptoms if score was greater or equal to 21. Results indicated that moderate depressive symptoms (p=0.004) and severe depressive symptoms (P < 0.001) were significantly

associated with poor adherence among the 10.4 % of the participants who had a pharmacy refill rate of 95%.

In conclusion, the findings from these studies supports the evidence from many other studies conducted in high-income and middle-income countries that depressive symptoms are strong predictors of non-adherence to ART medication. A meta-analysis by Uthman et al. (2015) on depression and ART adherence in LMIC showed a consistent association between adherence and depression across all countries income groups (pooled OR = 0.58, 95% CI 0.55-0.62).

2.8.2 Alcohol Use Disorder (AUD) and ART Adherence

AUD is mainly defined according to alcohol intake over a period of time that leads to health and social problems. AUD is usually classified as mild, moderate or severe. AUD is especially critical because of its association with general public health outcomes e.g. individual health deterioration, increased sexual risk-taking behaviors leading to increased virus transmission, poor medication adherence resulting in drug resistance and a decline in cognitive functions (Azar et al., 2010). Studies have reported a high prevalence of AUD among PLWHA as well as an association with ART adherence (Nakimuli-Mpungu, 2012).

Studies examining the association between risky alcohol use and ART adherence have been conducted in various sub-Saharan countries, such as South Africa (Magidson et al., 2017; Morojele & Kekwaletswe, 2013), Lesotho (Cerutti et al., 2013), Benin (Jacquet et al., 2010), Mali (Jacquet et al., 2010), Ivory Coast (Jacquet et al., 2010) and Ethiopia (Negash & Ehlers, 2013). For example, in a multi-national cross-sectional study conducted in Benin, Mali and Ivory Coast, Jacquet et al. (2010) examined alcohol use and ART adherence in 2920 patients attending ART clinics. Risky alcohol use was measured by the Alcohol Use Disorders Identification Test (AUDIT). The AIDS Clinical Trials Group self-report questionnaire was used to measure ART adherence and 91% of participants reported optimal adherence levels. The results showed that participants who reported sub-optimal adherence were more likely to be alcohol consumers (OR=1.4; CI= 1.1-2.0) and high-risk drinkers (OR=4.7; CI=2.6-8.6) compared to non-drinkers. Another cross-sectional observational study by Magidson et al. (2017), investigated risky alcohol use and the association with nonadherence among 101 PLWHA attending regular ART clinics in South Africa. Alcohol use and related harms were measured by the AUDIT while ART nonadherence was assessed by

self-report event-level measurement which assessed medication taking behavior over the past weekends. The results showed that 17% of participants scored in the elevated ranges for AUD. Alcohol use was significantly associated with ART nonadherence (AOR = 1.15; 95%; CI = 1.02–1.29) Similarly, in another cross-sectional study, Morojele & Kekwaletswe (2013) investigated whether alcohol use was independently associated with ART nonadherence among ART recipients attending ART clinics in Tshwane, South Africa. The study enrolled 304 participants. Risky alcohol use was measured by the AUDIT. ART adherence was assessed by the CASE Adherence Index , which is a three-item measure assessing challenges in taking ART on time, how often doses are missed (frequency) and the last time a dose was missed. Using hierarchical multiple regression, the results showed that the percentage of variance in adherence of 24% ($p<0.001$) was significantly elevated after AUDIT scores were included in the model. Compared to other factors, demographic details, structural barriers and psychosocial variables, 4%, 16% and 19% ($p<0.001$) respectively. This indicates that alcohol use was found to be independently associated with ART adherence.

In Lesotho, Cerutti et al. (2013) examined the link between alcohol use and ART adherence and viral suppression among 1388 HIV-infected people receiving treatment at ten rural clinics. This was a cross-sectional observational study. Alcohol use was measured by the AUDIT and ART adherence was assessed by combining two visual analogue scale (VAS) and pill count, where ≥ 95% VAS score and pill count of less than 95%. The results showed that 6.3% of the participants had elevated scores for hazardous drinking. The results also indicated that participants who consumed alcohol were two times more likely to be non-adherent than those who were alcohol abstinent (adjusted odds-ratio: 2.09, 95% CI: 1.58-2.77). Participants using alcohol at risky levels (AUDIT-score ≥ 8) were had 2.73 times higher odds of being ART non-adherent than those who did not use alcohol (OR=2.73, 95 % CI: 1.68-4.42). Another cross-sectional study in Ethiopia looked at alcohol usage influencing ART adherence among 355 ART recipients (Negash & Ehlers, 2013). ART adherence was assessed by pill count while alcohol usage was assessed by a specifically designed structured survey which asked participants to self-rate their frequency of alcohol usage in a week. The results showed that 42.6 % of the non-adherent participants (94 in total) were light drinkers, 53.2% were non-drinkers, 1.1 % were frequent light consumers and 3.2% were heavy drinkers; hence, a statistically significant link between alcohol use and ART adherence

(p=0.001). A recent meta-analysis of 32 studies investigating alcohol use and ART non-adherence in Sub-Saharan Africa has also found that participants who reported any alcohol usage had double the odds of being non-adherent to ART compared to non-drinkers (OR= 2.3; 95% CI: 1.90-2.70, P-value=0.001) (Velloza et al., 2020). These studies, therefore, also support the evidence from other studies conducted in high- and middle-income countries that alcohol use is strongly associated with ART nonadherence (Hendershot et al., 2009).

2.8.3 Anxiety disorder and ART adherence

Most of studies investigating the association between mental health and ART adherence have focused on depression. There is a paucity of studies examining the link between anxiety and ART adherence. However, anxiety has been shown to have an impact on the quality of life for people living with HIV and is linked to risky sexual behaviours resulting in increased transmission, poor retention rates and medication adherence among PLWHA (Brandt et al., 2017). A recent meta-analysis examined the association between anxiety and ART adherence in LMIC (Wykowski et al., 2019). Eleven studies were selected and included in the final meta-analysis representing nine countries: Nigeria, Cameroon, South Africa, Nepal, Thailand, China, India, Brazil and Vietnam. The meta-analysis results showed that anxiety is strongly associated with ART nonadherence (OR: 1.61, 95%; CI 1.18–2.20; p = 0.003).

Few studies have investigated the association between ART adherence and anxiety in sub-Saharan Africa. This remains a crucial area to be explored. However, surprisingly, the few studies that have examined the association between anxiety and ART adherence in Africa have not indicated a positive association. For instance, a cross-sectional study by Nel et al. (2013) on the association between depression and anxiety and ART adherence among ART recipients in South Africa found that anxiety was not significantly associated with ART adherence (OR=1.425, CI=0.54-0.76, p=0.474) compared to depression (OR= 3.169, CI=1.391-7.221, P=0.03). Additionally, the comorbid association of depression and anxiety did not significantly predict adherence (p=0.475). Similar studies in Nigeria and Cameroon have also failed to find a statistically significant association between anxiety and ART adherence (Adejumo et al., 2016; Yunusa et al., 2014; Pefura-Yone et al., 2013). In contrast, some studies in high- and middle-income countries have found a significant association between anxiety and ART nonadherence. For example in the United

States, Tao et al. (2018) conducted a prospective study among 228 Chinese men who have sex with men (MSM) to examine the association between anxiety and ART at baseline, 6 months and 12 months. The Hospital Anxiety and Depression Scale (HADS) was used to measure depression and anxiety while ART adherence was assessed by a self-report questionnaire evaluating missed doses in the past three months. The results indicate that anxiety was significantly associated with ART nonadherence (OR=4.79; 95% CI, 1.12–20.50). In another study, Campos et al. (2010) conducted a longitudinal study to examine whether depression and anxiety at initiation predict ART nonadherence among 293 ART recipients at two public hospitals in Brazil. HADS was used to measure depression and anxiety while ART adherence was assessed by self-report items assessing missed doses in the three days prior to the interview. The results indicated that only severe anxiety was significantly associated with ART nonadherence, therefore, a strong predictor of nonadherence (OR=1.87; 95% CI=1.14–3.06).There is a need for more studies in Africa to establish how anxiety is associated with ART adherence across different populations.

2.8.4 Rationale

These studies highlight that there is evidence for the link between mental health problems and non-adherence among HIV-infected populations. To achieve the last UNAIDS target of having 90% of people living with HIV be virally suppressed, ART adherence is critical. So far, Malawi has made remarkable progress towards achieving the 90-90-90 targets, particularly in identifying those infected with the virus. According to the UNAIDS Malawi HIV country profile, by the end of 2020, 91% of people living with HIV had been tested and knew their status, 86% of people diagnosed were on treatment and 81% of people on treatment were virally suppressed (UNAIDS, 2021). The findings indicate there is still a huge gap in addressing barriers to ART adherence. There is a need for comprehensive adherence programs that include mental health interventions as mental health has been shown to be a critical component in many countries. However, in Malawi there is limited evidence regarding ART adherence barriers due to the paucity of published studies and no studies specifically investigating the association between mental disorders and ART adherence in Malawi.

To address this gap, the current study examined the association between symptoms of common mental disorders and ART adherence among HIV-positive people attending an HIV clinic in Malawi. Evidence from this study could potentially inform HIV service development to integrate

mental health services into HIV standard care for ART adherence improvement in order to reduce the impact of HIV in Malawi.

CHAPTER 3: METHODOLOGY

3.1 Type of Study

This was a facility-based quantitative study with a cross-sectional descriptive design conducted to determine the association of symptoms of CMDs, namely depression, anxiety and alcohol use disorder with ART adherence among HIV-positive people attending an ART clinic in Blantyre.

3.2 Study Setting and Study Population

The study was conducted in Malawi. Malawi is a landlocked country in South-Eastern Africa bordering Zambia (West and North West), Tanzania (North and North East) and Mozambique South and South West). The picture below shows a map of Malawi (Figure 2).

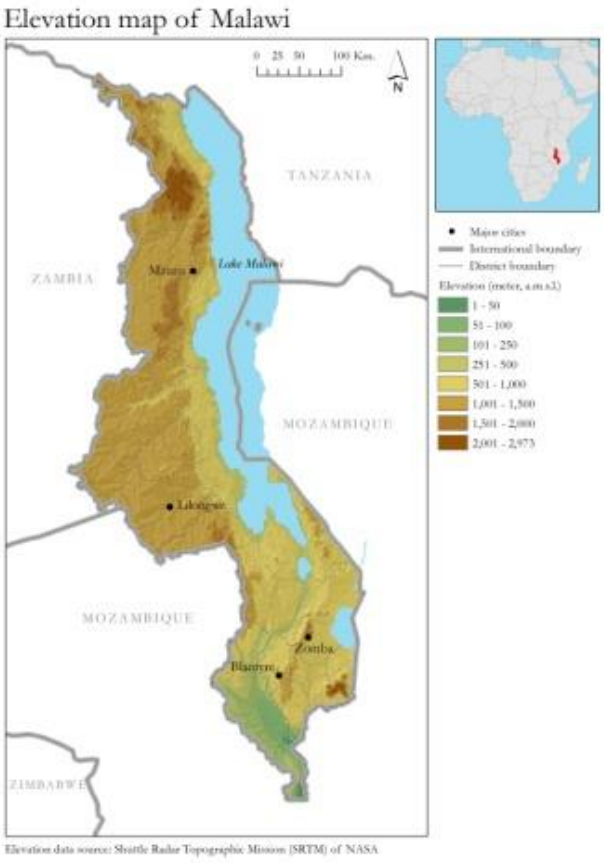

Fig 3. Map of Malawi, Source: http://www.masdap.mw/documents/281

The study took place at Queen Elizabeth Central Hospital (QECH) ART clinic in Blantyre. Blantyre is the commercial city for the southern region of Malawi and has a population of around 1 100 000 people. Blantyre has one of the highest HIV prevalence statistics in Malawi, estimated

to be at 18.2% compared to the national prevalence of 10% (MPHIA, 2016). QECH is the largest hospital in Malawi and the main referral hospital for the southern region. The ART clinic at QECH was established in 2000 and currently serves a cohort of around 12 000 people on ART. This study enrolled 211 patients attending the routine ART clinic at QECH according to the inclusion criteria detailed below.

3.3 Definitions and Eligibility

Patients were eligible for the study if they met the following inclusion criteria:

1) 18 years of age or older
2) HIV-positive on any ART regimen (regardless of regimen line)
3) Initiated ART ≥ 6 months prior to study recruitment
4) Attending QECH for ART services
5) Able and willing to consent to study participation.

3.4 Measures

Participants were asked to complete a short survey including questions related to socio-demographics, mental health, HIV and clinical characteristics. The following measures were included in the questionnaire:

3.4.1 Socio-demographics

Socio-demographics details on marital status, employment status, number of children and education level were obtained using a survey adapted from Robert et al. (2014). This socio-demographic survey was used in assessing the relationship between social support, antenatal depression and ART adherence in Malawi (Robert et al., 2014).

3.4.2 ART adherence

ART adherence was measured by pill count and a six-item self-report measure. In Malawi, routine ART adherence assessment is done by pill count as stipulated in the national ART guidelines (MOH, 2014). Pill count was calculated using the following formula:

Pill count %= (Number of dosage units dispensed − number of dosage units remained)/ (prescribed number of dosage unit per day × number of days between 2 visits) x 100

The six-item self-report adherence tool was developed by Nel & Kagee. (2013) and was adapted from items proposed by Simoni et al. (2006) based on a comprehensive systematic review of self-report adherence tools for measuring adherence to ART. The tool has been used in South Africa, in a resource-limited setting, to assess ART adherence in HIV-positive people with common mental disorders (Simoni et al., 2006; Nel & Kagee, 2013). The tool has six questions that assess medication-taking patterns and missed doses at different intervals (2 weeks, during the previous weekend, 7 days) and a visual self-adherence rating on a scale of 0%-100% (Nel & Kagee, 2013). Combining self-report and pill count results in assessing ART adherence levels has been shown to be a strong adherence assessment method which correlates well with viral load measurements (Wu et al., 2014). Viral load testing in Malawi is quite expensive, hence, only done at few central laboratories where samples from all ART clinics nationwide are processed. Routine viral load testing in Malawi is only done at a six-month point after ART initiation and there after every other two years, except for targeted testing for patients with suspected ART failure (Health, 2014). Consequently, viral load details were not collected for the participants in this study.

3.4.3 Depression (PHQ-9)

Depression symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 is a brief nine–item tool that focuses on the nine diagnostic criteria for DSM-IV depressive disorders. The tool is a short version of the Patient Health Questionnaire (PHQ), that was developed for primary care use (Kroenke, Spitzer, & Williams, 2001). The score range is 0-27, with 1-4 being minimal, 5-9 mild, 10-14 moderate, 15-19 moderately severe and 20-27 severe levels of depressive symptoms. The tool has been validated in sub-Saharan Africa among people living HIV/AIDS (Cholera et al., 2014). In Western Kenya, the tool showed good internal consistency reliability (0.87) among people living with HIV (Monahan et al., 2008). PHQ-9 has recently been validated to identify depression in non-communicable diseases clinics in Malawi (Udedi et al., 2019).

3.4.4 Alcohol use disorder (AUDIT)

The Alcohol Use Disorders Identification Test (AUDIT) was used to assess problem alcohol use among the participants. The tool was designed to identify hazardous use, harmful use and probable alcohol dependence (Bohn, Babor, & Kranzler, 1995). The highest tool score is 40 and a score of 8 or more is recommended as a cut-off for identifying hazardous drinking (Saunders et al., 1995).

Although the tool has not been validated in Malawi, it has been used to screen for harmful alcohol use among Malawian university students and has also been validated in Zambia among HIV patients with 60% sensitivity and 60% positive predictive value for identifying alcohol use disorder (Zverev, 2008; Chishinga et al., 2011).

3.4.5 Anxiety (GAD-7)

The Generalized Anxiety Disorder 7-tem scale (GAD-7) is a seven-item tool used to screen for generalized anxiety disorder and was developed for the primary care setting. The tool scores range from 0-21 with 5, 10 and 15 being cut points for mild, moderate and severe levels of generalized anxiety disorders respectively (Spitzer, Kroenke, Williams, & Löwe, 2006). The tool has primarily been used in high-resourced settings but its use in African settings (Ivory Coast and Ghana), showed good reliability with a Cronbach alpha of 0.68 (Bindt et al., 2012). Although the tool has not been validated in Malawi, it has been validated and used in other Southern African countries. For instance, the GAD-7 has also been validated in a primary care setting in Zimbabwe using the Structured Clinical Interview for DSM-IV (SCID) as the gold standard. The investigators reported that the GAD-7 showed good sensitivity, specificity of 89% and 73% respectively, and a good internal consistency reliability with a Cronbach alpha of 0.87 (Chibanda et al., 2016).

3.4.6 Social support (MSPSS)

The Multidimensional Scale of Perceived Social Support (MSPSS) was used to measure participants' perception of the social support they received. The 12-item tool has been validated and translated into two local Malawian languages, Chichewa and Chiyao, and displayed excellent reliability with a Cronbach's alpha of 0.90 (Stewart, Umar, Tomenson, & Creed, 2014).

3.4.7 Clinical characteristics and knowledge

A simple 6-item questionnaire assessing ART side-effects, length of time on ART and knowledge of the importance of using ART was included. The questionnaire was adapted from an interview guide that was developed after consultation with expert health professionals following a literature review on barriers and facilitators to ART adherence. The interview guide was used to identify facilitators and barriers to adherence among mothers on the Option B+ plan in Lilongwe, Malawi (Kim et al., 2016).

3.5 Study Procedures

Two special nurses were recruited as research assistants by the candidate to screen, recruit and administer the study questionnaire at the ART clinic. The nurses had just completed their general

required internship and were waiting for placement by the ministry of health. They had previous research experience and were not part of the nursing staff at the ART clinic. The candidate played a supervisory role of the study nurses during recruitment. The ART clinic was starting at nine o'clock in the morning with special health talk by service providers (clinician/nurse). The health talk highlighted general medication adherence and health living tips for the patients on ART. After each talk, the study nurses introduced themselves, the study and its purpose in broad terms with the support from the ART clinic staff before the clinical consultations started. The study nurses were allocated a special room next to a consultation room. After routine clinical consultations, the clinician referred the patients to the study nurses for further information on the study. The study nurses explained the study objective and sought patients' consent to ask the brief screening questions to ensure that they met inclusion criteria. If consent was granted, the study nurse screened the patients for eligibility. If found eligible, the study nurses explained the study in detail and the patient was given time to ask questions and think about their participation. Patients willing to participate in the study were asked to sign a written informed consent form. Upon signing the consent (See Appendix C), the study nurses administered the self-report questionnaires (See Appendix B). The patients' ART number (special identification number assigned to every patient receiving ART at the clinic) was documented to check their pill count results in the electronic database. The survey took approximately 30 minutes to conduct and was administered in Chichewa. The candidate thereafter reviewed the questionnaires and made sure all queries were resolved by the study nurses. Participants were given refreshments (soft drink) during the survey and 1000 Malawi Kwacha (R20) as compensation for their time.

3.6 Screening Report

During the study period (June-August 2018), out of 1651 patients seen, 226 patients were referred to the research staff by the clinic staff. The selection was based on specific time points of referrals. The target was to recruit five within the day, three in the morning hours and two in the afternoon hours. The clinician would refer any patient seen at 9, 10, 11 hours in the morning and two and three hours in the afternoon for screening. After screening, 8 patients were not eligible as they had been on ART for less than 6 months. Of the patients screened, 218 patients were eligible and approached for consent. Three patients refused to take part in the study and 215 patients gave consent and were enrolled. Two of the refusals did not state the reason for refusal while one patient cited time constraints as reason for refusal. Out of the 215 patients, 213 participants were included

in the final analysis as two participants were further excluded after data cleaning due to missing critical variables, mental health and adherence scores.

3.7 Sample Size

G*Power version 3.1.9 software (Faul, Erdfelder, Buchner, & Lang, 2009) was used to calculate the sample size for a multivariable logistic regression analysis. The alpha was set at 0.05 and desired power at 0.80. These estimates were based on the following assumptions: (i) 30% of non-adherent HIV-positive participants will score above threshold on a screening tool for symptoms of a common mental disorder and (ii) 10% of adherent HIV-positive participants will score above threshold on a screening tool for symptoms of a common mental disorder. Malawian studies investigating the prevalence of mental disorder among people with HIV report that between 14 % and 19 % of this population will score above threshold for symptoms of a common mental disorder (Kim et al., 2015; Stewart et al., 2007). The estimated sample size was 206 participants. However, slightly more participants were recruited per caution to ensure that estimated sample size was still maintained after potential exclusion of some participants due to data incompleteness.

3.7.1 Statistical Analysis

Statistical analysis was done using SPSS version 25. Binary variables were generated to indicate presence or absence of a particular phenomenon. Summary statistics were computed for continuous variables using mean and standard deviation (SD) or using the median and interquartile range (IQR) according to whether there was normal or skewed distribution, respectively. Frequencies were computed for categorical variables. Several variables were dichotomized. These variables included knowledge of ART where a maximum score of 3 was possible for each participant. The scores were categorized as scores 0 to 2 indicating none or insufficient knowledge, and 3 as sufficient knowledge. For PHQ-9, the binary variable computed categorized participants as not having clinically relevant depressive symptoms if the score was between 0-4 and having clinically relevant depressive symptoms if the score was from 5 to 27. In this sample, if depression symptoms were present, participants only scored in the minimal and mild depressive symptoms group. Similarly, this applied to alcohol use and participants were simply categorized as having used alcohol before or never having used alcohol before because the majority of participants (75 %) scored 0 on AUDIT with an average score of 1.25. The anxiety variable was also dichotomized as participants only scored in the minimal and mild range. The cut-off scores used for the GAD-7

were 0-4 indicating no clinically relevant anxiety symptoms and 5-21 indicating anxiety symptoms.

Self-rated adherence was calculated using the scores from five questions and the visual analogue scale (VAS). Adherence was categorized as optimal if a participant scored 0 on the five questions and a VAS percentage of 95% or above and suboptimal if a participant scored more than zero on the questions and endorsed a VAS percentage of less than 95%. Pill count adherence was categorized as suboptimal if a participant scored less than 95% and good if 95% or more. A combined adherence variable was generated combining the self-reported adherence and pill count adherence. If a participant was adherent on both self-report and pill count the combined adherence was coded as 1 and 0 if otherwise. A social support variable was generated from the 12-item Multidimensional Scale of Perceived Social Support (MSPSS) tool. The total score was divided by 12 and categorical groups coded as: 1-2.4 low support; 2.5-3.5 mild support; and 3.6-5 high support.

Two-way associations were assessed using t-tests for continuous variables and Chi-square tests for categorical variables to compare participant characteristics and mental health scores by gender. Fisher's exact test was used instances where cells had an expected count of less than 5 cases. P-values from all tests were considered statistically significant if less than 0.05 on a two-sided test. Three logistic regression models were developed to investigate the association between self-report, pill count and combined adherence and symptoms of common mental disorders. Covariates were included in the multiple logistic regression model based on the literature and natural confounders: age and sex. Covariates which were found significant in the unadjusted models or, in some cases, very close to significance were included in the adjusted models in addition to age and sex. The significance cut-off for inclusion was set at p-value of equal or less than 0.05. Odds ratios (OR) and associated 95% confidence intervals (CI) were computed from the logistic regression models.

3.8 Ethical Considerations

The study protocol was approved by University of Cape Town Human Research Ethics Committee (HREC 121/2018) and the National Health and Scientific Research Committee of Malawi (NHSRC 18/05/2063) (See Appendix). Permission to carry out the study at the Queen Elizabeth Central Hospital was sought from the hospital director and the medical director of HIV services.

3.8.1 Voluntary Informed Consent

Prior to the study, the study nurses attended a good clinical practice (GCP) training organized by the College of Medicine Research Support Centre where they were trained in ethical considerations and taking informed consent. The study nurses were also trained on study data collection procedures by the candidate. The informed consent procedure for this study was designed to maximize understanding of potential risks (see Appendix D). Participant consent forms were translated into the local language, Chichewa. The study nurses read the consent form aloud to participants. After reading the consent form and prior to seeking a signature, the staff person asked participants to summarize the study to ensure that information was understood. Individuals were provided with information on how to contact the study staff to report adverse events related to the study.

3.8.2 Confidentiality

Confidentiality was strictly maintained for all study participants. For all test results as well as for demographic and clinical data collected during the study, participants were assigned a unique identification number. Study staff involved were trained on procedures for maintaining confidentiality and asked to sign documentation to agree to protocols that ensure confidentiality for participants.

3.8.3 Potential Risks to Participants

Given the observational nature of the study, there were limited potential risks. The risk of loss of confidentiality was possible and was minimized by using unique identification numbers and by training of study staff. Participants had the right to refuse to answer specific questions on surveys if they felt uncomfortable or preferred not to answer and they were assured that they could leave the study at any time. Patients with harmful or hazardous drinking behavior (cut off score 8 or more on the AUDIT) and severe depressive symptoms (score of 15 or more on the PHQ-9) were provided with a referral to specialized support at QECH psychiatric unit. No clinical information for referrals was shared with other clinicians without the permission of the patient.

3.8.4 Potential Benefit to Individual Participants and Value to the Host Country

There was no direct benefit for participants in this study; however, participants might have benefited from being aware of their mental health status and being referred for specialized care if necessary. In this study, two participants were referred to the psychiatric unit, one for severe

depressive symptoms and the other for hazardous alcohol use. There was also no direct benefit to Malawian health system, but results may inform recommendations on improving the quality of care and strategies to improve ART adherence.

3.8.5 Adverse Event Reporting

Given the observational nature of the study, serious adverse events were unlikely. No serious adverse events associated with this study were reported. Individuals were given information on how to contact local researchers and ethics committees when they needed to report adverse incidents, and staff were trained on accurate recording and reporting of events to the investigator.

3.8.6 Data and Safety Monitoring Plan

Loss of confidentiality was a potential adverse event and several mechanisms to ensure the confidentiality of participants were set up. No identifying information was used; each participant was given a unique study ID. Data were stored on a password–protected laptop and study forms were kept in a locked file cabinet in a locked office accessible only to the PI and research assistants. Research assistants signed a confidentiality agreement form and had extensive experience in HIV research.

3.8.7 Data Sharing Plan

Data from the study were made available to MPhil supervisors at University of Cape Town and the results will be published in this dissertation and in a peer-reviewed journal.

3.8.8 Reimbursements

Participants were given refreshments (bottled water/soda) during the survey interview and 1000 Malawian Kwacha (R20) as compensation for their time away from work or other responsibilities.

CHAPTER 4: RESULTS

4.1 Participant Characteristics

A total of 213 participants were recruited with more women (n=122, 57.8%) than men (n=89, 42.2%) and an overall mean age of 42.72 (SD: 10.11) (See Table 3). Nearly three quarters of participants were either married or had a long-term partner (n=154, 74%) and in the sample, the mean number of alive children per participant was 3.23 (SD: 1.99). While most (n=197, 93.4%) had attended formal education, less than half had completed secondary education (n=84, 39.4%). The majority of participants were in informal employment within past three months (n=120, 58.3%). For HIV-related variables, the overall mean of duration on ART treatment was 78.68 months (SD=49.65). The majority of participants (n=167, 78.4%) were on the 5A ART regimen (first-line drug comprising of Lamivudine, Tenofovir and Efavirenz) and 63.7% had experienced at least one side effect from the treatment. The majority of participants (n=150, 82.4%) were knowledgeable about ART treatment.

The participant characteristics were further compared by sex. Female participants were significantly younger than male participants with a mean age of 40.83 (SD: 8.96) years as compared to 45.10 (SD: 11.04) years, (p-value=0.003). Among the males, the majority were significantly more likely to report being married or having a long-term partner (79.5%) and were less likely to be widowed or divorced (12.5%) compared to females reporting being married or having a long-term partner (70.3%) or being widowed or divorced (27.1%) (P-value=0.012). The education level completed for males was also significantly different from females with more males (48.3%) having completed secondary education compared to females (32.8%), (p-value=0.044). The mean number of live children was significantly higher for men (mean=3.63, SD 2.25) than for women (mean=2.91, SD 1.70) with a p-value of 0.013. The ART regimen for males was also significantly different from females (p-value=0.003), with more females (90%) being on first-line regimens (2A-6A) compared to males (84%) and more males (10%) being on second-line regimens (7-8A) compared to females (7%). Finally, the mean alcohol score was significantly higher for males (mean=2.51, SD= 4.51) than females (mean=0.26, SD=1.29), p-value=<0.001. There were no statistically significant differences in depression or anxiety scores between the groups.

Table 3: Participants' Sociodemographic, HIV-related and Mental Health Characteristics				
	Total (n=211) N (%)	**Male (n=89) N (%)**	**Female (n=122) N (%)**	**P-values**
Age (mean, SD)	42.72 (10.11)	45.10 (11.04)	40.83(8.96)	0.003*
Marital Status *m				0.012*
Relationship	154 (74)	70 (79.5)	83 (70.3)	
Single	10 (4.8)	7 (8.0)	3 (2.5)	
Widow/divorce	44 (21.2)	11 (12.5)	32 (27.1)	
Education *m				0.564
No	14 (6.6)	4 (4.5)	9 (7.4)	
Yes	197 (93.4)	84 (95.5)	112 (92.6)	
Education				0.044*
None	13 (6.1)	4 (4.5)	8 (6.6)	
Primary	83 (39)	26 (29.2)	57 (46.7)	
Secondary school	84 (39.4)	43 (48.3)	40 (32.8)	
Higher	33 (15.5)	16 (18.0)	17 (13.9)	
Employment *m				0.173
Unemployed	26 (12.6)	10 (11.8)	16 (13.4)	
Informal work	120 (58.3)	44 (51.8)	74 (62.2)	
Formal work	60 (29.1)	31 (36.5)	29 (24.4)	
Number of children (M, SD)	3.23 (1.99)	3.63 (2.25)	2.91(1.70)	0.013*
HIV-Related Variables				
ART knowledge *m				0.605
No	32 (17.6)	15 (19.5)	17 (16.5)	
Yes	150(82.4)	62 (80.5)	86 (83.5)	
Side effects *m				0.251
No	77 (36)	37 (41.6)	41 (33.6)	
Yes	135 (63.7)	52 (58.4)	81 (66.4)	
ART Regimen *m				0.003*
2A	7 (2.8)	4 (4.5)	3 (1.4)	
4A	2 (0.9)		2 (1.6)	
5A	167 (78.4)	61 (68.5)	105 (86.1)	
6A	10 (4.7)	10 (11.2)	0	
7A	7 (3.3)	3 (3.4)	4 (3.3)	
8A	10 (4.7)	6 (6.7)	4 (3.3)	
ART duration(months)	78.68 (49.65)	76.89 (50.51)	80.46 (49.22)	0.607
Social Support (mean, SD)	4.27 (0.54)	4.26 (0.53)	4.28 (0.55)	0.857
Mental Health Scores				
Depressive symptoms (mean, SD)	3.62 (1.84)	3.74 (1.85)	3.57 (1.83)	0.502
Yes	66 (32)	32 (48)	34 (52)	

No	140 (68)	54 (39)	86 (61)	
Anxiety symptoms (mean, SD)	3.46 (1.90)	3.58 (1.88)	3.39 (1.92)	0.450
Yes	54 (26)	22 (41)	32 (59)	
No	157 (74)	67 (43)	90 (73)	
Alcohol (mean, SD)	1.22 (3.28)	2.51(4.51)	0.26 (1.29)	<0.001*
Alcohol use	33 (16)	27 (81)	6 (19)	
No alcohol use	176 (84)	61 (35)	115 (65)	

*p<0.05

*m= missing Values
Gender= 2
Education= 2
Marital status= 5
Employment= 7
Side effects= 1
Knowledge= 31
Regimen= 10

4.2 Self-Report Adherence

Overall, 88 (41.7 %) the participants self-reported good adherence to ART. For crude odds ratios, logistic regression analysis was employed to investigate the associations between each variable and the dependent variable, self-report adherence. The crude odd ratios showed a statistically significant association with self-report adherence for two variables: age and alcohol use. For every increase in age by one year, the odds of being adherent to treatment were increased by 1.03 (OR=1.03; 95%CI= (1.00-1.06), p-value=0.050) (Table 4). Participants who scored higher on the AUDIT were less likely to adhere to ART treatment. For every increase in alcohol usage by score of one on the AUDIT, the odds of participants being adherent were 16% less (OR=0.84; 95% CI=0.78-0.98), p-value=0.018). There was no significant association between self-report adherence and the other mental health variables (anxiety and depression) in the univariate analysis. After adjusting the association by age, gender and alcohol usage, only alcohol usage showed significant association with self-report adherence. Participants who scored higher on the AUDIT were less likely to be adherent to treatment (OR=0.88; 95% CI=0.76-0.99, p-value=0.031).

Table 4: The unadjusted and adjusted associations with self-reported adherence				
	Unadjusted OR (95% CI)	**Unadjusted p-value**	**Adjusted OR (95% CI)**	**Adjusted P-values**
Age	1.03 (1.00-1.06)	0.050*	1.02 (0.99-1.05)	0.116
Gender				
Male	1.00		1.00	
Female	1.09 (0.62-1.90)	0.766	0.96 (0.51-1.80)	0.899
Marital Status				
Single	1.00			
Relationship	1.14 (0.31-4.20)	0.846		
Widow/Divorce	0.80 (0.20-3.30)	0.761		
Education level				
None	1.00			
primary	0.35 (0.10-1.16)	0.087		
secondary	0.39 (0.12-1.28)	0.119		
Higher	0.85 (0.23-3.15)	0.806		
Number of kids	1.10 (0.96-1.26)	0.187		
Duration on ART	1.00 (1.00-1.01)	0.585		
Employment				
No	1.00			
Yes	0.49 (0.21-1.14)	0.097		
Side Effects				
No	1.00			
Yes	0.80 (0.45-1.40)	0.428		
ART Regimen				
1st line	1.00			
2nd line	1.25 (0.46-3.38)	0.664		
ART knowledge				
No	1.00			
Yes	0.91 (0.42-1.96)	0.801		
Alcohol	0.84 (0.78-0.98)	0.018*	0.88 (0.78-0.99)	0.031*
Anxiety				
No	1.00			
Yes	0.56 (0.29-1.07)	0.079		
Depression				
No	1.00			
Yes	1.00 (0.55-1.81)	0.993		
Social Support	0.64 (0.36-1.12)	0.115		

*p<0.05

4.3 Pill Count Adherence

For pill count-based adherence, 161 (75.6%) participants were found to have optimal adherence. The univariate logistic regression showed that only having side-effects was significantly associated with pill-count adherence. Participants who experienced one or more side effects from the treatment were less likely to adhere than participants who reported no side effects (OR=0.34; 95%

CI (0.16-0.73), p-value=0.006). (Table 5). Alcohol use and ART knowledge were also close to being statistically significant and were included in the multivariable model. Participants who scored higher on the AUDIT were less likely to adhere than those with lower scores (OR=0.92 (0.84-1.00), p-value=0.053). ART knowledge was also at the margin of statistical significance where participants with more knowledge of ART were less likely to adhere than participates with no to less knowledge of ART (OR=0.29; 95% CI=0.09-1.02, p-value=0.054). Only side effects remained significantly associated with pill count adherence after adjusting with age, gender, side effects, ART knowledge and alcohol usage (OR=0.19; 95% CI=0.07-0.53, p-value=0.001).

Table 5: The unadjusted and adjusted associations pill count adherence

	Unadjusted OR (95% CI)	Unadjusted p-values	Adjusted OR (95% CI)	Adjusted P-values
Age	1.01 (0.98-1.04)	0.522	1.00 (0.96-1.03)	0.811
Gender				
Male	1.00		1.00	
Female	1.52 (0.81-2.86)	0.190	1.87 (0.83-4.24)	0.132
Marital Status				
Single	1.00			
Relationship	0.29 (0.04-2.33)	0.243		
widowed/divorce	0.59 (0.06-5.40)	0.638		
Education				
none	1.00			
primary	1.97 (0.58-6.70)	0.279		
secondary	2.46 (0.71-8.50)	0.153		
higher	1.44 (0.38-5.50)	0.596		
Number of kids	1.06 (0.90-1.25)	0.479		
Duration on ART	1.00 (1.00-1.01)	0.479		
Employment				
Yes	1.00			
No	0.96 (0.36-2.53)	0.928		
Side effects				
No	1.00		1.00	
Yes	0.34 (0.16-0.73)	0.006*	0.19 (0.07-0.53)	0.001*
ART Regimen				
1st line	1.00			
2nd Line	0.55 (0.19-1.58)	0.267		
ART knowledge				
No	1.00		1.00	0.133
Yes	0.29 (0.09-1.02)	0.054	0.37 (1.00-1.36)	
Alcohol score	0.92 (0.84-1.00)	0.053	1.00 (0.88-1.13)	0.968

Anxiety Score		
No	1.00	
Yes	1.06 (0.52-2.17)	0.876
Depression		
No	1.00	
Yes	1.02 (0.52-2.02)	0.95
Social Support	0.90 (0.48-1.68)	0.735

* $p<0.05$

4.4 Combined adherence (self-report and Pill Count)

Combined adherence was generally low compared to other adherence measures with only 70 (33.2%) of participants showing good adherence. For combined adherence, side effects and alcohol usage were significantly associated with combined adherence in the crude regression. Participants who experienced one or more side effects from the treatment were less likely to be adherent. The odds of participants who experienced any side effect from ART medication being adherent to treatment were 49% less than those who experienced at least one side effect (OR=0.51; 95% CI=0.29-0.93, p-value=0.027) (Table 6). Participants who scored higher on the AUDIT were also less likely to adhere to treatment. For every increase in alcohol usage by score of one on the AUDIT, the odds of participants being adherent were 15% less (OR=0.85; 95% CI=0.74-0.98, p-value=0.026). After further adjusting the model with age, gender, side effects and alcohol usage, only side effects experienced remained significantly associated with combined adherence (OR=0.45; 95% CI=0.24-0. 83, p-value=0.011).

Table 6: The unadjusted and adjusted associations with combined adherence

	Unadjusted OR (95% CI)	Unadjusted p-value	Adjusted OR (95% CI)	Adjusted P-values
Age	1.02 (0.99-1.05)	0.137	1.03 (1.00-1.06)	0.104
Gender				
Male	1.00		1.00	
Female	1.35 (0.75-2.44)	0.315	1.24 (0.64-2.43)	0.524
Marital Status				
Single	1.00			
Relationship	0.73 (0.20-2.70)	0.635		
widow/divorce	0.65 (0.16-2.70)	0.553		
Education				
none	1.00			
primary	0.63 (0.19-2.14)	0.464		
secondary	0.80 (0.24-2.67)	0.717		
higher	1.18 (0.32-4.38)	0.806		
Number of kids	1.11 (0.96-1.28)	0.147		
Duration on ART	1.00 (1.00-1.01)	0.717		
Employment				
No	1.00			
Yes	0.65 (0.28-1.51)	0.320		
Side effects				
No	1.00		1.00	
Yes	0.51 (0.29-0.93)	0.027*	0.45 (0.24-0.83)	0.011*
ART Regimen				
1st Line	1.00			
2nd Line	0.83 (0.28-2.45)	0.731		
ART knowledge				
No	1.00			
Yes	0.71 (0.32-1.55)	0.390		
Alcohol score	0.85 (0.74-0.98)	0.026*	0.87 (0.75-1.00)	0.057
Anxiety Score				
No	1.00			
Yes	0.63 (0.32-1.26)	0.192		
Depression				
No	1.00			
Yes	0.91 (0.49-1.70)	0.889		
Social Support	0.74 (0.44-1.25)	0.260		

*p<0.05

CHAPTER 5: DISCUSSION

This study explored mental health and ART adherence among HIV-positive people attending an ART clinic in Blantyre, Malawi. This chapter will highlight key findings according to the study objectives, explore the relationship of the findings with other literature, present the limitations of the study, and conclude with recommendations for further research and practice.

5.1 Summary of Key Findings

5.1.1 Prevalence of Mental Disorder Symptoms

The first objective was to estimate prevalence of probable common mental disorders (depression, anxiety and alcohol use disorder) among ART clinic attendees. For depression, there was a high prevalence of depressive symptoms among the participants with 32% presenting with minimal and mild depressive symptoms. The prevalence of anxiety symptoms was also relatively high with 26 % of participants screening positive for mild to moderate symptoms. Unlike for anxiety and depressive symptoms, the majority of participants (84%) scored 0 on the AUDIT. Consequently, the participants were only categorized according to alcohol usage based on whether they had ever used alcohol or not. Only 16% of the participants reported to have ever used alcohol.

5.1.2. ART Adherence Prevalence

Three adherence assessment methods, namely self-report, pill count and combined (self-report and pill count), were used to ascertain adherence levels among the participants. For the self-report adherence measure, 41.7% of the participants showed optimal adherence to ART treatment. A high number of participants (75.6%) showed optimal adherence levels using the pill count adherence measure, which was considerably higher than the scores on the self-report measure. Currently, routine ART adherence assessment is mostly done by pill count as stipulated in the national ART guidelines. The data from this sample suggests that this method may overestimate adherence as very few participants (33.2%) showed optimal adherence using the combined adherence measure.

5.1.3. Association between depression, anxiety and alcohol use disorder symptoms and ART adherence

This study's main objective was to examine the association between depression, anxiety and alcohol use disorder symptoms and ART adherence among ART clinic-attending HIV-positive

people. The prevalence of both depressive and anxiety symptoms among the participants was relatively high, being 32% and 26% respectively. However, there was no significant association between depression and anxiety and ART adherence across all the three adherence assessment measures. Strikingly, depression did not show any statistical significance with all the adherence measures, even after adjusting for different variables. Unlike depressive and anxiety symptoms, alcohol use was relatively low among the participants with only 16 % of participants indicating ever having used alcohol at least once in their lives. There was a significant association between any alcohol use and self-report adherence with those scoring higher on the AUDIT being less likely to be adherent (OR=0.84, p-value=0.018). Similarly, alcohol usage was also significantly associated with combined adherence with the participants who scored higher on the AUDIT more likely to be non-adherent to treatment (OR=0.85, p-value=0.026).

Apart from mental health variables, there were also other factors associated with ART adherence that showed statistical significance. Age of participants was significantly associated with self-report adherence, with older participants more likely to be adherent to treatment compared to younger participants (OR=1.03, p-value=0.050). Side effects from treatment experienced by the participants were also significantly associated with both the pill-count and combined adherence measures with those who experienced at least one side effect, less likely to be adherent (OR=0.34; p-value=0.006 and OR=0.51, p-value=0.027 respectively).

According to the socio-ecological framework, the variables included in this thesis centered on the relationship between the personal and social factors and ART adherence. The majority of variables were individual factors such as mental health variables, side effects, and the clinical variables. Social factors included social support, education and employment status. The findings show that according to the framework, only few individual factors (age, alcohol and side effects) had a significant association with ART adherence. No social factor was significantly associated with ART adherence in this study.

5.2 Relationship of key findings with literature

5.2.1 Adherence Assessment Methods

The results indicated that there were high non-adherence levels (58.3%) for the self-reported adherence measure compared to the pill count (24.4%). The self-report measure was adapted from Nel & Kagee (2013) and the low adherence levels on the self-report measure was in line with Nel & Kagee (2013) who found that 54.5 % of the participants were adherent while 45.5% were non-adherent. While some studies have shown consistence with this finding, most studies often report optimal (higher) ART adherence on self-report measures in comparison to pill count (Haberer et al., 2010; Senkomago et al., 2011; Hardy et al., 2011). For instance, a cross-sectional study in Malawi comparing self-report and pill count adherence among women living with HIV attending an ART clinic showed that 96.7% reported optimal self-report adherence, whilst only 79% of the same subjects showed good pill count adherence (McKinney et al., 2016). The self-report measure was used for the first time in Malawi, hence, there is a need for more work to understand how this will perform across other HIV populations in Malawi. There is also a need to validate sensitivity and specificity of this measure against viral load. Even though both measures have been shown to predict viral failure and suppression, they also have limitations; self-report has been associated with overestimating adherence (Minzi OM, 2008) and using the pill count also has limitations because there is possibility of some patients hiding unused pills pending clinic visits (Agot et al., 2015). As an alternative, combining both self-report and pill count has also shown to be effective in predicting viral load (Wu et al., 2014; Minzi, 2008). Further investigation into different adherence assessment methods is fundamental to determine the most effective measures that can accurately assess adherence levels among people living with HIV in low-resource settings.

5.2.2 Prevalence of Common Mental Health Problems among PLWHA

Studies have shown that mental disorders are highly prevalent among people living with HIV in LMIC (Chibanda et al., 2014). The present study was consistent with other studies showing that symptoms of mental disorders are highly prevalent among PLWHA, with 32% of participants positive for probable depression. Similarly, a recent study in Lilongwe, Malawi of 1091 HIV-positive individuals initiating on ART, found that 27% had clinically significant depressive symptoms (PHQ-9 score ≥5) (Stockton et al., 2020). This is similar to other studies in southern African that showed elevated levels of depression among HIV-positive people with ranges from

37.6% to 40.4 % of the sample sizes (Nel & Martin, 2010; Nel & Kagee, 2013). For anxiety, the present study showed that 26% of the sample had probable anxiety disorder. This is in line with a number of studies in sub-Saharan Africa (Tanzania, Ethiopia and Nigeria) that have also shown elevated levels of anxiety symptoms among people living with HIV with a range of 23.5% to 32.6% (Ngocho et al., 2019; Tesfaw et al., 2016; Adeoti, Dada & Fadare, 2018).

Alcohol consumption is also common among HIV-positive people, although in this study, 16% of the participants indicated ever having used alcohol with more males (81%) reporting alcohol usage compared to females (19%). This is similar to a cross-sectional survey by Magidson et al. (2017) which explored prevalence of alcohol usage among ART-clinic attendees in South Africa. Only 17% of the participants reported alcohol usage. Other studies have reported much higher alcohol usage among people living with HIV. For instance, a cross-sectional survey among 2920 HIV-positive people in three West African countries (Ivory Coast, Mali and Benin) showed that 37.9 % reported alcohol usage with more males (40%) compared to females (15%) as seen in the present study. Even though alcohol usage was not further categorized into harmful and hazardous drinking in this study given the small number of participants reporting alcohol use, participants who reported alcohol use were deemed at risk compared to those who scored zero on the AUDIT. However, self-reported alcohol use is susceptible to social desirability bias and amount of alcohol consumed is often underreported (Adong et al., 2019). We suspect this may have been the case in the present study, although in Malawi, population surveys have shown that general alcohol usage is relatively low with women drinking far less compared to men (Mwangomba et al., 2018). For instance, a field-based survey conducted in 2012 exploring social drinking norms in Malawi found out that 14.5% of Malawians used alcohol in the preceding year representing 27.6% of the male population and only 1.6% of the female population (Natvig et al., 2014).

5.2.3 Association between mental health disorder symptoms and ART adherence

The present study examined the association between symptoms of three common mental disorders (depression, anxiety and alcohol use disorder) and ART adherence. Depression and anxiety symptoms were not found to be significantly associated with adherence. In a number of studies, depressive symptoms have been found to be significantly associated with ART non-adherence (Uthman et al., 2014; Wagner et al., 2017; Wagner et al., 2011). The present study finding of depression not showing any association with all the three adherence assessment methods is,

somewhat, divergent from the majority of similar studies; although the symptoms reported were in the mild to moderate range according to the cut-off score on the PHQ-9, which may have accounted for the difference in findings. A recently published Malawian paper examined six-month post-ART initiation viral suppression outcomes between patients with depressive symptoms and no depressive symptoms (Stockton et al., 2021). PHQ-9 was also used to screen for depressive symptoms in this study. The results showed that there was no difference in viral suppression between the patients with depressive symptoms and those without at 6-month point. Again, this finding is consistent with the present study and highlights a knowledge huge gap on the relation between depression and ART adherence in Malawi. This implies for further studies to assess if this trend applies to other PLWHA populations in Malawi especially using the PHQ-9.

However, in line with these results, other studies in similar settings have also not found significant associations between depression and ART adherence. A cross-sectional study by Naidoo & Kitshoff. (2012) among 146 HIV-positive people in Kwazulu Natal, South Africa found that there was no significant association between high levels of depressive symptoms and non-adherence. This is despite a high prevalence of depressive symptoms in the sample with 62% of the participants having elevated levels of depressive symptoms (CES-D score ≥16) (Naidoo & Kitshoff, 2012). Similarly, in a recent study in Malawi, Stockton et al., (2020) found that there was no significant difference in viral suppression six months after ART initiation between participants with and without depressive symptoms at initiation, suggesting that adherence levels were similar across the groups.

Similar to findings reported in the present study, other studies have also not found significant associations between anxiety symptoms and ART non-adherence. Despite finding a significant association between depressive symptoms and ART non-adherence among HIV-positive people attending an ART clinic in South Africa, Nel & Kagee (2013) did not also find any statistically significant association between anxiety symptoms and ART adherence. Similarly, another study in Ibadan, Nigeria examining adherence among ART-using patients diagnosed with psychiatric disorders (depression and anxiety) found that there was no significant association between anxiety and adherence as reported by missed doses in previous one week and month. However, depression was found statistically significantly associated with depression (Adejumo et al., 2016). In addition, another study by Yunusa et al. (2014) in Sokoto, Nigeria and Pefure-Yone et al. (2013) in Yaounde,

Cameroon, both similarly found no statistically significant associations between anxiety symptoms and ART adherence.

Any alcohol use was significantly associated with ART non-adherence in the current study. This finding is consistent with numerous studies that have shown that alcohol consumption, especially harmful or hazardous drinking is strongly associated with ART treatment non-adherence (Braithwaite &Bryant, 2010; Morojele et al., 2014; Kalichman et al., 2013; Kekaletse &Morojele, 2014; Tran et al., 2014; Hendershot &Stoner, 2009). Interventions to reduce alcohol use among PLWHA are of particular significance because alcohol consumption has been shown to have a negative impact on survival of HIV-positive people. Alcohol-induced immunosuppression aggravates HIV-associated immunosuppression and heavy alcohol use is likely to amplify ART toxicity through metabolic pathways that exacerbates oxidative stress associated with liver failure, thereby, leading to increased mortality among HIV-positive people (Braithwaite & Kendall, 2010). In a longitudinal study, Kahler et al. (2017) studied direct (viral load and CD4 count) and indirect (decreased kidney function and liver fibrosis) effects of alcohol use among HIV patients on ART medication with a follow up period of six months. The results indicated that heavy drinking was associated with low CD4 count and liver fibrosis, which were mediated through decreased ART adherence levels. This further highlights the deleterious effects of harmful alcohol use among PLWHA on ART. To address this challenge, different interventions have been studied to reduce alcohol use among PLWHA to improve adherence. In a meta-analysis of 21studies, Scott-Sheldon et al., (2017) evaluated the efficacy of behavioral interventions to reduce alcohol use among PLWHA. The findings demonstrated that behavioral interventions were successful in reducing alcohol consumption among PLWHA, improving ART adherence and reducing plasma viral load in intervention groups compared to controls. Similarly, in the two recent clinical trials, cognitive behavioral therapy and motivational enhancement therapy interventions were successful in reducing alcohol consumption, improving ART adherence and viral suppression among PLWHA (Go et al., 2020; Glasner et al., 2020). This demonstrates that further investigation into efficacy of behavioral interventions to reduce alcohol consumption among PLWHA is of paramount importance especially in low-resource settings like sub-Saharan Africa.

Apart from the mental health variables, age and side-effects were also found to be statistically significantly associated with adherence in the current study. Side effects were associated pill count

and combined non-adherence. This is also in line with other studies that have shown that experiencing side-effects from ART is linked to ART non-adherence (Cauldbeck et al., 2009; Adeniyi et al. 2018). A systematic review and meta-analysis of 19 studies examining the impact of treatment-related adverse events (AEs) on ART adherence showed that specific AEs like fatigue, taste disturbance and nausea were significantly associated with poor adherence (Al-Dakkak et al., 2013). Similarly, a qualitative study in Lilongwe, Malawi examining barriers and facilitators to ART adherence among pregnant women found that most women cited side-effects as the main reason for defaulting from ART (Kim et al., 2016). In this study, older participants were more likely to be adherent compared to younger participants. This is also consistent with a meta-analysis of 20 studies which reported that older individuals with HIV are at a significantly reduced risk of non-adherence compared to younger PLWHA both during short and long-term assessments (Ghidei et al., 2013). Similarly, another meta-analysis of 20 African studies comparing adherence between older and younger PLWHA found that a higher proportion of older patients were adherent to ART compared to younger patients in the studies using objective measures (medication possession ratio and clinician count) (OR= 1.01; 95% CI= 0.94-1.09) (Soomro et al., 2019) Consistent with the present study, a cohort study of pregnant and breastfeeding women starting ART at 13 heath facilities in Malawi found that ART initiation at younger age was a risk factor for non-adherence (Haas et al., 2016). This highlights the need for education regarding ART side effects and targeted inquiry by HIV care providers at follow-up visits, as well as intensive support for younger people starting ART.

5.3 Study Limitations

The study had a number of limitations. Firstly, the study data collection may have been hampered by social desirability bias. The surveys were administered by two research nurses who were, however, not part of the ART clinic staff. The research nurses explained their research roles to the participants during the introductions and that they were not directly involved with clinical care at the clinic. However, it is probable that responses to survey questions might have been influenced by social desirability and this might have been specifically amplified with medical personnel (research nurses) administering the surveys. This could partly be the reason for participants scoring low on the mental health and alcohol use screening tools. This could also partly explain why depressive symptoms were not found statistically significant in the present study due to the low

scores. Secondly, the present study used GAD-7 and AUDIT for screening anxiety and alcohol use disorder symptoms. Although these tools have been used in previous studies in Malawi and similar Southern African settings, their validity and reliability in Malawian setting and population has not been investigated. Thirdly, the present study was a cross-sectional survey. This poses a challenge in establishing the temporality of the common mental disorder symptoms and ART adherence as compared to other longitudinal study designs. As much as it is well established that depression, anxiety and alcohol use may result in ART non-adherence, it could be the other way around that non-adherence to ART results in PLWHA experiencing common mental disorder symptoms due to worsening health or other reasons. Further longitudinal studies would be useful in exploring this question. Fourthly, the study was conducted at only one ART clinic. Consequently, the findings cannot be generalized across the whole ART clinic-attending population of Malawi. Fifthly, the present study had a limited sample size. Power calculation based on previous studies conducted in Malawi only indicated a small sample size. Large sample size studies have the advantage of high statistical power which gives greater precision and reliable results (Royall, 1986). Therefore, there is a need to conduct large studies among ART clinic-attending population. Lastly, the present study did not investigate the mediating effects of other non-mental health factors such as knowledge and social support in the association between mental disorder symptoms and ART adherence. A much more complex analysis to establish mediating effects of other associated factors on the relationship between common mental disorder symptoms and adherence would have been desirable. On the other note, the study had some strength. Firstly, this is the first paper in Malawi that assessed three mental health problems in relation to ART adherence at the same time. Most of the studies have mainly focused on depression only. Secondly, the study used three adherence measures, self-report, pill count and combined, which balanced both subjective and objective approaches to ART adherence assessment.

5.4 Recommendations for future research and practice

The current study findings add to the growing evidence that common mental disorder symptoms are highly prevalent among HIV-positive people who are on ART. This implies that that there is a need to routinely screen ART clinic attendees for mental disorder symptoms. In Malawi, ART clinic attendees are currently not routinely screened for mental disorder symptoms. A recent pilot study at two public ART clinics in Lilongwe, Malawi has demonstrated that it is feasible for

clinicians to administer the PHQ-9 during routine clinical consultations (Pence et al., 2019; Kulisewa et al., 2019). This calls for further investigation into the feasibility of screening ART clinic attendees for other mental disorder symptoms like anxiety as well as alcohol use to assess whether scaling up screening across all ART clinics in Malawi is possible. Secondly, there is also a need to come up with innovative ways to address the shortage of mental health specialists especially in primary health care settings in limited-resource setting like Malawi. Task-shifting of mental health services to lay health workers has been proven to be effective in addressing the screening and treatment gap among PLWHA. For instance, in Zimbabwe, training nurses, community health workers and traditional medicine practitioners to screen for harmful alcohol and drug use was found to be feasible and acceptable (Duffy et al., 2017). Similarly, in South Africa using a task-shifting model, a group-based counselling intervention among HIV-positive patients with depressive symptoms delivered by trained lay HIV counsellors led to significant improvements in depressive symptoms as measured by the PHQ-9 (Petersen et al., 2014). Again in Zimbabwe, a problem-solving intervention for depression delivered by lay adherence counselors was found acceptable by patients and led to improvement in depression symptoms and ART adherence (Nyamayaro et al., 2020). Further research into the feasibility and effectiveness of task-shifting interventions in detection and management of mental disorders using lay health workers in resource-constrained settings like sub-Saharan Africa is critical.

Thirdly, the effectiveness and efficacy of integrating mental health services and HIV care in resource-constrained settings needs to be further explored. Currently, there is very limited literature on the integration of mental health services into HIV care in limited-resource settings. Studies conducted in Cameroon and Uganda have shown promising findings on the feasibility and effectiveness of integrating depression treatment and HIV care (Pence et al., 2014; Nakimuli-Mpungu et al., 2015). In Malawi, a pilot quasi-experimental study was conducted to evaluate effectiveness of integrating depression treatment into routine HIV care (Udedi et al., 2019). Preliminary results revealed that screening for depression during HIV routine care was feasible. However, as reported by Stockton (2020), depression management (counseling and antidepressants) did not reveal promising results for HIV care outcomes, such as retention and viral suppression when compared between the intervention and control groups. The program was deemed not feasible and sustainable due to health systems challenges (Stockton, 2020). This calls

policy makers to scrutinize and review the current HIV health system structure and to champion further research using implementation science approaches and robust designs such as randomized clinical trials to evaluate the feasibility and effectiveness of integrating depression treatment into HIV care in the Malawian health system. Considering the huge shortage of mental health personnel in Malawi, it is also important to study the feasibility of using lay health workers in the management of mental health problems among PLWHA. For instance, the Friendship Bench program in Zimbabwe has been successful and proven feasible where lay health personnel provide mental health interventions (Chibanda et al., 2016). Strikingly, the limited literature on evaluating integration of mental health services into HIV care in limited-resource setting has largely focused on depression treatment. This calls for additional research to evaluate the feasibility and effectiveness of integrating treatment of other common mental disorder symptoms, including anxiety and symptoms of hazardous or harmful alcohol use into routine HIV care.

Fourthly, as older participants were found to be more likely to be adherent compared to younger participants in the present study, there is a need for HIV care providers to design innovative adherence-enhancement interventions targeting younger PLWHA. Approaches like text messaging and mobile phone applications have shown promising efficacy, feasibility and acceptability in improving adherence among the youth living with HIV/AIDS (Badawy et al., 2017). The feasibility and effectiveness of using these approaches with limited resources needs to be explored.

Fifthly, side effects from treatment were also associated with ART non-adherence in the current study. HIV care providers could adopt the policy of routinely ask HIV-subjects if they are experiencing any side effects during their visits as subjects might not report the side-effects due to not being asked by the clinicians (Fonsah et al., 2017). There is a huge need for service providers to adequately educate PLWHA especially during treatment initiation on the potential side effects associated with the regimen provided. Interventions for coping skills and self-management of HIV treatment adverse events need to be explored as some studies have shown that such interventions are effective in reducing non-adherence to treatment (Johnson et al., 2011). There is also a need to further develop and improve availability of optimized and less toxic regimens in low-resourced settings to reduce the pill burden, toxicity and side effects in order improve adherence and overall quality of life for PLWHA (Nachega et al., 2011).

Lastly, the socio-ecological framework used in this study only covered social and individual factors. Future research should also expand to include structural and health factors that have shown to impact ART adherence (Musheke et al., 2012). Usage of other recent prominent theories like COM-B and the behavior change wheel to assess relationship between different factors and ART adherence will also be commendable for development of targeted interventions to adherence (Mitchie et al., 2011; Mitchie et al., 2014).

5.5 Conclusion

The present study aimed at examining the association between common mental disorder symptoms (depression, anxiety and alcohol use) and ART adherence among PLWHA attending an ART clinic in Blantyre, Malawi. The findings show that mild to moderate symptoms of depression and anxiety were highly prevalent among PLWHA. Alcohol use, younger age group and experiencing side-effects from ART were statistically significantly associated with ART non-adherence.

The study adds to the body of evidence that mental health problems are highly prevalent among PLWHA. Further research is required to investigate how depression, anxiety and any alcohol use may be associated with ART adherence among PLWHA in a Malawian population. The current study also highlights the need to routinely screen PLWHA for mental health problems and offer interventions targeting younger PLWHA and education regarding management of side effects. Further research using advanced designs such as randomized clinical trials incorporating implementation science approaches is also needed to evaluate feasibility and effectiveness of integrating mental health services for common mental disorders and alcohol use into HIV care to improve ART adherence and wellbeing among PLWHA in Malawi.

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APPENDICES

APPENDIX A: SCREENING FORM

1. How old are you?	_____ 18 years or older(eligible) □ <18 years old □
2. Are you HIV positive?	Yes □ No □
If Positive, 3. Are you currently taking ART	Yes □ No □
4. How long have you taken ART for? or do you remember when you started taking ART for?	6 months or more □ Less than 6 months □
5. Are you attending this clinic (QECH) for ART services	Yes □ No □
Screening should be conducted privately, ask patients permission first before asking the questions. Any red response woud mean patient is ineligible to participate in the study.	

APPENDIX B: SURVEY QUESTIONNAIRE

I. **Socio-demographic & clinical characteristics questionnaire**

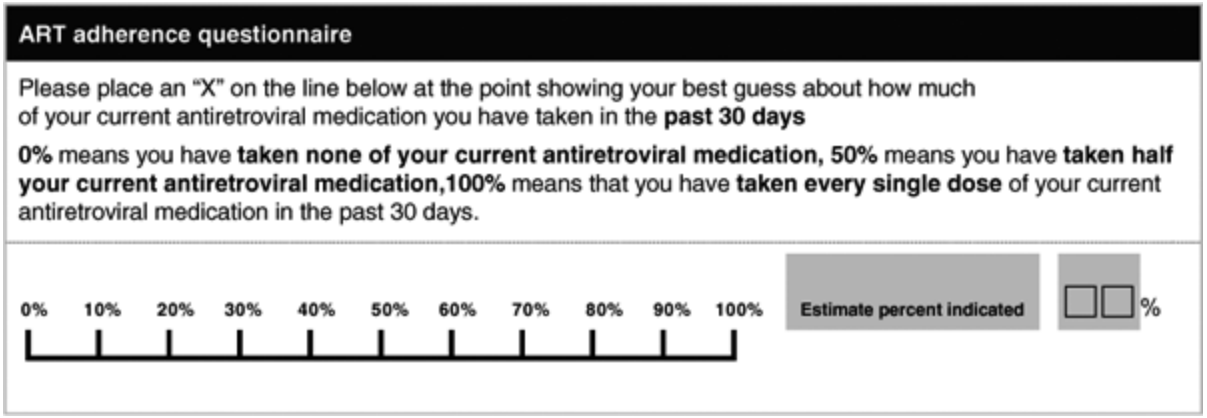
Socio-demographics	
Gender	☐Male ☐Female
What is your marital status	☐ Single or no long-term partner ☐ Married or long-term partner ☐ Other (widowed, divorced, separated) ☐ Unknown/refuses to answer
How many living children do you have, including children you are caring for as if they are your own?	_____
Have you ever attended formal education?	☐yes ☐No
What is the highest level of school you attended?	☐None ☐Primary School ☐Secondary ☐Higher
What is the highest class you completed?	_____
Did you work for pay this week (you received money for the work you did)?	☐Yes ☐ No
How would you describe your work over the past 3 months?	☐ Unemployed ☐ Working informally

	□ Working formally □ Unknown/refuses to answer
Clinical characteristics	
When you were first diagnosed with HIV?	Date: _____/_____/_____
When did you start taking ART?	Date: _____/_____/_____
Have you experienced any of the following problems when taking ARVs that you believed came from the treatment?	☐ Nausea or vomiting ☐ Skin rash ☐ Difficulty sleeping ☐ Dizziness ☐ Sadness or depressed mood ☐ No side effects experienced ☐ Participant did not answer??
ART Knowledge	
1. For how long is ART needed?	☐ Don't know ☐ 1 month ☐ Until the person regains a healthier immune system ☐ Forever
2. Does ART help to protect people with HIV from getting sick?	☐ **Yes** ☐ **No** ☐ **Don't Know**

	☐
3. Do you think it is best for the Viral Load test to be	☐ **To be as low as possible** ☐ **To be as high as possible** ☐ **Don't know**

II. ART adherence self-report Questionnaire

1. During the last 2 weeks, did you forget to take your HIV medications?
   a. Always b. Sometimes c. Never
2. When you feel better, do you sometimes stop taking your HIV medications?
   a. Always b. Sometimes c. Never
3. Sometimes if you feel worse, do you stop taking your HIV medications?
   a. Always b. Sometimes C. Never
4. Did you forget to take any of your HIV medications over the past weekend?
   a. Always b. Sometimes c. Never
5. How many doses of your HIV medication have you missed in the past 7 days? ___
6.



III. MENTAL HEALTH SCREENING TOOLS

a) DEPRESSION (PHQ-9)

	Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed, or hopeless	0	1	2	3
3	Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4	Feeling tired or having little energy	0	1	2	3
5	Poor appetite or overeating	0	1	2	3
6	Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7	Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8	Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9	Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

A11 – PHQ9 total score ☐

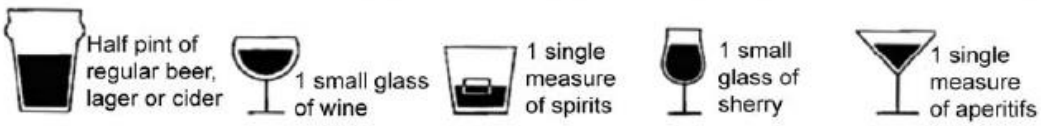
b) ANXIETY DISORDER (GAD-7)

	Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1	Feeling nervous, anxious or on edge	0	1	2	3
2	Not being able to stop or control worrying	0	1	2	3
3	Worrying too much about different things	0	1	2	3
4	Trouble relaxing	0	1	2	3
5	Being so restless that it is hard to sit still	0	1	2	3
6	Becoming easily annoyed or irritable	0	1	2	3
7	Feeling afraid as if something awful might happen	0	1	2	3

GAD7 total score

c) ALCOHOL USE DISORDER (AUDIT)

[Prompt to participant] This is one unit of alcohol…



…and each of these is more than one unit

Questions	Scoring system					Your score
	0	1	2	3	4	
How often do you have a drink containing alcohol?	Never	Monthly or less	2 - 4 times per month	2 - 3 times per week	4+ times per week	
How many units of alcohol do you drink on a typical day when you are drinking?	1 -2	3 – 4	5 - 6	7 - 9	10+	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	

How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you needed an alcoholic drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	

Have you or somebody else been injured as a result of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

Scoring: 0 – 7 Lower risk, 8 – 15 Increasing risk,

16 – 19 higher risk, 20+ possible dependence

TOTAL Score: _____

IV) Multi-dimensional scale of perceived support (MSPSS)

Instructions: We are interested in how you feel about the following statements. Read each statement carefully. Indicate how you feel about each statement.

Circle the "1" if you Very Strongly Disagree
Circle the "2" if you strongly disagree
Circle the "3" if you mildly disagree
Circle the "4" if you are Neutral
Circle the "5" if you mildly agree
Circle the "6" if you strongly agree
Circle the "7" if you Very Strongly Agree

Statement	Very strongly agree	Strongly disagree	Mildly disagree	neutral	Mildly agree	Strongly agree	Very strongly agree
1. There is a special person who is around when I am in need.	1	2	3	4	5	6	7
2. There is a special person with whom I	1	2	3	4	5	6	7

can share joys and sorrows.							
3. My family really tries to help me.	1	2	3	4	5	6	7
4. I get the emotional help and support I need from my family.	1	2	3	4	5	6	7
5. I have a special person who is a real source of comfort to me.	1	2	3	4	5	6	7
6. My friends really try to help me.	1	2	3	4	5	6	7
7. I can count on my friends when things go wrong.	1	2	3	4	5	6	7
8. I can talk about my problems with my family.	1	2	3	4	5	6	7
9. I have friends with whom I can share my joys and sorrows.	1	2	3	4	5	6	7
10. There is a special person in my life that cares about my feelings.	1	2	3	4	5	6	7
11. My family is willing to help me make decisions.	1	2	3	4	5	6	7
12. I can talk about my problems with my friends.	1	2	3	4	5	6	7

Data extraction table (patient records)

Date	Study ID #	Pill count Results (%)	Self-report (%)	Overall adherence (pill count+ self-report (%)

APPENDIX C: INFORMED CONSENT

Please find below the study consent forms. The consent form pertinent to the study participants has been translated to Chichewa.

CONSENT TO PARTICIPATE IN RESEARCH – PATIENT PARTICIPANT (English version)

INFLUENCE OF MENTAL HEALTH ON ART ADHERENCE AMONG HIV POSITIVE PEOPLE ATTENDING ART FACILITY IN BLANTYRE, MALAWI

INTRODUCTION

You are being requested to take part in this research project. Please make sure that you understand well information presented here. If you have any questions or do not understand any part of this study, please do not hesitate to ask study staff or provider. Your participation in this research project is voluntary and you are free to decline.

Why is this study being done?

This study is being carried out to find out whether being depressed, anxious or problem drinking has influence on the medication-taking behavior of people living with HIV/AIDS.

Why are you being asked to take part?

You have been asked to participate in this study because you are at least 18 years of age; you are HIV positive and have been on ART for at least the past six months.

How many people will take part in the study?

206 people attending this clinic will be asked to take part in the study

How long will you be in the research study?

You will only be requested to take part during your clinic visit today by taking part in a survey interview that will take approximately 20-30 minutes.

What will happen if you decide to take part in the study?

If you agree to participate in this study, we will ask you to answer some questions for about 20 to 30 minutes, and then we are also request that we may ask your doctor/medical officer to write down your pill count on a card for us. (Your name will not be on the card, but will have a special study number.) The questions will include the following: questions about how well you take your ART, questions about whether you feel sad or anxious, whether you use alcohol and if so how much, and questions about you, such as age, how long you have taken ART, and what type of support you have from other people. You will also be asked by the doctor about how many pills you have left over from your last collection.

What are the potential risks or discomforts you can expect from this study?

Participation in this study may involve some added risks or discomforts. These may include:

Discomfort associated with answering questions

You may have some discomfort when answering questions about your health, HIV diagnosis, mental health and your medication taking behavior. If there are any questions that are too uncomfortable to answer, you may choose not to answer. The questions will be asked in a private place where no other patients or health center staff will hear your answers. If the questions show that you are depressed or may be at risk due to high alcohol use, you will be provided with a referral letter to QECH mental health clinic (Room 6) for a confirmatory review, counseling and treatment by a registered psychiatric clinician.

Inconveniences associated with time to take the Survey

As mentioned earlier, the survey will take approximately 20-30 minutes. You may feel inconvenienced by extending your clinic visit time to complete the survey. . The survey will be kept reasonably short to minimize the time you spend here and your number in the waiting line will be kept to avoid starting at the back of the line after completing the survey interview.

What are the potential benefits you can expect from the study?

There are no direct benefits to you from participating in this interview; however, if you have depression or other mental health problems, these will be identified and you will be referred for specialized mental health care at QECH psychiatry unit for further support.

What are the potential benefits to society?

Information obtained from this study may be beneficial to others in Malawi since findings will help to identify better ways of supporting medication behavior and promote checking patients for mental health problems and able to receive mental health help at the ART clinic.

What will happen if I decide to withdraw from the study?

Your participation in this research study is **VOLUNTARY.** If you choose not to be in the study, it will not affect your relationship with your provider, hospital, or health center, or your right to health care. You are free to stop participating in the study at any time and can continue to receive health care from the same provider and clinic where you currently receive care. The study staff may stop your participation in this study if he/she feels this is best for your health and safety.

What other choices do you have?

You may decide not to take part in this study. If you decide not to take part in the study, you will still receive the care you need and ART from your current provider. Not taking part in the study will not influence your care in any way.

What are the costs of participating in this study?

There are no costs to participate in this study.

Will you receive any reward for taking part in this study?

You will receive refreshment (soda or bottled water) during the survey interview and will be compensated for time taken to complete the survey with 1000 MK.

WILL INFORMATION ABOUT YOU BE KEPT CONFIDENTIAL?

The researchers are the only people who will know about your or any information that you have provided in this study. However, if we find that there are possible risks to you or to others; specific information about you may be made available to providers or relevant authorities.

The principle investigator will be responsible for ensuring that rules related to confidentiality are followed. Any violation of confidentiality will be reported to relevant representatives of the College of Medicine Research & Ethics Committee (COMREC) and Human Research Ethics Committee, University of Cape Town. When the results of this research study are published or discussed in meetings, no information will be included that would reveal your identity. Any paperwork related to the study will be kept in a locked cabinet in a locked office. Only staff members of the study will have access to this information. A code will be assigned to each individual participating in the study. This code will be stored on a computer in a locked file. The key to unlock the information will only be known by the research staff. All data entered into a computer will be entered using this code, so information will no longer have any information that can identify you such as your name.

What will happen after the study?

All study paperwork will be destroyed five years after the study is completed.

WHO TO CONTACT IF YOU HAVE QUESTIONS ABOUT THIS STUDY?

Dennis Chasweka

Mobile: 265991492070

College of Medicine

P/Bag 360

Chichiri

Blantyre

If you have any questions about your rights while taking part in this study, please contact:

DR D Kathyola

National Health Sciences Research Committee

+265 88 834 4443

P.O. Box 30377

Capital City, Lilongwe 3, Malawi

UCT Faculty of Health Sciences Human Research Ethics Committee
021 406 6338

SIGNATURE OF THE PARTICIPANT

I have read (or someone has read to me) all of the information provided above. I have been given an opportunity to ask questions, and all of my questions have been answered to my satisfaction. I have been given a copy of this form.

BY SIGNING THIS FORM, I WILLINGLY AGREE TO PARTICIPATE IN THE RESEARCH STUDY:

_____

Name of Participant

_____

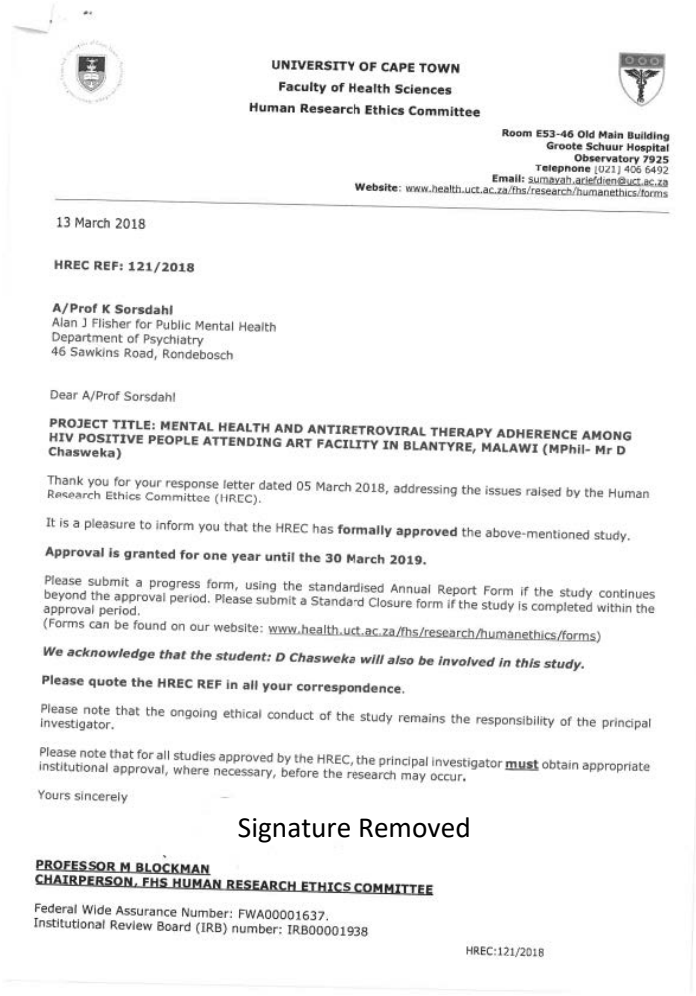
Name of Legal Representative (if applicable)

_____ _____

Signature of Participant or Legal Representative Date
(Day/Month/Year)

APPENDIX D: ETHICAL APPROVALS

1) UCT APPROVAL



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

13 March 2018

HREC REF: 121/2018

A/Prof K Sorsdahl
Alan J Flisher for Public Mental Health
Department of Psychiatry
46 Sawkins Road, Rondebosch

Dear A/Prof Sorsdahl

PROJECT TITLE: MENTAL HEALTH AND ANTIRETROVIRAL THERAPY ADHERENCE AMONG HIV POSITIVE PEOPLE ATTENDING ART FACILITY IN BLANTYRE, MALAWI (MPhil- Mr D Chasweka)

Thank you for your response letter dated 05 March 2018, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 March 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: D Chasweka will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC:121/2018

2) National Health Sciences Research Committee-Malawi

Telephone: + 265 789 400
Facsimile: + 265 789 431

All Communications should be addressed to:

The Secretary for Health and Population

In reply please quote No.

.....

MINISTRY OF HEALTH AND POPULATION
P.O. BOX 30377
LILONGWE 3
MALAWI

21 June, 2018

Dennis Chasweka
University of Cape Town

Dear Sir / Madam

Re: Protocol # 18/05/2063: Mental Health and Antiretroviral Therapy Adherence Among HIV Positive People Attending ART Facility in Blantyre, Malawi

Thank you for the above titled proposal that you submitted to the National Health Sciences Research Committee (NHSRC) for review. Please be advised that the NHSRC has **reviewed** and **approved** your application to conduct the above titled study.

- **APPROVAL NUMBER : 2063**
- The above details should be used on all correspondences, consent forms and documents as appropriate.
- **APPROVAL DATE : 21/06/2018**
- **EXPIRATION DATE**
  This approval expires on **20/06/2019**. After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the NHSRC Secretariat should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING:** All serious problems having to do with subject safety must be reported to the NHSRC within 10 working days using standard forms obtainable from the NHSRC Secretariat.
- **MODIFICATIONS**: Prior NHSRC approval using forms obtainable from the NHSRC Secretariat is required before implementing any changes in the protocol (including changes in the consent documents). You may not use any other consent documents besides those approved by the NHSRC.
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the NHSRC using standard forms obtainable from the NHSRC Secretariat.
- **QUESTIONS**: Please contact the NHSRC on phone number *+265 888 344 443* or by email on mohdoccentre@gmail.com.
- **OTHER**: Please be reminded to send in copies of your final research results for our records (Health Research Database).

SECRETARY FOR HEALTH
2018 -06- 21
P.O BOX 30377, CAPITAL CITY, LILONGWE 3

Kind regards from the NHSRC Secretariat.

Signature Removed

For: **CHAIRPERSON, NATIONAL HEALTH SCIENCES RESEARCH COMMITTEE**
Promoting Ethical Conduct of Research