College of Medicine

Burden of and factors associated with virological failure among HIV positive patients on antiretroviral therapy (ART) in Nsanje district, Malawi

By

Shupe Mphande

(Bachelor of Science in Environmental Health)

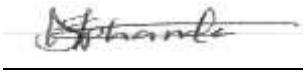
A Dissertation Submitted to the School of Public Health in Partial Fulfilment of the Requirements of the Master of Public Health Degree

18th August, 2021

DECLARATION

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

Name of Candidate: Shupe Mphande

Signature: 

Date: 5th May, 2021

CERTIFICATE OF APPROVAL

The thesis of Shupe Mphande is approved by the Thesis Examination Committee:

_____

Prof. Fanuel Lampiao

(Chairman, Post Graduate Committee)

_____

Prof. Adamson S. Muula

(Supervisor)

_____

Dr. Evanson Z. Sambala

(Internal Examiner)

_____

Dr. Charles Mangani

(Head of Department)

ACKNOWLEDGEMENTS

I wish to acknowledge the support of Prof. Adamson S Muula, my academic supervisor for his guidance throughout preparation of this research report. I also thank Nsanje DHO for granting permission to use their viral load database, registers, master cards and the support rendered during data collection. Special thanks to Bintel analytics for their statistical support. My acknowledgement would be incomplete without as a special thanks to family for their prayers and support not forgetting friends who have contributed to this success in one way or another. I salute you all.

ABSTRACT

In efforts to fight HIV, many countries including Malawi started implementation of universal ART eligibility for all HIV infected individuals as a strategy for reaching the 90-90-90 targets. This led to the increase in ART coverage hence intensifying the need for scale-up of ART monitoring, for which the current gold standard is Viral Load (VL) testing. Despite the increasing access to ART and VL monitoring, numerous studies have demonstrated suboptimal levels of viral suppression (VS) in different populations in many low-resource settings. Therefore, this research will help to determine the burden of virological failure and focus on factors leading to virological failure which will in turn lead to better targeting strategies and policy change.

The main objective of the study was to determine the burden of virological failure and factors associated with virological failure among HIV patients on ART in Nsanje district.

This was a cross sectional quantitative study using Laboratory information system database, ART master cards and registers. The study targeted HIV positive patients on ART for > 6 months from July 2015 to June 2019 in 14 facilities in Nsanje district. The criteria for the study was a VL result within the stated period. Data was analyzed using STATA version 16.

451 participants were enrolled in this study. 267(59.2%) participants were married, and 278 (61.6%) started ART due to WHO clinical stage. Of the 451 study participants, 321(71.2%) failed to achieve viral suppression (VL=<1000 copies). In univariate analysis, age at ART initiation, occupation (OR 0.203, 95% CI 0.11, 0.39; p<0.003), marital status, duration on ART (OR 0.55, 95% CI 0.33, 0.92; p=0.023) and ART adherence (OR 5.125, 95% CI 3.01, 8.74; p<0.0001) were associated with VF. Age and Fair/poor adherence (AOR 4.221, 95% CI 2.41, 7.38; p<0.0001) was statistically significant in multivariate analysis.

Age, ART adherence, marital status, occupation and duration on ART were identified as some of the factors associated with VF. Proper strategies should be developed in order to reduce VF and improve adherence.

TABLE OF CONTENTS

LIST OF TABLES

DEFINITION OF TERMS AND CONCEPTS

Acquired Immunodeficiency Syndrome (AIDS): AIDS is a disease caused by infection with HIV. AIDS results in severe damage to the immune system, leaving the body vulnerable to life threatening.

Antiretroviral Therapy (ART): Treatment with antiretroviral (ARV) drugs that inhibit the ability of HIV to multiply in the body, leading to improved health and survival among HIV-positive persons.

Enhanced Adherence Counselling (EAC): This is one of the strategies used to improve adherence in patients with confirmed High viral load. The main aim is to identify ART patients who fail to suppress HIV replication due to poor adherence from those truly failing as a result of drug resistance.

High Viral Load (HVL): A viral load of 1000 copies per ml and above

Human Immunodeficiency Virus (HIV): The Virus that cause AIDS. It can be transmitted from person to person through blood, semen, vaginal fluids, and breast milk. It weakens the immune system by attacking the CD4 cells, leaving the HIV-positive person vulnerable to illnesses

HIV Drug Resistance (DR): Ability of HIV to mutate and multiply itself in the presence of antiretroviral drugs. HIV resistance may be acquired or transmitted to one another.

HIV Viral Load (VL): The amount of HIV in a sample of blood plasma. It is reported as the number of HIV RNA copies per milliliter of blood.

Routine Viral Load Monitoring: It's a way of monitoring progress on ART routinely according to the national HIV Guidelines. It is done at 6 months, 2 years and thereafter every two years.

Targeted Viral Load Monitoring (TVL): It's a VL monitoring strategy used to confirm suspected treatment failure based on clinical and/ or immunological criteria and can reduce inappropriate switching to second-line ART.

Treatment Failure (TF): The inability of the ART regimen to control HIV infection leading to progression of disease after initiation on ART. It can be categorized into clinical failure, immunologic failure, virological failure or any combination of the three.

Viral Load Suppression (VLS): An HIV viral load of less than 1000 copies per ml.

Virological Failure (VF): A type of HIV treatment failure. It occurs when ART fails to suppress and sustain a person's viral load to less than 1000 copies per milliliter.

ABBREVIATIONS/ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
AOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
ARV	Antiretroviral
CAG	Community ART Groups
CD4	CD4+ T Cells
CHAM	Christian Health Association Management
CI	Confidence Interval
COMREC	College of Medicine Research and Ethics Committee
EFV	Efavirenz
EAC	Enhanced Adherence Counselling
EMR	Electronic Management Records
HIV	Human Immunodeficiency Virus
HVL	High Viral Load
IQR	Interquartile range
IAC	Intensive Adherence Counselling
LAC	Latin American Countries
LMIC	Low and Middle Income Countries
LIMS	Laboratory Information Management System
MSF	Medecins Sans Frontieres
NGO	Non-Governmental Organization
NVP	Niverapine

OR	Odds Ratio
UK	United Kingdom
UNAIDS	Joint United Nations program on HIV/AIDS
RVL	Routine Viral Load
SPSS	Statistical Product and Service Solutions
TB	Tuberculosis
TVL	Targeted Viral Load
VL	Viral Load
VF	Virological Failure
VS	Viral Suppression
WHO	World Health Organization

CHAPTER 1: INTRODUCTION AND OBJECTIVE OF THE STUDY

1.1 Background and Introduction

Human immunodeficiency virus (HIV) is a leading cause of global burden of deaths around the world. In 2017 an estimated 36.9 million people were living with HIV (including 1.8 million children) with a global HIV prevalence of 0.8% among adults [1] nearly 71% of the global total were from the Sub-Saharan Africa [2]. Over the past years, there has been efforts to provide access to antiretroviral therapy (ART) for HIV infected individuals in sub-Saharan Africa, the region with the highest HIV burden [3]. Malawi is among the sub-Saharan Africa countries burdened with HIV infection, with a prevalence of 10.6% of those aged 15–64 infected [4]. An estimated 834,000 Malawians have died of AIDS since the start of the epidemic in the country (1985-2014) [5].

In 2014 the Joint United Nations Programme on HIV/ AIDS (UNAIDS) set new targets towards elimination of HIV, including diagnosis of 90% of HIV infected individuals, access to treatment for 90% of identified HIV infected persons, and 90% viral suppression among those initiated on treatment [6]. These targets have since been adopted by several countries including Malawi in 2016. In an effort to control the HIV epidemic and meet the ambitious "90-90-90" targets set forth by the UNAIDS in 2014 [6], low and middle income countries (LMICs) have rapidly expanded the number of individuals on antiretroviral therapy (ART). Globally, the number increased by an estimated 2.3 million to more than 21.7 million people on ART between the end of 2017 and up from 8million in 2010 [1]. In efforts to scale up further, Malawi started implementation of universal ART eligibility for all HIV infected individuals as a strategy for reaching the 90-90-90 targets [6,7]. Thus from 2016, all HIV infected Malawians were universally eligible for ART. This led to the increase in ART coverage hence intensifying the need for scale-up of ART monitoring,

for which the current gold standard and World Health Organization (WHO) recommendation is viral load (VL) testing [8].

Efforts to reach UNAIDS' treatment and viral suppression targets have increased demand for viral load (VL) testing [9]. This is despite VL testing coverage remaining low among most parts of the world with only half of the people on ART receiving an annual test [10]. In sub Saharan Africa only 55% of the people living with HIV had access to VL testing as of 2016 [11]. Efforts to increase access and demand for VL were made in different countries. A study conducted in central and Southern Malawi established a 164% increase in mean number of VL testing in a month with a simple quality improvement program [12]. The current Malawian HIV national guidelines recommend that viral load testing be performed 6 months after ART initiation, and after every 12 months [13]. A detectable or non-suppressed VL (≥1000 copies/ml) in a patient who has been on ART for at least six months can indicate either therapeutic failure due to antiretroviral (ARV) resistance or poor adherence to treatment in Malawi [7]. To distinguish between these two conditions, a patient with a detectable VL undergoes intensive adherence support followed by retesting after 3 months [7,14]. According to the WHO guidelines, patients whose VLs are not suppressed at retesting can be classified as having virological failure (VF) due to probable drug resistance, and should be switched to second line therapy [3].

Despite the increasing access to ART, numerous studies have demonstrated suboptimal levels of viral suppression (VS) in different populations in many low-resource settings [15,16]. In Eastern and Southern Africa, for example, UNAIDS estimates that 65% of people living with HIV have achieved viral suppression (VS) as of 2019 [17] Similarly a South African study showed that almost

85% of HIV infected patients in care and on first line, had achieved viral suppression [18]. A national study conducted in Malawi from 2015 to 2016 established that 68.3% adults on ART are viral suppressed. However, 2019 UNAIDS estimates shows a viral suppression of 72% for all ages and 48% among children in Malawi [17]. On the other hand only 55% achieved viral suppression in United States in 2013 [19] while 86.6% achieved VS in European and Asian countries [20].

The 65% viral suppression in Eastern and Southern Africa and the 72% in Malawi [17] shows that there are gaps that needs to be addressed in order to reach the 95% targets. 29% viral suppression in sub Saharan Africa [6] calls for action to be taken. Although previous studies in Sub-Saharan Africa have addressed this question, and some studies in Malawi have studied the same, it is no possible to generalize these findings to Malawi as a whole and particularly Nsanje district hence this study. This paper serves to establish the burden and the factors associated with VF among HIV positive patients on ART in Nsanje district.

1.2 Rationale of the Study

Since the roll out of VL in 2014 as a way of assessing progress on ART treatment in Malawi, most ART patients have had a VL tested among which some have failed to suppress their viral load despite being on ART longer or undergoing intensive adherence counselling. Identification of factors leading to virological failure is important for health programmers since it enables better targeting of adherence support. Identification of risk factors helps to define early predictors of treatment efficacy that permit better use of these drugs, avoid unnecessary switching to second line drug, prevent drug resistance, and decrease economic burden [21], especially in a resource limited setting like Malawi. In addition, despite the increasing number of HIV positive patients

accessing ART due to test and treat strategy there is limited information about non suppression rates and factors affecting it amongst children and adults enrolled in care in Malawi. In addition, previous studies that have highlighted the factors associated with virological suppression in most developed countries and resource limited settings have used lower cut-offs points to determine non-suppression. The thresholds used range from 50 to 500 copies/ml of blood [22–25] as compared to that of Malawi which is currently at 1000 copies/ml of blood [7]. This makes it difficult to generalize the results to other settings. Furthermore, the effects or the contribution of the factors leading to virological non-suppression may vary across settings and population groups and context specific data are critical to the implementation of corrective measures.

Therefore, it is expected that the research will help to determine the burden of virological failure and focus on real reasons leading to virological failure which will in turn lead to better targeting strategies to address the issue and policy change.

1.3 Objectives of the Study

1.3.1 Broad Objective

To determine the burden of virological failure and factors associated with viral non suppression/ virological failure among HIV patients on ART in Nsanje district.

1.3.2 Specific Objectives

1. To describe the demographic and clinical characteristics of patients on ART with virological failure

2. To determine the proportion of patients with virological failure amongst patients on ART
3. To determine the factors associated with virological failure amongst patients on ART

1.4 Hypothesis

1. Null Hypothesis: Virological failure is not related to any patient, institution or drug related factors
2. Alternative hypothesis: There is an association between virological failure and patient, institution or drug related factors

1.5 Literature Review

1.5.1 Expanded Access to ART

In the fight against HIV, efforts to expand access to ART have been prioritized globally. Expanded access to ART has a significant role to play in the global strategy to control the pandemic, reduce its impact on people living with HIV and improving the survival and quality of life of the patients globally [9]. A cross national analysis study in 37 European and Central Asian countries showed that, test and treat was strongly associated with substantial improvements in population level access to ART and viral suppression [20]. Similar study conducted in sub Saharan Africa established that, the expansion of HIV prevention and treatment services has improved treatment outcomes and reduced mortality [26]. The Malawi's rapid and successful ART scale up between 2004 and 2014 critically influenced the HIV epidemic in the country and has mitigated its impact [5]. By June 2014, 505,123 (48%) of the estimated 1,056,000 HIV infected Malawians were already on ART through the national treatment program [5]. The number of people accessing ART

in Malawi has gradually increased recently with the coming in of the test and treat strategy in 2016 [14].

Despite these promising result, regular monitoring of people on ART is recommended to ensure whether there is an effective treatment response or not [21].

1.5.2 Viral Load Monitoring

Viral Load (VL) testing is the gold standard for HIV treatment monitoring that shows the amount of HIV genetic material circulating in the blood plasma [7,14]. WHO introduced VL monitoring as a gold standard to monitor patient's response to ART and follow up the treatment effectiveness in 2013 [27]**.** Virological monitoring improves the diagnosis of ART failure, enabling a better use of resources as established by a cross sectional study in Mozambique [28]. Similarly a study conducted in six Eastern Caribbean countries showed the importance of VL through improvement in viral suppression after strengthening VL monitoring [29]. Early identification of patients with inadequate response to ART is critical for achieving optimal HIV treatment outcomes [30]. VL testing is the most important parameter in monitoring ART and can be categorized into routine and targeted VL monitoring [7]. Routine VL (RVL) testing is recommended by WHO as the preferred approach for patients on ART in LMIC since it enables more accurate and earlier detection of VF, allowing patients to switch to a second line regimen at higher CD4 cell counts and before the accumulation of drug resistance mutations [31]. A systematic review of observational studies in Africa showed that routine VL monitoring is beneficial when used as a tool to identify people in need of adherence interventions [32]. On the other hand targeted viral load (TVL) monitoring strategy, is used to confirm suspected treatment failure based on clinical and/ or immunological

criteria and can reduce inappropriate switching to second-line ART [7]. A study conducted in Vietnam showed that routine screening is better to identify patients on ART who experience significant viremia and requires a comprehensive structure for follow up and intervention [33]. Similarly a study in Switzerland, Lesotho and Uganda showed that frequent VL monitoring lowers levels of resistance even when treatment failure occurs [34]. This shows that accurate and early identification of VF is crucial as HIV patients may benefit from interventions to improve ART adherence [35].

Despite the benefits of VL monitoring, a study in Lesotho showed that in real life setting the potential of routine VL monitoring for patients taking ART is not optimized [36]. The study revealed that, lack of timely follow up after a first unsuppressed VL as well as low switching rates among patients with confirmed VF, reduce the potential benefit of routine VL monitoring in resource limited settings [36]. WHO defines VL suppression as <1000 copies/ml which is similar to the Malawian HIV guideline [7]. On the other hand, European and American HIV guidelines define VL suppression as undetectable and <200 copies/ml, respectively [21,29]. Despite the significant reduction in morbidity and mortality among the HIV infected patients receiving combination ART, a considerable number of patients still fail to achieve a sustained virological and immunological response to therapy [21].

1.5.3 Virological Failure

The inability to achieve or maintain suppression of viral replication to recommended levels indicates virological failure. As a global target, 90% of patients receiving ART should have HIV viral suppression [6]. A study conducted in Malawi at Ndirande Health Centre (H/C), established

a 9.4% prevalence of VF among stable adults who had been on ART for at least 6 months [37]. Patients are at risk of developing VF if maintained on a failing regimen leading to accumulating resistance mutations. A national study conducted in Malawi from 2015 to 2016 established that 68.3% of adults are viral suppressed [4]. Similarly a cross sectional analysis of an observational cohort in 5 South African districts showed that almost 85% of HIV infected patients in care and on first line, had achieved viral suppression [18]. Despite this, poor adherence to treatment is still a key problem, which has led to the high rate of VF [38]. Achieving viral suppression protects the body's immune system, helps people living with HIV stay healthy and prevents transmission of HIV to other people [39]. If a patient on treatment is found to have detectable viral replication, it may be due to poor drug adherence and/or drug resistance [4,7]. Thus, regular monitoring and evaluation about VS is very important to achieve the established targets and take necessary corrective actions. A qualitative study on the perceptions of VF and VL monitoring in rural Mozambique showed that most patients and healthcare workers placed great importance to VL testing in order to reduce VF [40].

1.5.4 Factors Associated with Virological Failure

There are so many factors that can contribute to virological failure of which the main culprits are poor adherence and drug resistance [41]. A study in Botswana established a statistically significant association between non adherence, drug resistance and VF [42]. Previous studies on VL monitoring have highlighted factors that may be associated with virological failure. Among these are WHO clinical staging 4 at the time of starting [43,44]. Children and adolescents mainly due to adherence challenges [44,45], Suboptimal adherence [33,46], poor tolerability, and drug and food interactions, CD4 cell count [15,24,44,47], Patients on treatment for more than one year, treatment

history [24,44], poor linkage to care and drug-resistance (primary or transmitted) have also been associated with virological non-suppression [48,49]. Virological non-suppression may also be caused by patient-related factors such as comorbidities, challenges with adherence to ART [15,46,47], economic hardships, and AIDS-related stigma [46]. Furthermore, Socio-demographic factors including missed clinic appointment and interruption of or intermittent access to ART, and ARV regimen related factors such as drug adverse effects [46], drug side effects, drug toxicity to certain ART regimen combinations, prior exposure to ART monotherapy [24,33]. A cross sectional study in Tanzania highlighted that factors such as ART adherence, Niverapine based regimen, HIV status disclosure to those caring for the child need to be addressed to achieve sustained virological suppression [50].

1.5.4.1 Poor Adherence

Poor adherence is the most frequent cause of treatment failure and the subsequent development of resistant strains of HIV among patients on ART [51]. In the absence of sufficient levels of drugs, the virus rapidly multiplies leading to an increase in VL mutations, unsuppressed VL, leading to opportunistic infections, drug resistance and ultimately mortality. Different studies done across the world suggests that poorer adherence is strongly associated with a higher risk of VF [15,33,43,46,52–54]. Similarly, a study conducted in Cameroon also showed that most patients develops VF after being on first line ART for 1 year due to incomplete adherence on ART [38]. A study in Botswana showed that, the odds of having treatment failure was 2.25 times higher among individuals with refill non adherence compared to those with good adherence [42]. However, a good adherence, together with non-suppressed VL highlights the presence of drug resistance among patients on ART. This is supported by previous findings which showed that good adherence

does not protect from the development of drug resistance as revealed in a study conducted in South Eastern Ethiopia which showed that a total of 16.36% of ART clients with fair drug adherence at the first visit after ART initiation experienced treatment failure [41]. Thus suboptimal adherence is the strongest predictor of both low detectable VL and unsuppressed VL [55]. Closer monitoring of drug resistant mutations at the start of HIV treatment or at first line failure can better inform clinical decision making and HIV treatment regimen programing as observed from a cross sectional study in Zambia [56].

Another study conducted in Latin American Countries (LAC) showed that 30% of PLHIV may be at risk of developing AIDS related illnesses and transmitting the virus to others due to incomplete adherence to ART as required for successful viral load suppression [57]. Findings from a cohort study in Tanzania indicates that, initiating treatment early and ensuring optimal adherence are vital for the success and durability of first-line ART in these settings [49]. However a study conducted in Ethiopia among children showed that there was no association between adherence and VF [58]. This entails that there are other factors apart from adherence that may lead to VF.

1.5.4.2 ART Resistance

Drug resistance (DR) is among the factors affecting viral suppression and disease control [59]. Resistance may be acquired or transmitted to another person. Acquired drug resistance develops when patients interrupt their treatment, do not take it according to prescription, or the drugs are not absorbed properly due to other medical issues [21]. On the other hand transmitted drug resistance develops when people are infected from others who had HIV drug resistance and that carry resistant HIV strains [7,14,21]. Results from a sub Saharan African study indicated that HIV

drug resistance inevitably causes attenuation of the potential full health benefits of ART and adds cost to the programs [60]. Resistance in patients with VF compromises the success of adherence interventions [21]. A multicenter retrospective cohort study has showed drug resistance in a high proportion of patients after VF on a tenofovir containing first line regimen across Low and Middle Income regions [59]. Similarly a study in Zambia found significant resistance to NRTIs and NNRTIs at the time of VF which increased with prolonged failing on first line regimen [48]. Resistance testing remains costly and inaccessible in most Low and Middle Income Countries (LMIC) but may become more important for patients failing on ART in the long term [21,59]. Delayed failure detection and continuation of a failing regimen results in the multiplication of viruses with extensive resistance to ARV drugs [7]. The accumulation of mutations associated with cross-resistance within a particular drug class may compromise the effectiveness of standard second-line regimens, which are based on a dual backbone of that class [7,14,21].

1.5.5 Strategy to Support Clients with Viral Suppression

1.5.5.1 Enhanced Adherence Counselling

Intensive adherence counselling (IAC) also known as enhanced adherence counselling (EAC) is one of the strategies used to improve adherence on patients with a confirmed high VL (HVL). The aim of IAC/EAC is to identify ART patients who fail to suppress HIV replication due to poor adherence from those failing to suppress as a result of acquired or transmitted drug resistance [7]. The IAC/EACs sessions aim to explore behavioral, socio-economic, cognitive and emotional barriers to adherence and to identify strategies to overcome these barriers [55]. In Malawi patients with HVL are being subjected to IAC/EAC for 3 months and later a repeat VL is collected [7]. There is no standard way of counselling in Malawi, hence each district adapts to its own structure based on

the NGOs supporting the program in the district. Nsanje is one of the districts with a well-structured IAC/EAC program championed by Medecins Sans Frontieres (MSF). A study conducted in Harare, Zimbabwe showed that ART patients who underwent EAC session were more likely to achieve viral suppression than those who did not undergo any EAC session [61].

CHAPTER 2: METHODOLOGY

2.1 Study Design

This is a cross sectional quantitative study using a Laboratory information system data set and data from registers that was routinely collected from all health facilities in Nsanje for 3 years from July 2015 to June 2019. The rationale behind the study design was its ability to assess the burden of the disease and analyze multiple variables at once.

2.2 Study Area

The study was conducted in Nsanje district, due to its high HIV prevalence of 12.5% in 2019 from 16.3% in 2015 [55,62]. The prevalence is above the national HIV prevalence which is currently at 9.2% [62]. In addition, Nsanje district was among the first districts to implement routine VL monitoring with the help of Medecins Sans Frontieres (MSF) at the end of 2013 [55]. However in 2016 about 20% of clients who had a VL taken, failed to suppress their VL leading to Virological failure [55]. Nsanje district is located in the lower Shire in the Southern part of Malawi bordering with Mozambique. The district has a population of 299,168 [63] but also serves people from Mozambique. In total there are14 health facilities in the district, 10 government facilities and 4 CHAM facilities. The district is served by 1 district hospital which acts as the referral, 2 community CHAM hospitals and health centers. In total there are 15 ART sites in Nsanje including a private hospital. A total of 21475 people were alive and on ART treatment as of December 2019.

2.3 Study Population

The study involved people living with HIV and on antiretroviral therapy with a documented high VL result during the period of study in Nsanje district. All patients who underwent VL testing in

the health facilities from July 2015 to June 2019 and had a virological failure were included in the study. Furthermore, by this period most clients on ART have VLs collected to monitor progress on ART, of which some were failing to suppress the virus due to virological failure. Laboratory information for all patients who underwent VL monitoring in this period were sought and analyzed using unique patient identifiers.

2.3.1 Inclusion Criteria

1. Patients on ART for ≥6months during the study period with documented VL results.

2.3.2 Exclusion Criteria

1. Patients with VL ≥ 1000/ml with an outcome of death or lost to follow up before accessing results.
2. Patients less than 6 months on ART with a VL test of ≥ 1000.
3. Patients on ART without a VL test.

2.4 Sample Size

The sample size for this study was 326, calculated using Epi info version 7.2 statistical calculator at 95% confidence interval. With an estimated population being 2148 at an expected frequency of 50% and Margin error 5%. However due to availability of data 451 participants were enrolled in the study. The sample size was based on the sampling frame of 21475 patients who were active on ART as of 2019. In total, the district has 43646 patients on ART with 11627 lost to follow up and 3145 who died while on ART. Assumptions were made that 50% of the 21475 patients active on ART have had their VL taken and 20% of them might have VF within the study period of July

2015 to June 2019. The study used stratified random sampling technique to select participants at each health facility with each year being regarded as a stratum. A simple random sampling technique was used to select patient's records from each strata to ensure equal representation from each year group in the study.

2.5 Study Period

The study took place from December 2019 to March 2021 as follows

	2019	2020											2021	
ACTIVITY	Dec	Jan	Feb	Mar	Apr	May	Jun	July	Aug	Sept	Oct	Nov to Feb	Mar	Jun
Topic Identification														
2 page proposal development														
Proposal development														
Literature review														
Proposal submission & COMREC feedback														
Data collection														
Data Analysis														
Report writing and review														
Submission of dessertation														
Dissemination														

2.6 Data Collection

Permission was sought from the DHO in order to access the data obtained from the Malawi Laboratory Information Management System (LIMS), which includes viral load data from the facilities. Data was collected from the viral load database at the district. The data does not include names it only contains numbers that are used to identify the patients. Additional data was collected by reviewing patients' medical charts and electronic records. Data was collected by the researcher

and ART data clerks who were oriented on the documentation and techniques of data collection. Data was checked for its completeness every day to ensure data quality, edited, cleaned, and analyzed.

The study investigated the following social, demographic and clinical characteristics: gender (Male and Female), age at ART initiation (0-19 year, 20-24 years, 25-34 years, 35-44 years and 45 years and above), duration on ART(0-3 years, 4-7 years and 8 years and above), marital status (child/single, married and divorced/widowed), occupation (unemployed and employed/self-employed), reasons for starting ART (PMTCT/test and treat, WHO clinical stage and other), ART regimen at viral load(2P, 5A and other) , drug adherence at viral load (good and fair/poor), history of TB (yes and no), TB co infection (yes and no) , history of substance abuse (yes and no), history of side effects (yes and no), reasons for VL collection, history of depression (yes and no) and facility size (low, medium and high). A binary virological failure variable (yes versus no) using viral load results of 1000 and more copies/ml categorized as virological failure.

A data collection checklist (Appendix 1) was used to complement the routine clinical data retrieved from medical records in ART clinics.

2.7 Data Management

Data was stored electronically and protected with a password to ensure data security. This data was only available to the researcher and some research assistants such as ART clerks themselves or HTS Counsellors within the ART Clinic. Coding was done before processing the data for analysis. The extracted data was entered into an excel sheet then analyzed with STATA.

2.8 Data Analysis

Collected data was entered into an excel spreadsheet which was later analyzed using STATA version 16.1**.** Descriptive statistics were used to summarize the study variables and the results presented as frequencies and percentages. Binomial logistic regression model was used to assess social, demographic and facility factors associated with the virological failure amongst HIV infected patients. Unadjusted and adjusted odds ratios (ORs and AORs respectively) were calculated at 95% confidence intervals (CIs) and included all factors with a p-value < 0.05 from the univariable model in the multivariable logistic regression model. All data management and analyses were performed using STATA version 16.1 (Stata Corporation, College Station, Texas, USA) at 5% significance level.

2.9 Results Presentation

Results from this study have been presented in tables of percentages and mean for continuous and categorical variables such as age, sex and viral suppression. Odd ratio have also been obtained and presented in tables to show association. The results are presented in a manner where readers can understand and interpret the meaning.

2.10 Dissemination

Results from this study will be disseminated to Nsanje DHO and relevant stakeholders in the district. The data will also be disseminated to College of Medicine Research Ethics Committee (COMREC) being the institution which approved this research and also to the college itself. The data may further be disseminated at research dissemination at COM and other forums in order to ensure policy change**.**

A copy of the final report and any published papers or abstracts of papers read at conferences out of the research findings will be shared with the COMREC, College of Medicine Library, and to all relevant stakeholders through the COMREC Secretariat.

2.11 Ethical Considerations

Prior to the study an approval was granted by COMREC at College of Medicine in Blantyre. Furthermore, the study used laboratory and program data collected for routine patient care from health facilities in Nsanje which does not contain patient names but only has ART numbers. To protect patient's confidentiality all data collected did not carry personal identifiers. The data was not made available to third parties other than the study team. Permission to use the data was sought from the District Health Office (DHO) and the ART Coordinator.

2.12 Possible Constraints

In proper categories of reasons for VL on whether it is routine VL or Targeted/repeat VL. Most VL results are labeled routine VL when in real cases they might be Targeted VL. This affected the results of the study.

The study being retrospective in nature meant that we had to go through past records of patients. This is prone to missing data since some information might have been lost along the way. This leads to exclusion of clients who would have been potential participants in the study. Data was not collected from one facility (Makhanga) since the facility does not have enough records and information for the period of study due to heavy floods which hit the facility

The study constraints were minimized by reviewing the data which was clearly indicated whether it was routine monitoring and targeted monitoring. Furthermore, missing data in the LMIS database was complemented with medical records such as VL results, master cards, VL registers and Electronic Management Records (EMR) if available at the site. Only patients with complete data were recruited for the study and Makhanga was left out due to loss of data.

CHAPTER 3: RESULTS

3.1 Socio-Demographic and Clinical Characteristics of Study Participants

A total of 451 HIV positive individuals on ART were included in this study, among which 289 (64.1%) were females with a median age at ART initiation of 30 years (IQR: 22-38). 267 (59.2%) participants were married, and 278 (61.6%) started ART because of WHO clinical stage. Majority of the study participants were employed or self-employed (332) representing 73.6% of the total participants. Table 1 shows the socio-demographic and clinical characteristic of the participants.

Table 1: Socio-demographic characteristics of HIV infected individuals on ART (n = 451)

Characteristic	Frequency (%)
Gender	
Male	162(35.9)
Female	289(64.1)
Age at ART initiation (years)	
0-19	95(21.1)
20-24	44(9.8)
25-34	150(33.3)
35-44	93(20.7)
45+	68(15.1)
Median(IQR)	30(22-38)
Duration on ART (years)	
0-<4	162(35.9)
4-<8	160(35.5)
≥8	129(28.6)
Marital status	
Child/single	133(29.5)
Married	267(59.2)
Divorced/Widowed	51(11.3)
Occupation	
Child/student/unemployed	119(26.4)
Employed/self-employed	332(73.6)
Reason for starting ART	
PMTCT/Test and treat	140(31.0)
WHO clinical stage	278(61.6)
Other	33(7.3)

3.2 Proportions of Patients with Virological Failure

Of the 451 study participants, 321(71.2%) failed to achieve viral suppression (Table 2). Most of those who failed to achieve viral suppression were aged 0-19 years (96.8%), males (74.7%), children or single (86.5%), and had fair to poor adherence (88.8%) (Table).

Table 2: Virological failure and associated risk factors

	Virological Failure, n (%)		Univariable Logistic Regression		Multivariable Logistic Regression	
Characteristic	**Yes**	**No**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**
Number of patients (%)	321(71.2)	130(28.8)				
Age at ART initiation						
0-19	92(96.8)	3(3.2)	1		1	
20-24	29(65.9)	15(34.1)	0.063(0.017-0.233)	<0.0001	0.087(0.018-0.413)	0.002
25-34	100(66.7)	50(33.3)	0.065(0.02-0.216)	<0.0001	0.112(0.027-0.465)	0.003
35-44	57(61.3)	36(38.7)	0.052(0.015-0.175)	<0.0001	0.075(0.017-0.325)	0.001
>=45	42(61.8)	26(38.2)	0.053(0.015-0.184)	<0.0001	0.090(0.020-0.396)	0.001
Facility type						
Low volume	34(68.0)	16(32.0)	1			
Medium volume	95(70.9)	39(29.1)	1.146(0.568-2.312)	0.703		
High volume	192(71.9)	75(28.1)	1.205(0.628-2.311)	0.575		
Sex						
Male	121(74.7)	41(25.3)	1			
Female	200(69.2)	89(30.8)	0.761(0.494-1.174)	0.218		
Marital status						
Child/single	115(86.5)	18(13.5)	1		1	
Married	176(65.9)	91(34.1)	0.303(0.173-0.529)	<0.0001	1.175(0.581-2.373)	0.654
Divorced/Widowed	30(58.8)	21(41.2)	0.224(0.106-0.472)	<0.0001	0.964(0.398-2.339)	0.936
Occupation						
Child/student/unemployed	107(89.9)	12(10.1)	1		1	

Employed/self-employed	214(64.5)	118(35.5)	0.203(0.108-0.385)	<0.0001	0.646(0.297-1.405)	0.271
Duration on ART						
0-<4yrs	124(76.5)	38(23.5)	1		1	
4-<8yrs	114(71.3)	46(28.8)	0.759(0.461-1.251)	0.28	0.855(0.491-1.489)	0.581
≥8yrs	83(64.3)	46(35.7)	0.553(0.331-0.922)	0.023	0.682(0.384-1.212)	0.192
Reason for starting ART						
PMTCT/Test and treat	99(70.7)	41(29.3)	1			
WHO clinical stage	195(70.1)	83(29.9)	0.973(0.623-1.519)	0.904		
Other	27(81.8)	6(18.2)	1.864(0.716-4.851)	0.202		
ART regimen at VL						
2P	39(100)	0(0)				
5A	170(65.4)	90(34.6)	0.674(0.433-1.050)	0.081		
Other	112(73.7)	40(26.3)	-			
Drug adherence at VL						
Good	171(60.6)	111(39.4)	1		1	
Fair/Poor	150(88.8)	19(11.2)	5.125(3.005-8.739)	<0.0001	4.221(2.413-7.383)	<0.0001
History of TB						
No	303(71.0)	124(29.0)	1			
Yes	18(75.0)	6(25.0)	1.228(0.476-3.166)	0.671		
TB co infection						
No	312(70.7)	129(29.3)	1			
Yes	8(88.9)	1(11.1)	3.308(0.41-26.714)	0.262		
History of substance abuse						
No	318(71.1)	129(28.9)	1			
Yes	3(75.0)	1(25.0)	1.217(0.125-11.808)	0.866		
History of side effects						
No	311(71.5)	124(28.5)	1			
Yes	10(62.5)	6(37.5)	0.665(0.236-1.868)	0.438		
History of depression						
No	306(71.2)	124(28.8)	1			

Yes	15(71.4)	6(28.6)	1.013(0.384-2.671)	0.979		

3.3 Factors Associated with Virological Failure

Factors associated with virological failure were also assessed. In univariate analyses factors associated with a statistically significant increased odds of virological failure were Age at ART initiation, occupation, marital status, duration on ART and ART adherence at VL (Table 2). The study findings revealed that, poor to fair ART adherence increased the odds of virological failure four times (OR = 4.221, 95% CI; 2.413-7.383) after adjusting for all factors that were significant in univariable analysis. Participants aged 20–24 years (OR = 0.087, 95% CI; 0.018-0.413), 25–34 years (0.112; 0.027-0.465), 35–44 years (0.075; 0.017-0.325), or 45 years and older (0.090; 0.020-0.396) were less likely to experience virological failure than those aged 19 years or younger. Factors that were associated with virological failure in univariable analysis but were not significant in the adjusted analysis included marital status, occupation and duration on ART. There were no significant differences in odds of virological failure between female and male participants in both univariable and adjusted analysis.

CHAPTER 4: DISCUSSION

4.1 Introduction

The results of this study are discussed in this chapter. The aim of the study was to identify socio-demographic and clinical characteristics of study participants, to determine the proportion of patients with virologic failure and to identify factors associated with virologic failure among patients receiving antiretroviral therapy in Nsanje district.

The findings show that about 71.2% (321) patients on ART experienced virological failure within the period of study. This is contrary to other studies conducted in Malawi and other countries which showed a range of 9.4% to 43% of VF [18,30,37,45,64–67]. This may be attributed to involvement of the whole ART cascade for this study as other studies only concentrate on specific groups such as children, adolescents, adults, men having sex with men, drug users and second line patients. Furthermore the study dwelled on data for a particular period of time of which routine VL was being role out in Nsanje hence samples were being collected for catch up despite poor adherence. Furthermore some studies used a small sample size and a short period of the study (6 months) [18,30,37] unlike this study which was for over a period of 3 years. Two studies showed different finding on patients with VF (VL ≥1000 copies per mL) as follows; Malawi (32%) [66], Ethiopia 14.7% [64]. Similarly cross sectional studies in Uganda and Ethiopia found the overall proportion of VF among children to be 11% and 28% respectively [45,58]. In addition, cross sectional and cohort studies in South Africa showed that 15.3% & 30.1% had poor VL suppression (VL ≥400 copies/mL) at 6 months on ART respectively [18,30]. Similarly a cross sectional study at Ndirande health facility in Malawi demonstrated a 9.4% prevalence of VF in clinically stable adults who had been on ART for at least 6 months [37]. It should be highlighted that it's difficult

to compare this study with other studies since different countries use different cut off points of VL (VL ≥200) and age [65,68]. This is supported by a Study conducted in Southern part of Malawi, which also highlighted the difficulties to compare non suppression results with other studies due to variations in the thresh-holds utilized [67].

The univariate analysis of this study demonstrated that, age, occupation, marital status, duration on ART and adherence on ART are associated with virological failure. However, only age and adherence on ART were significantly associated with VF in multivariate analysis. The findings were expected since adherence issues are directly associated with age in most cases and working on adherence has proven to work for some clients failing on ART due to adherence. This is supported by other studies which demonstrated that factors associated with unsuppressed VL were initiating ART before 15 years of age, being on ART for less than one year, or more than ten years [18]. Also a cross sectional study in Mozambique showed that factors associated with VF included younger age and estimated low adherence [28]. Similarly a case control study in Ethiopia showed that age <35 years, poor adherence to treatment, and higher duration of taking ART were positively and significantly associated with VF [69]. Furthermore studies conducted in South Eastern and Northern Ethiopia showed that age of clients and ART adherence level were significantly associated with viral non suppression [41,70].

Adherence on ART (fair/poor) was a significant factor associated with VF in this study. A case control study in Ethiopia showed that, patients with poor adherence to ART were 16 times likely to have VF as compared to those who were adherent to their treatment [69]. This is strongly supported by several studies which established that poor adherence to treatment was significantly

associated with VF [23,45,75–77,47,52,69–74]. In Malawi, a study at Ndirande health facility concurred with this study by revealing that suboptimal self-reported ART adherence is an independent risk factor for VF [37]. This shows that poor adherence is a key problem in ART hence proper strategies needs to be developed to address adherence issues before switching to second line. In Nsanje, it was observed that poor adherence among patients with HVL was due to lack of support system, illiteracy leading to missing of appointments and competing priorities as revealed during IAC/EAC sessions in the district. In support to the study, a multicenter study in Ethiopia established that the rate of second line ART failure was higher in patients who started second line ART with poor drug adherence [78]. Poor adherence is attributed to: working away from home, stigma, non HIV status disclosure, relaxed continuous ART adherence education/counselling, alcohol use or misuse, availability of other HIV treatment options, treatment fatigue, experiences or fear of ART side effects, belief that God and ART can cure HIV, food insecurity and incarceration as highlighted in a qualitative study in Uganda [79]. There is need for targeted interventions such as EAC and Community Action Groups(CAGs) to be implemented in order to improve adherence on ART, which in turn helps to suppresses VL [69].

Despite poor adherence being a key problem leading to VF in patients on ART, other studies found no association between adherence and VF [58]. A study in Uganda showed that even when adherence was more than 95%, 71% of adolescents failed to achieve viral suppression [80]. Similarly a study in Kenya demonstrated that there was no association between missing ARVs or clinic visits with virologic failure [15]. This was attributed to screening and managing for non-adherence before requesting for a VL test [15]. Furthermore, a retrospective cohort study in Ethiopia showed that a total of 16.36% of ART clients with fair drug adherence at the first visit after ART initiation experienced treatment failure whereas below 2% of poor adherence ART

clients experienced treatment failure [41]. This can be related to this study where some patients with good adherence were also failing on ART due to other medical reasons not related to adherence and drug resistance. This shows that even with good adherence some patients will still experience VF.

The study further, indicated that younger age (0-19) significantly increased the odds of VF. This is supported by several studies in Africa which also demonstrated the significant association of younger age with VF [45,53,81]. Similarly a cross sectional study in South Africa showed that being younger than 15 years old at ART initiation increased the odds of VF compared to initiating ART at 15–49 years [18]. The study went further to highlight that this could be due to behavioral factors such as not taking medication daily and as prescribed, or structural issues, like not being able to attend the health facility during the weekday because of school [18]. This is consistent with another study which revealed that adolescents and young adults have greater risk of virologic failure since this age group faces multiple social, psychological and adherence challenges increasing their vulnerability to treatment failure [82]. In this study, increased odds of VF for younger age can be attributed to lack of child disclosure which in turn affected adherence and school going age since ART clinics are only run during week days unless if the facility has a teen club. Further studies in Kenya and Uganda revealed that, younger age was associated with delayed ART initiation, failure to achieve viral suppression, and increased risk of virologic rebound [83]. This can help to explain why this age group is mainly at risk.

Furthermore, studies in Uganda and Togo showed a VF rate among children and adolescents on ART at 34.5% and 51.1% respectively [80,84]. This is supported by 2 studies which stated that

being a child and an adolescent is a predictor of VF [44,85]. Similarly a case control study conducted in Ethiopia showed that the likelihood of developing VF for patients aged <35 years was 2.5 times as likely as compared with their older counterparts [69]. This is supported by an observational cohort study in UK which revealed that older age is associated with better adherence [86]. Several studies in Kenya, Vietnam, Uganda and Ethiopia also revealed that age below ≤ 40 years was significantly associated with VF [15,76,87]. However, a prospective cohort study in Uganda showed that VF was significantly associated with age >40 years [88]. This was also established in this study where age groups 40 above were significantly associated with VF.

The findings further revealed that, duration on ART was also associated with VF. Significant differences were observed in this study, patients who have been on ART longer (8 years or more) were associated with VF compared to their counterparts. This is supported by a case control study in Ethiopia which showed that duration on ART was a significant factor associated with VF [69]. This study reported that, patients who took ART for 24–47 months and for >48 months were 3 times and 7 times respectively, as likely to have VF as those who took the treatment for 6–24 months [69]. In our context, this might be related to the development of drug resistance after a long time of taking first line ARVs coupled with adherence issues due to familiarity with the drugs. Similarly a cross sectional study at Ndirande health facility in Malawi demonstrated that longer ART duration was among the independent risk factors for VF in the study [37]. Furthermore a descriptive study in Swaziland revealed, longer time on ART as a key predictor of detectability of VF [44]. Despite this, period of time on ART, was not of statistical significance in a study done in Kenya [15]. This is probably since the Kenyan study did not find significant differences related to duration on ART unlike this study.

In this study an association was observed between marital status and VF. Being married, divorced or widowed were associated with VF than being single. This was not expected as mostly VF is associated with being single (Unmarried, Child). Therefore, the findings are related to issues of disclosure to partners and fear for stigma and discrimination which in turn affects adherence to ART among married people. This is contrary to other studies which showed that being single was highly associated with VF [53]. Other studies in Tanzania and Ethiopia further demonstrated that, there was no association between marital status and treatment failure [64,89].

Furthermore, this study did not find any association between VF and history of depression. This may be due to lack of properly developed structures for assessing depression or mental health in Malawian health facilities including Nsanje district. This is confirmed by a similar study in Southern Malawi which showed that years knowing one's HIV status and depression were not significantly associated with non-suppression after adjusting for confounders [67].

Similarly, gender was not significantly associated with VF but the study showed that males (74.7%) were more likely to experience VF than females, This is confirmed by a study in South Africa which revealed that the odds of having a recent unsuppressed VL test were greater in men compared to women [18]. Also a study in Morocco demonstrated that males were associated with a higher risk of not completing viral suppression after 6 months of ART [68]. In another study, being male, was significantly associated with viral non suppression [70]. In our context (Nsanje), this may be due to more females visiting the facility than men. Women who visit the facility tends to have more information and are likely to adhere to ART than men who shun away from the facilities. Contrary to the findings, a cross sectional study conducted in Lilongwe Malawi, showed

that male gender was not associated with increased risk of VF [90]. This is supported by a Kenyan study, where gender was found not to be associated with VF [15]. In addition a randomized control trial in Tanzania also established that the risk of VF did not differ significantly by gender [49].

Contrary to other studies, this study demonstrated that a history of TB and co infection with TB at the time of VL are not associated with VL unsupression. This might be attributed to few patients having a history of TB/Co infection at the time of the study or due to proper management of opportunistic infections within the district. On the other hand, a cohort study in Ethiopia, showed that co infection during ART initiation and developing TB after ART initiation was one of the significant factors associated with treatment failure [41]. The study further explains that, TB co infected patients and patients who had developed TB after ART initiation had higher odds of experiencing treatment failure as compared to their counter parts [41]. Similarly, studies from South Africa and Uganda showed that being on TB treatment or having active TB increased the odds of virological non suppression [18,46].

The study demonstrated that, substance abuse was not associated with VF in this study. Probably since it is difficult for clients to give honest information related to substance abuse at the facility for fear that it may be used against them or deprive them of the services. Furthermore, Malawi as a country do not have well established structures to address issues of substance abuse. Contrary to this, a retrospective cohort study in Morocco found that alcoholism was associated with unsuppressed VL [68]. Similarly an unmatched case-control study in Harare, Zimbabwe showed that alcohol consumption and non-disclosure increased the odds of VF [77]. This is further

supported by another study which showed alcohol consumption alongside other factors (ART adherence and decreased age) as an independent predictor to conventional and pragmatic VF [52]. In determining whether the current regimen type has any association with VF, there was no association recorded. This is supported by results for a study in Kenya where ARV regimen, CD4 and indication for VL testing were not of statistical significance [15]. This shows that ARV regimen has no impact on VF among the study participant in this study. This can be attributed to the current starting regimens in Malawi which are much better than the previous regimens which had more side effects. However, a study conducted in Zimbabwe showed that those on 2nd line treatment were less likely to have VF as compared to those on first line [77]. This is contrary to an African cohort study which showed that being on second line ART regimen was significantly associated with risk of VF [53]. This is probably due to the increase in number of pills on second line. This shows that there is need for intensive adherence counselling in order to reduce VF patients on second line treatment. Another study conducted in Vietnam also showed that Efavirenz (EFV) use was associated with a lower probability of VF compared to Niverapine (NVP) [87]. At the time of the study Malawian guidelines had both EFV and NVP combinations being used, with EFV and NVP being used as a starting regimen for adults and children respectively [7,14]. Further studies need to explore if the presence of NVP in pediatric formulas in Malawi is related to young age likelihood of experiencing VF in this study.

Lastly, the study demonstrated an association between occupation (employed/ self-employed) with VF. This is supported by a prospective cohort study in Uganda which established that VF was significantly associated with self-employment compared to unemployment [88]. A clear significant relationship was identified between self-employment and VF outcome when compared

to unemployment [88]. This might be attributed to self-employed and employed people working away from home and having competing priorities which affects their adherence to ART. Similarly a case control study in Ethiopia showed that occupation, was associated with ART VF [69]. However, a cross sectional study in France showed that, employment was not a main risk factors for virological non-suppression [91]. This was also noted in a study in 6 provinces of China, where occupation was not associated with VF [74]. Contrary to the findings, a study in Australia showed that unemployment was associated with VF [92].

4.2 Limitations of the Study

This study has several limitations. The first limitation is the study being a cross sectional study which meant that temporal relationship among variables studied is unknown and associations observed cannot be interpreted as causal [67]. For instance, the relationship between being married, widowed and divorced with VF and also Self-employment with VF is unknown.

Secondly, this is a retrospective study involving past records hence accuracy of the analysis depends on the completeness of data. This affected the study in a way that the selection criteria excluded some clients with important information due to incomplete data. Future studies should consider a prospective cohort study in order to follow up clients and address this challenge.

Furthermore, the quantitative nature of the study and the use of retrospective data limited the factors identified to be associated with VF. The factors analyzed were only those that were available in the database and those collected from registers. Interviews with clients would have unearthed other factors related to VF which are not in the registers and databases. Therefore, future researchers should consider a qualitative study or studies using both qualitative and quantitative

methods in order to identify behavioral, psychological, structural, socio economic and cultural factors which requires a face to face interaction with client.

Lastly, data was not collected from one facility (Makhanga) due to loss of data for the period that was required for this study during the previous floods. This affects the generalization of this data to the whole district.

CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

In conclusion, the findings demonstrate that more than half of the HIV infected patients established on ART for more than 6 months in the district experience VF while continuing to be on ART. The study further established that age at initiation, marital status (married, divorced or widowed), Occupation (employed/ self-employed), duration on ART (8 years and more) and ART adherence (Fair/poor) are important predictors of VF that should be monitored and proper strategies should be put in place in order to reduce VF, improve adherence and avoid switching to more expensive second line or third line ART drugs. Intensive adherence counselling/education and Community ART Groups (CAG) are some of the strategies to improve adherence. Lastly, further research is necessary to explore and determine underlying causes of VF in relation to age, marital status, occupation, duration on ART and poor adherence to provide more definite conclusions.

5.2 Recommendations

The recommendations below are made for Ministry of Health and Nsanje DHO to ensure improvements in delivery of ART and policy change:

1. Development and strengthening of comprehensive interventions targeting young people in order to reduce VF in young people in all facilities.
2. Development of strategies to ensure screening for routine VL and offering support to those with adherence issues before VL collection

REFERENCES

1. UNAIDS. Global HIV and AIDS statistics 2017 [Internet]. 2018. Available from: http://www.avert.org
2. WHO. Antiretroviral therapy (ART) coverage among all age groups [Internet]. 2015. Available from: http://www.who.int/gho/hiv/epidemic_response/ART_text/en/
3. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: 2013 [Internet]. 2013. Available from: http://www.who.int/hiv/pub/arv/arv-2016/en/
4. Ministry of Health. Malawi Population-Based HIV Impact Assessment (MPHIA) 2015 - 2016: final report [Internet]. Lilongwe: Ministry of Health; 2018. Available from: http://phia.icap.columbia.edu
5. National AIDS Commission. National Strategic Plan for HIV and AIDS 2015-2020. Lilongwe; 2015. 1–91 p.
6. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. 2014.
7. Ministry of Health and Population. Malawi guidelines for clinical management of HIV in children and adults 2018. 4th ed. Lilongwe: Ministry of Health; 2018. 1–128 p.
8. WHO. Technical brief on HIV viral load technologies. 2010. Available from: http://www.who.int/hiv/topics/treatment/tech_brief_20100601_en.pdf.
9. Minchella PA, Chipungu G, Kim AA, Sarr A, Ali H, Mwenda R, et al. Specimen origin , type and testing laboratory are linked to longer turnaround times for HIV viral load testing in Malawi. PLoS One. 2017;12(2):1–13.
10. UNAIDS. Knowledge is power: know your status, know your viral load [Internet]. 2018. Available from: http://www.unaids.org/.

11. WHO. HIV diagnostic tests in low and middle income countries: forecasts of global demand for 2014-2018. Geneva: WHO; 2015. 1–24 p.
12. Hubbard J, Kakwesa G, Nyirenda M, Mwambene J, Bardon A, Balakasi K. Towards the third 90 : improving viral load testing with a simple quality improvement program in health facilities in Malawi. Int Health. 2019;11:215–20.
13. Ministry of Health and Population. 2019 policy updates: Addendum to the 4th edition of the Malawi integrated guidelines and standard operating procedures for clinical HIV services. Lilongwe: Ministry of Health; 2019. 1–26 p.
14. Ministry of Health and Population. Malawi guidelines for clinical management of HIV in children and adults 2016. 3rd ed. Lilongwe: Ministry of Health; 2016. 1–114 p.
15. Sang RKA, Miruka FO. Factors associated with virologic failure amongst adults on Antiretroviral Therapy in Nyanza region, Kenya. IOSR J Dent Med Sci [Internet]. 2016;15(7):108–21. Available from: http://www.iosrjournals.org
16. Haberer JE, Sabin L, Amico KR, Orrell C, Galárraga O, Tsai AC, et al. Improving antiretroviral therapy adherence in resource-limited settings at scale : a discussion of interventions and recommendations. J Int AIDS Soc [Internet]. 2017;20:1–15. Available from: http://dx.doi.org/10.7448/IAS.20.1.21371
17. UNAIDS. UNAIDS data 2020. Geneva; 2020.
18. Davey DJ, Abrahams Z, Feinberg M, Prins M, Serrao C, Medeossi B, et al. Factors associated with recent unsuppressed viral load in HIV-1-infected patients in care on first-line antiretroviral therapy in South Africa. Interntional J STD AIDS. 2018;29(6):1–8.
19. Center for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas,

2014. HIV Surveillance Supplemental Report [Internet]. Vol. 21. 2016. Available from: http://www.cdc.gov/hiv/library/reports/ surveillance/

20. Mendez-Lopez A, Mckee M, Stuckler D, Granich R, Gupta S, Noori T, et al. Population uptake and effectiveness of test-and-treat antiretroviral therapy guidelines for preventing the global spread of HIV : an ecological cross-national analysis. HIV Med. 2019;20:501–12.

21. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV [Internet]. Vol. 40. Department of Health and Human Services; 2019. 1–351 p. Available from: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf

22. Daskalopoulou M, Lampe FC, Sherr L, Phillips AN, Johnson MA, Gilson R, et al. Non-disclosure of HIV status and associations with psychological factors, ART non-adherence, and viral load non-suppression among people living with HIV in the UK. AIDS Behav [Internet]. 2017 Jan;21:184–95. Available from: https://doi.org/10.1007/s10461-016-1541-4

23. Metsch LR, Feaster DJ, Gooden L, Matheson T, Stitzer M, Das M, et al. Effect of patient navigation with or without financial incentives on viral suppression among hospitalized patients with HIV infection and substance use: A Randomized clinical trial. JAMA [Internet]. 2016;316(2):156–70. Available from: https://jamanetwork.com/

24. Bello KJ, Mesner O, Bryan TAO, Won SH, Lalani T, Ganesan A, et al. Factors associated with 10 years of continuous viral load suppression on HAART. BMC Infect Dis [Internet]. 2016;16:1–8. Available from: http://dx.doi.org/10.1186/s12879-016-1677-x

25. Zanoni BC, Sibaya T, Cairns C, Lammert S, Haberer E. Higher retention and viral

suppression with adolescent-focused HIV clinic in South Africa. PLoS One. 2017;12(12):1–12.

26. Ortblad KF, Baeten JM, Cherutich P, Wamicwe JN, Judith N, Cancer H. The arc of HIV epidermics in sub-Saharan Africa: New challenges with concentrating epidemics in the era of 90-90-90. Curr Opin HIV AIDS. 2020;14(5):354–65.

27. World Health Organisation (WHO). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendation for a public health approach: 2nd ed. Geneva: World Health Organization; 2016. 1–480 p.

28. Ruperez M, Pou C, Maculuve S, Ceden S, Luis L, Rodrı J, et al. Determinants of virological failure and antiretroviral drug resistance in Mozambique. J Antimicrob Chemother. 2015;70:2639–47.

29. Landis RC, Carmichael-simmons K, Hambleton IR, Best A. HIV viral load trends in six eastern Caribbean countries utilizing a regional laboratory referral service: Implications for treatment as prevention. PLoS One. 2015;10(4):1–9.

30. Salam Mbengue MA, Chasela C, Onoya D, Mboup S, Fox MP, Evans D. Clinical predictor score to identify patients at risk of poor viral load suppression at six months on antiretroviral therapy: results from a prospective cohort study in Johannesburg, South Africa. Clin Epidemiol [Internet]. 2019;11:359–73. Available from: http://doi.org/10.2147/CLEP.S197741

31. Pollack TM, Duong HT, Pham TT, Nguyen TD, Libman H, Ngo L, et al. Routine versus targeted viral load strategy among patients starting antiretroviral in Hanoi, Vietnam. J Int AIDS Soc [Internet]. 2019;22:1–9. Available from: https://doi.org/10.1002/jia2.25258

32. Bonner K, Mezochow A, Roberts T, Ford N, Cohn J. Viral load monitoring as a tool to

reinforce adherence: a systematic review. J Acquir Immune Defic Syndr [Internet]. 2013;64(1):74–8. Available from: https://doi.org/10.1080/09540121.2017.1344767

33. Trinh TT, Montague BT, Flanigan TP, Gerard HM. HIV suppression among patients on treatment in Vietnam: a review of HIV viral load testing in a public urban clinic in Ho Chi Minh city. AIDS Res Treat. 2011;2011:1–8.

34. Bachmann N, Braun A Von, Labhardt ND, Kadelka C, Gu HF, Sekaggya-wiltshire C, et al. Importance of routine viral load monitoring: higher levels of resistance at ART failure in Uganda and Lesotho compared with Switzerland. J Antimicrob Chemother. 2019;74(2):468–72.

35. Ssempijja V, Chang LW, Nakigozi G, Ndyanabo A, Quinn TC, Cobelens F, et al. Results of early virologic monitoring may facilitate differentiated care monitoring strategies for clients on ART, Rakai, Uganda. Open Forum Infect Dis. 2018;1–8.

36. Glass TR, Motaboli L, Nsakala B, Lerotholi M, Vanobberghen F, Id AA, et al. The viral load monitoring cascade in a resource-limited setting: a prospective multicentre cohort study after introduction of routine viral load monitoring in rural Lesotho. PLoS One. 2019;14(8):1–11.

37. Mungwira RG, Divala TH, Nyirenda OM, Kanjala M, Muwalo F, Mkandawire FA, et al. A targeted approach for routine viral load monitoring in Malawian adults on antiretroviral therapy. Trop Med Int Heal. 2018;23(5):526–32.

38. Zoufaly A, Jochum J, Hammerl R, Nassimi N, Raymond Y, Burchard G., et al. Virological failure after 1 year of first-line ART is not associated with HIV minority drug resistance in rural Cameroon. J Antimicrob Chemother [Internet]. 2015;70:922–5. Available from: https://academic.oup.com/jac/article-abstract/70/3/922/777195

39. Lecher S, Williams J, Fonjungo PN, Kim AA, Ellenberger D, Zhang G. Progress with scale-up of HIV viral load monitoring — seven sub-saharan African countries, January 2015–June 2016. Vol. 65. 2016.

40. Tarquino IA P, Venables E, Fidelis JM DA, Giuliani R, Decroo T. " I take my pills every day , but then it goes up , goes down . I don ' t know what ' s going on ": Perceptions of HIV virological failure in a rural context in Mozambique. A qualitative research study. PLoS One [Internet]. 2019;14(6):1–13. Available from: https://doi.org/10.1371/journal.pone.0218364

41. Haile D, Takele A, Gashaw K, Demelash H, Nigatu D. Predictors of treatment failure among adult antiretroviral treatment (ART) clients in Bale zone hospitals, south eastern Ethiopia. PLoS One. 2016;11(10):1–14.

42. Genn L. Refill non-adherence and immunologic failure as identifiers of HIV virologic treatment failure among adolescents in Botswana. 2016.

43. Tsegaye AT, Wubshet M, Awoke T, Alene KA. Predictors of treatment failure on second-line antiretroviral therapy among adults in northwest Ethiopia : a multicentre retrospective follow-up study. BMJ Open [Internet]. 2016;6:1–8. Available from: http://bmjopen.bmj.com/

44. Jobanputra K, Parker LA, Azih C, Okello V, Maphalala G, Kershberger B, et al. Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland. PLoS One [Internet]. 2015;10(2):1–12. Available from: https://doi.org/10.1371/journal.pone.0116144

45. Bulage L, Ssewanyana I, Nankabirwa V, Nsubuga F, Kihembo C, Pande G. Factors

associated with virological non-suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014--July 2015. BMC Infect Dis [Internet]. 2017;17:1–11. Available from: https://doi.org/10.1186/s12879-017-2428-3

46. Bulage L, Ssewanyana I, Nankabirwa V, Nsubuga F, Kihembo C, Pande G, et al. Factors associated with virological non- suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014–July 2015. BMC Infect Dis [Internet]. 2017;17:1–11. Available from: https://doi.org/10.1186/s12879-017-2428-3

47. Ayalew Biset, MohammedKumilachew D, Belay A, Getu S, Teju D, Endale D, Tsegaye Y, et al. First-line antiretroviral treatment failure and associated factors in HIV patients at the University of Gondar Teaching Hospital, Gondar, Northwest Ethiopia. HIV/AIDS - Res Palllative Care [Internet]. 2016;8:141–6. Available from: http://dx.doi.org/10.2147/HIV.S112048

48. Hudson FP, Mulenga L, Westfall AO, Warrier R, Mweemba A, Saag MS, et al. Evolution of HIV-1 drug resistance after virological failure of first-line antiretroviral therapy in Lusaka Zambia. Antivir Ther. 2019;29:1–21.

49. Hawkins C, Ulenga N, Liu E, Aboud S, Mugusi F, Chalamilla G, et al. HIV virological failure and drug resistance in a cohort of Tanzanian HIV-infected adults. J Antimicrob Chemother. 2016;212(71):1966–74.

50. Bitwale NZ, Mnzava DP, Kimaro FD, Jacob T, Mpondo BCT, Jumanne S. Prevalence and factors associated with virological treatment failure among children and adolescents on antiretroviral therapy attending HIV/AIDS care and treatment clinics in Dodoma municipality, central Tanzania. J Pediatric Infect Dis Soc [Internet]. 2020;10(2):1–10. Available from: https://academic.oup.com/jpids/advance-article-

abstract/doi/10.1093/jpids/piaa030/5848104

51. Ajose O, Mookerjee S, Mills EJ, Boulle A, Ford N. Treatment outcomes of patients on second-line antiretroviral therapy in resource-limited settings: a systematic review and meta-analysis. AIDS. 2012;26(8):929–38.

52. Kazooba P, Mayanja BN, Levin J, Masiira B, Kaleebu P. Virological failure on first-line antiretroviral therapy: associated factors and a pragmatic approach for switching to second line therapy–evidence from a prospective cohort study in rural South-Western Uganda, 2004-2011. PanAfrican Med J [Internet]. 2018;29:1–16. Available from: http://www.panafrican-med-journal.com/content/article/29/191/full/

53. Kiweewa F, Esber A, Musingye E, Reed D, Crowell TA, Cham F, et al. HIV virologic failure and its predictors among HIV-infected adults on antiretroviral therapy in the African cohort study. PLoS One [Internet]. 2019;14(2):1–16. Available from: https://doi.org/10.1371/journal.pone.0211344

54. Kan W, Teng T, Liang S, Ma Y, Tang H, Zuohela T, et al. Predictors of HIV virological failure and drug resistance in Chinese patients after 48 months of antiretroviral treatment , 2008–2012: a prospective cohort study. BMJ Open. 2017;7:1–15.

55. Medecins Sans Frontieres (MSF). Making viral load routine: successes and challenges in the implementation of routine HIV viral load monitoring. 2016. 1–36 p.

56. Miti S, Handema R, Mulenga L, Mwansa JK, Abrams E, Frimpong C, et al. Prevalence and characteristics of HIV drug resistance among antiretroviral treatment (ART) experienced adolescents and young adults living with HIV in Ndola, Zambia. PLoS One [Internet]. 2020;15(8):1–15. Available from: http://dx.doi.org/10.1371/journal.pone.0236156

57. Rebeiro PF, Cesar C, Shepherd BE, Boni RB De, Corte CP, Pape JW, et al. Assessing the HIV care continuum in Latin America: progress in clinical retention, cART use and viral suppression. J Int AIDS Soc [Internet]. 2016;19:1–8. Available from: http://dx.doi.org/10.7448/IAS.19.1.20636

58. Shiferaw MB, Endalamaw D, Hussien M, Agegne M, Amare D, Estifanos F, et al. Viral suppression rate among children tested for HIV viral load at the Amhara Public Health Institute , Bahir Dar , Ethiopia. BMC Infect Dis [Internet]. 2019;19:1–6. Available from: https://doi.org/10.1186/s12879-019-4058-4

59. The Tenores Study Group. Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study. Lancet Infect Dis [Internet]. 2015;16:565–75. Available from: http://dx.doi.org/10.1016/S1473-3099(15)00536-8

60. Phillips AN, Stover J, Cambiano V, Nakagawa F, Jordan MR, Pillay D, et al. Impact of HIV drug resistance on HIV/AIDS-associated mortality, new infections, and antiretroviral therapy program costs in sub–saharan Africa. J Infect Dis. 2017;215:1362–5.

61. Bvochora T, Satyanarayana S, Takarinda KC, Bara H, Chonzi P, Komtenza B, et al. Enhanced adherence counselling and viral load suppression in HIV seropositive patients with an initial high viral load in Harare, Zimbabwe: Operational issues. PLoS One [Internet]. 2019;14(2):1–13. Available from: https://doi.org/10.1371/journal.pone.0211326

62. Medecins Sans Frontieres (MSF). New model of care aims to reduce deaths among advanced HIV patients [Internet]. 2019. Available from: https://www.msf.org/new-model-care-reduce-deaths-aids-malawi ›

63. NSO. 2018 Malawi population & housing census: preliminary report. Zomba: NSO; 2018.

1–55 p.

64. Ayele G, Tessema B, Amsalu A, Ferede G, Yismaw G. Prevalence and associated factors of treatment failure among HIV/AIDS patients on HAART attending University of Gondar Referral Hospital Northwest Ethiopia. BMC Immunol [Internet]. 2018;19:1–13. Available from: https://doi.org/10.1186/S12865-018-0278-4

65. Davey DJ, Abrahams Z, Feinberg M, Prins M, Serrao C, Medeossi B, et al. Factors associated with recent unsuppressed viral load in HIV-1-infected patients in care on first-line antiretroviral therapy in South Africa. Int J STD AIDS. 2018;29(6):603–10.

66. Gupta-wright A, Fielding K, Oosterhout JJ Van, Alufandika M, Grint DJ, Chimbayo E, et al. Virological failure, HIV-1 drug resistance, and early mortality in adults admitted to hospital in Malawi: an observational cohort study. Lancet HIV [Internet]. 2020;7(9):e620–8. Available from: http://dx.doi.org/10.1016/S2352-3018(20)30172-7

67. Umar E, Levy JA, Bailey RC, Donenberg G, Hershow RC, Ellen M, et al. Virological non-suppression and its correlates among adolescents and young people living with HIV in Southern Malawi. AIDS Behav [Internet]. 2018;1–10. Available from: https://doi.org/10.1007/s10461-018-2255-6

68. Hicham T, Ilyas E, Tarik H, Noureddine B, Omar B, Rachid F, et al. Risk factors associated with unsuppressed viral load in HIV-1 infected patients at the first antiretroviral therapy in Morocco. Int J Mycobacteriol. 2019;8:113–7.

69. Bayu B, Tariku A, Bulti Balcha A, Habitu Ayanaw Y, Darso T, Teshome Fetene D. Determinants of virological failure among patients on highly active antiretroviral therapy in University of Gondar Referral Hospital, Northwest Ethiopia: a case–control study. HIV/AIDS - Res Palllative Care [Internet]. 2017;9:153–9. Available from:

http://www.dovepress.com/

70. Desta AA, Woldearegay TW, Futwi N, Gebrehiwot GT, Gebru GG, Berhe AA, et al. HIV virological non-suppression and factors associated with non-suppression among adolescents and adults on antiretroviral therapy in northern Ethiopia: a retrospective study. BMC Infect Dis [Internet]. 2020;20:1–10. Available from: https://doi.org/10.1186/s12879-019-4732-6

71. Leierer G, Grabmeier-pfistershammer K, Steuer A, Sarcletti M, Geit M, Haas B, et al. A single quantifiable viral load is predictive of virological failure in Human Immunodefi ciency Virus (HIV)-infected patients on combination antiretroviral therapy: the Austrian HIV cohort study. Open Forum Infect Dis [Internet]. 2016;1–9. Available from: https://academic.oup.com/ofid/article-abstract/3/2/ofw089/2399407

72. Shoko C, Chikobvu D. Determinants of viral load rebound on HIV/AIDS patients receiving antiretroviral therapy: results from South Africa. Theor Biol Med Model [Internet]. 2018;15(10):1–13. Available from: https://doi.org/10.1186/s12976-018-0082-0

73. Yassin S, Gebretekle GB. Magnitude and predictors of antiretroviral treatment failure among HIV-infected children in Fiche and Kuyu hospitals, Oromia region, Ethiopia: a retrospective cohort study. Pharmacol Res Perspect. 2017;5(1):1–9.

74. Zuo Z, Liang S, Sun X, Bussell S, Yan J, Kan W, et al. Drug resistance and virological failure among HIV-infected patients after a decade of antiretroviral treatment expansion in eight provinces of China. PLoS One. 2016;11(12):1–13.

75. Leierer G, Grabmeier-pfistershammer K, Steuer A, Geit M, Sarcletti M, Haas B, et al. Factors associated with low-level viraemia and virological failure: results from the Austrian HIV cohort study. PLoS One. 2015;10(11):1–12.

76. Hailu GG, Hagos DG, Hagos AK, Wasihun G, Dejene TA. Virological and immunological failure of HAART and associated risk factors among adults and adolescents in the Tigray region of Northern Ethiopia. PLoS One [Internet]. 2018;13(5):1–17. Available from: https://doi.org/10.1371/journal.pone.0196259

77. Sithole Z, Mbizvo E, Chonzi P, Mungati M, Juru TP, Shambira G. Virological failure among adolescents on ART, Harare City, 2017- a case-control study. BMC Infect Dis [Internet]. 2018;18:1–8. Available from: https://doi.org/10.1186/s12879-018-3372-6

78. Haftu AZ, Aregay A, Id D, Bezabih NM, Woldearegay W. Incidence and factors associated with treatment failure among HIV infected adolescent and adult patients on second-line antiretroviral therapy in public hospitals of Northern Ethiopia: multicenter retrospective study. PLoS One [Internet]. 2020;15(9):1–15. Available from: http://dx.doi.org/10.7448/IAS.20.1.21623

79. Bukenya D, Mayanja BN, Nakamanya S, Muhumuza R, Seeley J. What causes non-adherence among some individuals on long term antiretroviral therapy? Experiences of individuals with poor viral suppression in Uganda. AIDS Res Ther [Internet]. 2019;16:1–9. Available from: https://doi.org/10.1186/s12981-018-0214-y

80. Natukunda J, Kirabira P, Ing K, Ong C, Shibanuma A, Jimba M. Virologic failure in HIV-positive adolescents with perfect adherence in Uganda: a cross-sectional study. Trop Med Health [Internet]. 2019;47:1–10. Available from: https://doi.org/10.1186/s41182-019-0135-z

81. Haile GS, Berha AB. Predictors of treatment failure , time to switch and reasons for switching to second line antiretroviral therapy in HIV infected children receiving first line anti-retroviral therapy at a Tertiary Care Hospital in Ethiopia. BMC Pediatr [Internet].

2019;19(37):1–9. Available from: https://doi.org/10.1186/s12887-019-1402-1

82. Louis FJ, Buteau J, Franc K, Hulland E, Yang C, Boncy J, et al. Virologic outcome among patients receiving antiretroviral therapy at five hospitals in Haiti. PLoS One [Internet]. 2018;13(1):1–12. Available from: https://doi.org/10.1371/ journal.pone.0192077

83. Mujugira A, Celum C, Tappero JW, Ronald A, Mugo N, Baeten JM. Younger Age Predicts Failure to Achieve Viral Suppression and Virologic Rebound Among HIV-1-Infected Persons in serodiscordant partnerships. AIDS Res Hum Retroviruses. 2016;32(2):148–54.

84. Salou M, Dagnra AY, Butel C, Vidal N, Serrano L, Takassi E, et al. High rates of virological failure and drug resistance in perinatally HIV-1-infected children and adolescents receiving lifelong antiretroviral therapy in routine clinics in Togo. J Int AIDS Soc [Internet]. 2016;19:1–7. Available from: https://doi.org/10.1186/s41182-019-0135-z

85. Ford N, Orrell C, Apollo T, Vojnov L. HIV viral resuppression following an elevated viral load: a systematic review and meta-analysis. J Int AIDS Soc [Internet]. 2019;22:1–6. Available from: http://onlinelibrary.wiley.com/doi/10.1002/jia2.25415/full

86. Connor JO, Smith C, Lampe FC, Johnson MA, Chadwick DR, Nelson M, et al. Durability of viral suppression with first-line antiretroviral therapy in patients with HIV in the UK: an observational cohort study. Lancent HIV [Internet]. 2017;4:e295-302. Available from: https://doi.org/10.1016/j.ijid.2018.04.795

87. Tanuma J, Matsumoto S, Haneuse S, Cuong DD, Vu T Van, Thanh PT, et al. Long-term viral suppression and immune recovery during first-line antiretroviral therapy: a study of an HIV-infected adult cohort in Hanoi, Vietnam. J Int AIDS Soc [Internet]. 2017;20:1–8. Available from: https://doi.org/10.1002/jia2.25030

88. Flynn AG, Anguzu G, Mubiru F, Kiragga AN, Kamya M, Meya DB, et al. Socioeconomic position and ten-year survival and virologic outcomes in a Ugandan HIV cohort receiving antiretroviral therapy. PLoS One [Internet]. 2017;12(12):1–12. Available from: https://doi.org/10.1371/journal.pone.0189055

89. Gunda DW, Kilonzo SB, Mtaki T, Bernard DM, Kalluvya SE, Shao ER. Magnitude and correlates of virological failure among adult HIV patients receiving PI based second line ART regimens in north western Tanzania: a case control study. BMC Infect Dis [Internet]. 2019;19:1–7. Available from: https://doi.org/10.1186/s12879-019-3852-3

90. Ongubo DM, Lim R, Tweya H, Stanley CC, Tembo P, Broadhurst R, et al. A cross-sectional study to evaluate second line virological failure and elevated bilirubin as a surrogate for adherence to atazanavir / ritonavir in two urban HIV clinics in Lilongwe, Malawi. BMC Infect Dis. 2017;17:1–10.

91. Raho-moussa M, Guiguet M, Michaud C, Honore P, Palacios C, Boue F, et al. Respective roles of migration and social deprivation for virological non-suppression in HIV-infected adults on antiretroviral therapy in France. PLoS One [Internet]. 2019;14(3):1–10. Available from: https://doi.org/ 10.1371/journal.pone.0213019

92. Siefried KJ, Mao L, Kerr S, Cysique LA, Gates TM, Mcallister J, et al. Socioeconomic factors explain suboptimal adherence to antiretroviral therapy among HIV-infected Australian adults with viral suppression. PLoS One [Internet]. 2017;12(4):1–23. Available from: https://doi.org/ 10.1371/journal.pone.0174613

APPENDICES

Appendix 1: Data Collection Checklist

DATA COLLECTION CHECKLIST		
UNIQUE #:	**ART #:**	**HEALTH FACILITY:**
DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS		
Age:	At initiation	At VL
Gender:	Male	Female
Marital Status	Married Single Divorced Widowed Others specify…….	
Duration on ART	0 - < 2Years 2 - <4Yrs 4 - < 6Yrs 6 -< 8Yrs 8Yrs +	
Time on ART at Virological Failure (VF)	0 - < 2Years 2 - <4Yrs 4 - < 6Yrs 6 -< 8Yrs 8Yrs +	
Occupation	Farmer Business	

	Unemployed Teacher Health worker Others Specify……..
History of TB previously	Yes No
TB Co infection at VL	Yes No
History of Substance abuse	Yes No
Reason for starting ART	Test and treat CD4 WHO Clinical stage Others……..
WHO clinical Stage	At Initiation Stage 1 Stage 2 Stage 3 Stage 4
Burden Virological Failure	
Total patients with viral load ≥1000 copies	
Total patients with viral load ≥1000 copies from July 2016 to June 2019	
Characteristics associated with Virological Failure	
ART Regimen at VL	
Previous ART Regimen (s)	
Adherence Status at VL	Good (≥ 95%) Fair (≥ 85% - <95%) Poor (<85%)

Previous adherence status	Good (≥ 95%) Fair (≥ 85% - <95%) Poor (<85%)
EAC session conducted (Y/N)	Yes No
Viral load after EAC (Y/N)	Yes No
History of missed appointments	Yes No
How long?	< 1 Month 1Month < 2 months 2Months +
Lost to follow up (Y/N)	Yes No
Exposure to ART before starting	PEP PMTCT Others ……..
History of side effects (Y/N)	Yes No
Reasons for Viral Load	Routine Viral Load (RVL) Targeted Viral Load (TVL)
OTHER IMPORTANT INFORMATION	
History of depression?	Yes No
Participation in PLWHA Groups (Support group/ Teen club)	Yes No
If a child (Disclosure done or not)	Yes No

Appendix 2: Budget estimates and Justification

Budget Estimates

ITEM	DESCRIPTION	QUANTITY	AMOUNT
STATIONERY			
Ream of Papers	For Printing	3.00	18,000.00
Arch lever files	1 per facility	14.00	9,800.00
Pens	1 per facility	15.00	750.00
Envelopes	Data collection	3.00	300.00
SECRETARIAL SERVICES			
Proposal and dissertation Printing	1 each	2.00	10,000.00
Proposal and dissertation Photocopying	4 each	8.00	10,000.00
Proposal and dissertation Binding	4 each	8.00	12,000.00
Data Collection Guide	2 per 15 sites	30.00	3,000.00
Permission Letter	2 pages	14.00	1,120.00
Internet			10,000.00
ALLOWANCES			
Lunch Allowance for Research assistants	1 per facility for 2 days	14.00	112,000.00
Contigency money	10% of Budget		23,497.00
Transport Money	for Data Collectors	18.00	18,000.00
	Researcher	1.00	30,000.00
Accommodation for Researcher	28 Days	28.00	280,000.00
10% COMREC Fee	To be paid by Dept		53,846.00
TOTAL (MWK)			592,313.00

Budget Justification

The stationery was required to execute the study per facility. The ream of papers was required for printing the 4 copies of dissertation proposal and final paper. Lunch allowance was given to the ART Clerk (Research assistant) at each facility who helped with data collection. The principal investigator used transport money to and from the health facility for data collection and verification as well as travelling to the district itself. Accommodation was booked for the researcher since she is currently residing outside the district where the research was being conducted. The estimated cost was approximately 592, 313.00 Malawi kwacha for this research. The contingency money was added in readiness for any inconveniences to be met during the course of the study

Appendix 3: Certificate of Ethical Approval

CERTIFICATE OF ETHICS APPROVAL

This is to certify that the College of Medicine Research and Ethics Committee (COMREC) has reviewed and approved a study entitled:

P.02/20/2961 - Burden of virological failure and factors associated with virological failure among HIV positive patients on Antiretroviral Therapy (ART) by Shupe Mphande

On 21-Apr-20

As you proceed with the implementation of your study, we would like you to adhere to international ethical guidelines, national guidelines and all requirements by COMREC some of which are indicated on the next page for your study

21-Apr-20

Prof. E. Ulmer -Chairperson (COMREC)

Date

Approved by College of Medicine

21-Apr-2020

(COMREC)