# (COMPLETED RESEACRH)

# PREVALENCE OF BACTERIAL OPPORTUNISTIC INFECTIONS AND ASSOCIATED SOCIO-DEMOGRAPHIC FACTORS IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENTS INITIATED ON ANTIRETROVIRAL TREATMENT IN MOSES KOTANE SUB-DISTRICT, NORTH WEST PROVINCE

ΒY

Mangali Ongezwa

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Supervisor: Prof E Maimela

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# DECLARATION

I Mangali Ongezwa declare that this is my work and has never been submitted to any institution before.

Signature: Mangali. O

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#### ABSTRACT

**Background:** Human Immunodeficiency Virus (HIV) is a virus that destroys the immune system by weakening the body's defense (immune cells) against many infections (Anon, 2021). This study was about prevalence of bacterial opportunistic infections and associated socio-demographic factors in human immunodeficiency virus infected patients initiated on antiretroviral treatment in Moses Kotane Sub-District, North West Province.

**Methodology:** The study was a retrospective study design and the data collected included data from 2019-2021. The completed data collection resulted in 1682 records which were collected from five clinics which are Bakubung, Modderkail, Moruleng, Sandfontein and Sefikile. Data was analysed using the STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas).

**Results:** The prevalence of opportunistic infections in the current study was found to 7.4% which is very low however, this increased with increasing age. Occurrence of these opportunistic infections were significantly associated with age, gender, CD4 count and WHO clinical staging. Tuberculosis remained the number 1 OIs found in these patients and therefore, a significant concern that should be explored is the intervention that can reduce the burden of bacterial opportunistic infection with major focus on Tuberculosis. The current study revealed that there is a paucity of primary data on the contributory factors to opportunistic infections. The study strongly recommends future researchers to do an interventional study which could yield results to address factors influencing high rate of HIV infection amongst youth which will facilitate the development of better public health interventions to reduce the burden of prevalence of opportunistic infection in HIV infected patients. Therefore, it is recommended that clinics in Moses Kotane sub-district be provided with trained staff on screening and diagnose bacterial opportunistic infections

# Key words: Opportunistic infections, prevalence, Human immunodeficiency Virus, Antiretroviral treatment

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# LIST OF ABBREVIATIONS

SA	South Africa
ТВ	Tuberculosis
ART	Antiretroviral treatment
VL	Viral Load
HIV	Human Immunodeficiency Virus
Ols	Opportunistic Infection
CNS	Central Nervous System
CDC	Communicable Disease Coordinator
CD4	Cluster of Differentiation 4
SAHPRA	South African Health Products Authority
DoH	Department of Health
PLWHIV	Patient living with HIV
NWP	North-West Province
WHO	World Health Organization

# **DEFINITION OF CONCEPTS**

**Antiretroviral treatment-** drugs that inhibit the multiplication of the retrovirus like HIV and is given to HIV positive patients to stop the progression of the virus by decreasing the viral load in the body and boosting immune system (LU,WU,Yarta, XU,Ding & LU,2018). In the context of this study, antiretroviral treatment will be referring to the South African Health Products Authority (SAHPRA) approved treatment for HIV used in SA.

**Opportunistic Infections-** infections that crop up more often and severe to people with weakened immune system (Anon, 2021). In the context of this study, OIs will refer to TB, diarrhea and CNS associated infections.

**Human Immunodeficiency Virus-** is a virus that destroys the immune system by weakening the body's defense (immune cells) against many infections (Anon, 2021). In the context of the study, HIV will refer to the above.

# 1. CHAPTER ONE: OVERVIEW OF THE STUDY

#### 1.1. Introduction and background of the study

Human immunodeficiency virus (HIV) is a virus that alters the body's ability from fighting diseases by compromising the immune system. HIV attacks the body's CD4+ T cells which aids the body in fighting the diseases. It weakens the immune system and making it vulnerable to opportunistic infections (World health organization, 2021). HIV is still considered as a major public health issue. According to statistics, it is recorded that by the end of 2020 people living with HIV were recorded to approximately 37.7 million. Out of that 37.7 million two third of them are from the African region (WHO, 2021).

Highly active antiretroviral therapy (HAART) is a medication regimen used to manage and treat HIV type 1. It is composed of several drugs in the antiretroviral classes of medications (Eggleton & Nagalli, 2020). Only 21.7 million people infected with HIV have been reported to have accesses to antiretroviral therapy (ART), with the rest at risk of the potential complications of HIV infection (Ranganathan & Umadevi, 2019). Global targets for scaling up ART include ensuring that 90% of patients on ART achieve viral suppression. This gives a renewed emphasis to ensuring optimal levels of adherence (Shubber, Mills, Nachega, Vreeman, Freitas & Bock et al., 2016).

HIV became responsible for significant morbidity and mortality due to underlying immunesuppression which leads to life threatening opportunistic infections (OIs) during the natural course of the disease (Solomon, Angore, Koyra, Tufa, Berheto & Admasu, 2018). OIs associated with HIV remain the single main cause of ill-health and death among HIV/AIDS patients in resource poor settings. OIs lower the quality of life of HIV infected persons, speeds up the rate of progression to fully blown AIDS, reduces patients' response to ART especially when HIV-positive patients are co-infected with tuberculosis, increases stigma and limits one's ability to work and are usually associated with high medical care costs (Rubaihayo, Tumwesigye, Konde-Lule, Wamani, Nakku-Joloba, & Makumbi, 2016). It has been shown that oral lesions are diagnostic and prognostic of HIV infection, and many oral opportunistic infections continue to be a major problem, particularly in developing countries (Ranganathan & Umadevi, 2019).

Survival in people infected with HIV has improved because of an increasingly powerful array of antiretroviral treatments, but neurological symptoms due to comorbid conditions and opportunistic infections are still a public health concern (Tan, Smith, von Geldern, Mateen & McArthur, 2012; Pang, Shang, Li, Xu, Bi & Zhong 2018). One in three people seek health care for HIV/AIDS-related opportunistic infections globally and the rate of reoccurrence of OIs is increasing as in 2017 approximately 160,684 recurrent tuberculosis (TB) cases have been reported (Dembelu & Woseneleh, 2021). In Sichuan West of China it was found that the most opportunistic infection amongst HIV positive people on ART was bacterial pneumonia at 25.8% followed by candida infection; Pneumocystis jiroveci pneumonia, tuberculosis, infectious diarrhoea, cryptococcus infection, cytomegalovirus infection, toxoplasmosis, hepatitis C, nontuberculous mycobacteria desease and Penicillium marneffei infection at 18.3%, 11.9%, 11.5%, 9.3%, 7.3%, 4.9%, 4.6%, 4.0%, 2.2% and 0.3% respectively (Pang, Shang, Li, , Xu, Bi et al., 2018). There is no adequate information on the reoccurrence rate of OIs in Africa, however there were 310,000 OI-related deaths among AIDS patients in the eastern and southern Africa region (Dembelu & Woseneleh, 2021). In a study conducted in China, CD4+T cell counts of less than 100 cells/µL and not receiving antiretroviral therapy were found to be the two strongest risk factors for in-hospital mortality. As bacterial Opportunistic infections are the significant complication of HIV infection, the current study will focus on the investigating the prevalence of bacterial OIs in a rural area of North West Province of South Africa.

#### **1.2. Problem statement**

North West Province (NWP) has one of the highest HIV prevalence in South Africa. It is further challenged by severe poverty, a huge surface area housing a scattered community, and limited human resources. Despite this, it is one of the provinces that have successfully initiated large-scale ARV access in South Africa (Variava, 2006.). Opportunistic infections are one of the major causes of morbidity and mortality in patients

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with HIV infection throughout the world. Even if potent combination of ART has reduced the incidence of OIs for certain patients with access to care, for those patients in the developed and developing world did not have access to care and have OIs (Moges & Kassa, 2014).

The area is surrounded by lot of platinum mines and a lot of people come from different provinces to work in the mines, meanwhile others come to look for a job. Also the hospital is situated next to a well-known place, Sun City, where a lot of celebrities and tourists come to visit. Ols are less common now than in the early days of HIV and AIDS when there was no treatment however, researcher has noted that some people with HIV presenting at health facilities within Moses Kotane still develop OIs for various reasons. There are no studies that have analysed the prevalence of bacterial opportunistic infections in HIV -infected patients in Moses Kotane sub-district. Hence the researcher wanted to investigate the prevalence of bacterial opportunistic infections in patient starting ART in Moses Kotane Hospital and also determine the association between the patient's socio-demographic characteristics and types of bacterial opportunistic infections

# **1.3. Purpose of the study**

## 1.3.1. The aim of the study

The purpose of undertaking the study was to investigate the prevalence of bacterial opportunistic infections and associated socio-demographic factors in HIV infected patients taking ART in Mogwase cluster, Moses Kotane Sub-district, North-West Province from 2019-2021.

# 1.3.2. Objectives of the study

- To outline the socio-demographic characteristics of patients on ART.
- To describe the prevalence of the bacterial opportunistic infections in HIV infected patients taking ART. .
- To determine the association between the patient socio-demographic characteristics and categories of bacterial opportunistic infection.

### 1.4. Research question

What is the prevalence of bacterial opportunistic infection and associated sociodemographic factors in patients on ART?

#### 1.5. Literature review

The review of the literature in the current study provides an overview on the following areas of study: the prevalence of opportunistic infections globally; the prevalence of opportunistic infections in South Africa, factors associated with opportunistic infections, intervention and control of opportunistic infections. This review was informed by literature published from 2014 to date retrieved from the following databases: Google Scholar and Pub-Med. A detailed literature review is presented in detail in chapter 2.

## 1.6. Methodology

In this study, the approach which was used to address the research question was quantitative research approach, where the researcher used the retrospective study design to gather data from patient's files from five clinics which are Bakubung, Modderkail, Moruleng, Sandfontein and Sefikile.. This section has provided a detailed description of the research design, data collection procedures, data analysis, and data collection tools. Lastly, validity, reliability and ethical considerations were also described. A detailed methodology is presented in detail in chapter 3.

## 1.7. Ethical consideration

Ethics are defined as rules of conduct. When you exhibit acceptable practices in society and under governing bodies of instruction, you are delivering patterns of what is considered acceptable, good behavior (Wheeler & Bertram, 2019). Ethical clearance to conduct the study was granted by the Turfloop Research and Ethics committee. Ethical considerations will be discussed in depth in chapter 3.

# 1.8. Significance of the study

The study findings will be beneficial to the health department of North-West specifically to Moses Kotane sub-district in understanding the prevalence of OIs in HIV infected patients and how best can they do to help the community to prevent these opportunistic infection. The findings give the sub-district management a better understanding of the community they are serving in terms of illnesses and how they spread or develop into other conditions if not prevented earlier.

#### 2. CHAPTER 2: LITERATURE REVIEW

#### 2.1. Introduction

A literature review is a piece of academic writing demonstrating knowledge and understanding of the academic literature on a specific topic placed in context. A literature review also includes a critical evaluation of the material; this is why it is called a literature review rather than a literature report (Ridley, 2012). The review of research literature in the current study was conducted to provide a theoretical background for subsequent research and learning the breadth of research (Okoli & Schabram, 2010. Therefore, literature research reviews in current study followed the review of published scientific research from Google Scholar, PubMed, Science Direct and consultation of the University of Limpopo online library system.

## 2.2. Opportunistic infections amongst people living with HIV and taking ARTs

Opportunistic infections still remain to be a cause of morbidity and mortality in HIVinfected patients. They often develop because of severe weakened immune system resulting from poor adherence to antiretroviral therapy, failure of antiretroviral therapy, or unawareness of HIV infection by patients whose first clinical manifestation of AIDS is an opportunistic infection (Iribarren, Rubio, Aguirrebengoa, Arribas, Baraia-Etxaburu, & Gutiérrez, et al., 2016). The natural history of HIV disease may be indirectly affected by the occurrence of opportunistic diseases, because HIV viral load increases in patients with acute opportunistic diseases. Severely immunecompromised HIV patients may develop a variety of opportunistic infections that have a significant impact on their well-being, quality of life, health care costs, and their survival. These OIs are mostly caused by a variety of germs such as viruses, bacteria, fungi, and parasites (Moges & Kassa, 2014). The current study will only focus on bacterial opportunistic infections.

# 2.2.1. Global burden of bacterial opportunistic infection amongst people living with HIV and taking ART

Global burden of infectious disease estimates are crucial to guide prevention strategies and to determine treatment needs (Rajasingham, Smith, Park, Jarvis,

Govender & Chiller et al., 2017). The introduction of HAART led to substantial reduction in the incidence of OIs with more impressive percentage decline in HICs (43–97%) compared to 30–79% in LMICs. Disparities in the magnitude of HIV-related OIs between HICs and LMICs are evident both in the pre-HAART and post-HAART era. Efforts to optimize HAART-induced decline in HIV-related OIs should become a global health priority irrespective of prevailing socioeconomic circumstances (Iroezindu, 2016).

In the High Income Countries (HICs) and regions such North America, Europe and Australia, it was found that the conditions such as the Pneumocystis *jirovecii* pneumonia (PJP), Pneumocystis carinii pneumonia (PCP), (Iroezindu, 2016; Shenoy, Ramapuram, Shenoy, Ahmed & Srikant, 2017) candidiasis, Cytomegalovirus disease, Mycobacterium avium complex disease, and Kaposi's sarcoma were the most frequent while tuberculosis, candidiasis, chronic diarrhea, and cryptococcosis were predominant in Low Middle Income Countries (LMICs) (Iroezindu, 2016). In a retrospective study conducted in China using hospital admitted patients, they noticed that bacterial pneumonia was the most common bacterial opportunistic infection standing at 25.8%, tuberculosis 11.5%, infectious diarrhea 9.3%, Cryptococcus infection 7.3% (Pang, Shang, Li, Xu, Bi & Zhong et al. 2018). However, a study conducted in Brazil revealed that HIV/TB co-infection is the major cause of high morbidity and mortality. It was observed that the low CD4 T lymphocyte need for mechanical ventilation and presence of disseminated clinical presentation of TB also play a role in mortality risk hence they put an emphasis on the need to address the social determinants of health (da Silva Escada, Velasque, Ribeiro, Cardoso, Marins & Grinsztejn, 2017).

# 2.2.2. Burden of bacterial opportunistic infection amongst people living with HIV and taking ARTs in Africa

Cryptococcus is the most common cause of meningitis in HIV people living in the sub-Saharan Africa (Rajasingham et al., 2017). In a cross sectional series review

of observational data conducted in Uganda using 108 619 HIV positive adult before and after HAART they concluded that prevalence of diarrhea still remains high even after HAART more especially in Northern and Eastern Uganda (Rubaihay, Tumwesigye, Konde-Lule, Wamani, Nakku-Joloba, & Makumbi, 2016). Alem (2021) concluded in his review, where he based his conclusion on 13 articles collected from East Africa that bacterial pneumonia in HIV positive people is a major cause of morbidity and mortality. He further stressed that determination of prevalence of bacterial pneumonia in HIV seropositive people should be identified and recorded.

# 2.2.3. Burden of bacterial opportunistic infection amongst people living with HIV and taking in South Africa

Statistics projected in the WHO page shows that South Africa is the country with the high number of people infected with HIV. In Cherlot Maxeke Academic Hospital they conducted a study on presentation of HIV-positive patients into their emergency unit. In their study they concluded that there is a high prevalence of opportunistic infection in those patients and required a prolonged hospital stay (Laher, Venter, Richards & Paruk, 2021). Meanwhile in KwaZulu-Natal, the province with high HIV prevalence it was found that cryptococcal meningitis was the leading cause of confirmed meningitis among elderly people living with HIV (Britz, Perovic, Von Mollendorf, Von Gottberg, Iyaloo & Quan et al., 2016).

# 2.2.4. Implications of bacterial opportunistic infections on HIV positive patients and interventions to prevent and reduce their incidence

In sub–Saharan Africa, autopsy studies have shown that tuberculosis and bacterial diseases are the 2 most frequent causes of death in HIV-infected adults (MacPherson, Moshabela, Martinson & Pronyk, 2009), even though they are easier to diagnose and treat than many other types of opportunistic infections. Ols cause significant morbidity/mortality in HIV-infected individuals globally (Iroezindu, 2016) and this is due to a combination of 3 factors: poor access to healthcare facilities, poor access to specific diagnostic tests, and poor access to treatment

(Harries, Zachariah, Corbett, Lawn, Santos-Filho & Chimzizi et al., 2010). As a consequence of all 3 factors, not only is the frequency of active tuberculosis underestimated in most HIV infection care programs, but mortality from tuberculosis is also likely to be underestimated. Therefore, the WHO recommends that ART should be initiated regardless of CD4 cell count and this should be taken seriously worldwide and even more seriously in settings with a high burden of tuberculosis and non-tuberculous bacterial infections. The immediate initiation of ART reduces the risk of tuberculosis and non-tuberculous bacterial infections (Anglaret & Eholie, 2017).

#### 3. CHAPTER 3: METHODOLOGY

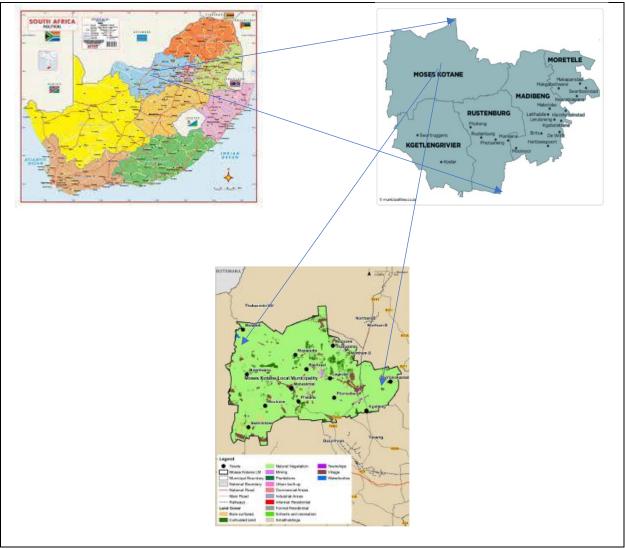
In this study, the approach which was used to address the research question was quantitative research approach, where the researcher used the retrospective study design to gather data from patient's files. Quantitative design in health care research is used to describe, predict, and compare characteristics or variables through the involvement or use of mathematical technique to measure characteristics (Jo Logan, 2021).

## 3.1. Research Design

The research design that the researcher used is retrospective cross sectional review of observational data, where the researcher made use of the secondary data which were obtained from existing patient's file to develop an objective conclusion regarding the research question.

## 3.2. Study Site

The study was conducted in Mogwase cluster in Moses Kotane sub-district, North West Province. The area is surrounded by lot of platinum mines and a lot of people come from different provinces to work in the mines, meanwhile others come to look for a job. The cluster is demarcated next to a well-known place, Sun City, where a lot of celebrities and tourists come to visit. Mogwase cluster in Moses Kotane sub-district has 14 clinics which are implementing ART program and purposive sampling has been used to select the clinics with high number of HIV positive patients initiated on ART on the basis of having enough sample for each clinic as the study is following a quantitative approach.



**Figure 1**: Maps of South Africa and the North West Province showing the district and Moses Kotane District with health facilities

# 3.3. Population and Sampling

# 3.3.1. Population

Population is the whole group in a community that we want to draw a conclusion about (McCombes, 2019). In this study population referred to all HIV positive patients who have been initiated on ART.

#### 3.3.2. Sampling technique

Sample is a subgroup of a population selected in order to represent a larger population (Acharya, Prakas, Saxena, Nigam, 2013). Therefore, in the current study there were 14 clinics which were implementing ART program. Thus purposive sampling was used to select the clinics with high number of HIV positive patients initiated on ART on the basis of having enough sample for each clinic per year as the study followed a quantitative approach.

## 3.3.3. Sample size determination

Sample size is the number of individuals selected in the population that are going to take part in the study or going to be used in the collection of data (McCombes, 2019). Sampling method is a technique used to select a subset of a population that is going to represent the whole population (McCombes, 2019). In the current study, probability proportional to size (PPS) sampling was used which is a method of sampling from a finite population in which a size measure is available for each population unit before sampling and where the probability of selecting a unit is proportional to its size (Skinner, 2014; Etikan & Bala, 2017; Nikolov, Singh & Tantipongpipat, 2022). Therefore, sampling was made from each clinic and sample size calculated using the following formula for each clinic:

# Sample size formula: $n = \frac{N}{1 + N(e)^2}$

## Where

- n is the sample size
- N is the population of ART initiated patients in a year
- e is the sampling error

During the determination of the sample size, the sample size can become an ethical issue if the sample is over-sized and under-sized. Over-sample size occurs when there are more people in the sample that needed in order to help address the research question. Whereas, under-sample size occurs when there is insufficient individuals in the sample. Furthermore, small sample size affects the

generalization of research findings. In this study, the sample size will be representative of the study population and the inclusion of a 10% non-response rate will be done to ensure that the non-response rate (patient records with incomplete information) will not result in an under-size sample, thereby affecting the generalization of the findings. Therefore, a 10% was added to the each clinic sample size as per calculations. A stratified sampling was used to get the sample for each clinic as presented in Table 1 below and therefore each clinic served as a strata in this study. After stratification was done, simple random sampling was applied in each strata to get the desired sample size per strata.

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#### **Table 1**: Distribution of sample size per clinic per year

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	inics	

	20	019 2020		020	2021		
	Population	Sample	Population	Sample size	Population	Sample size	
		size		plus10%		plus10%	
		plus10%					
Bakubung	335	201	311	192	250	169	
Modderkuil	119	101	120	102	107	93	
Mogwase	773	290	636	270	560	257	
Sandfontein	252	170	235	163	209	151	
Moruleng	79	73	127	106	107	93	
Sifikile	83	76	87	79	104	91	
Total	1479	762	864	727	1126	670	

## 3.3.4. Sampling procedure

Period in Years

In this study the researcher used a simple random sampling as a way of choosing which file to be used in the study per clinic to reach the sample size for each clinic.

Simple random sampling is defined as a method where everyone stands equal chance of being selected in the study and it does not have a formula of selection.

# 3.3.5. Inclusion Criteria

Inclusion criteria are set of predefined factors used to identify elements that will be included in a research study (Encyclopedia of research design, 2010). In this study the inclusion criteria were files of HIV positive patients initiated on ART from the year 2019 to 2021.

# 3.3.6. Exclusion Criteria

Exclusion criteria are characteristics used to prevent a person from being eligible for the study (Understanding Research, 2020). In this study the exclusion criteria were all the patient medical records from 2019 to 2021 without healthcare worker clinical notes, laboratory blood sticker and results, patient that demised and patient geographical information.

# 3.4. Data Collection and data sources

Data collection is defined as a method of obtaining information in a reliable and meaningful manner (Dictionary of Epidemiology). In this study the data was extracted by computer from Tier.net database system which be accessed from the Department of Health. Variables which were extracted included socio-demographic characteristics such as patient's age, sex, marital status, occupation; clinical information such as viral load, CD4 count, WHO baseline stage and final diagnosis of any bacterial opportunistic infection during the course on ART (see annexure 3).

# 3.5. Data Analysis

Data analysis is an ongoing process during research. Data will be extracted from the original patient files and then captured in Microsoft spreadsheet and later converted to the Statistical Package for Social Sciences software program version no.26 for analysis. Continuous variables are presented as mean and standard deviation while

categorical variables are presented as frequencies / percentages. The Chi square test was employed to investigate homogeneity in the demographic and clinical characteristics between age groups and types of bacterial opportunistic infections. Student's t-test (for non-normally distributed variables) was used to test for significant difference in mean values between the two groups. Stratified univariate logistic regression analysis was done to explore the epidemiological characteristics of opportunistic infections between age groups and gender. P-values less than 0.05 was considered statistically significant.

# 3.6. Reliability and Validity

## 3.6.1. Reliability

Reliability is the level at which the collection tool consistently measures the same characteristics that is supposed to measure and can be replicated (Jo Logan, 2012). In this study the focus was on inter-rater reliability where reliability was maintained by keeping the data collection tool standard to all the files which were used to review data from.

# 3.6.2. Validity

Validity refers to the extent to which the data collection tool accurately measures what it was designed to measure (Jo Logan, 2012). In this study the content validity was the focus where it is aimed to be achieved by contacting the in charge in this field to validate the data collection tool. The tool was tested using few patient files with aim of checking whether it really measures what it was intended to measure. This step started after the ethical committee had approved and granted permission to conduct the study.

## 3.7. Bias

Selection bias can be one of the biases that can be found in a study like this one where the researcher can select the files of the patient she knows that they are less likely ill and have all the relevant information that it needs. To minimize the selection bias, simple random sampling was used to select the patient files. Also reporting and interpretation bias was minimized by interpreting variables of interest only and reporting the exact findings of the study.

# 4. ETHICAL CONSIDERATION

In each and every study, authors are expected to report on the ethical consideration of their research (Gale Academic Onefile, 2014). The fundamental role of research ethics is to make sure that the research is conducted according to ethical procedures. This study will be conducted in line with National Health Act 61 of 2003.

# 4.1. Permission to conduct study and ethical clearance

The research proposal of this study was presented at University of Limpopo Department of Public Health, and then submitted to the School of Health care Sciences and Faculty of Health care Sciences' School Research Ethical Committee and lastly submitted to Turf loop Research Ethics Committee (TREC) for ethical clearance and approval. Also permission to conduct the study was granted by all the clinics which participated in the study from Moses Kotane.

# 4.2. Informed consent and voluntary participation

In this study the informed consent was not used since the data used was secondary data retrieved from patient files and tier.net database.

# 4.3. Privacy, confidentiality and anonymity

The information gathered from this study was kept highly confidential and as such patient files used for this study remained unknown and were only known only by the researcher. During collection of data no patient file number or personal information like identity number, name and surname of the patient were used. To also strengthen privacy, confidentiality and anonymity data collection in this study was done by only the researcher. The information received from this study was stored private in a USB and a hard copy was only made accessible to the researcher and supervisor only.

# 4.4. Respect and dignity

According to the South African bill of rights, everyone has a right to respect and human dignity. The researcher was guided against infringement of patient's right to respect and human dignity by not exposing the personal and confidential information of the patient to other people. The researcher used a unique code to label the patient's records and that code will only be known by the researcher and the supervisor.

# 4.5. Harm

In this study there was no harm caused to patients as there was no physical contact with patient. Only secondary data was used throughout the study.

#### 4 CHAPTER 4: RESULTS

#### 4.1 Introduction

This chapter describes the analysis of the collected data and the interpretation of the research findings. The data was analyzed to determine the prevalence of bacterial opportunistic infections and associated socio-demographic factors in human immunodeficiency virus infected patients initiated on antiretroviral treatment in Moses Kotane Sub-District, North West Province.

## 4.2 Data management and analysis

The completed data collection resulted in 1682 records which were collected from five clinics which are Bakubung, Modderkail, Moruleng, Sandfontein and Sefikile. The data was captured on excel spreadsheet and securely stored then transferred to STATA statistical software version 12 for Windows (STATA Corporation, College Station, Texas) for data analysis to produce descriptive statistical analysis in order to identify frequencies and percentages of answers to the research questions. The statistical significance of the relationships between the selected variables was determined using the t-test and the level of significance was set at 0.05. The accuracy of the records which were retrieved from the patients records was assessed and it was found that very few patients records did not have viral load results (2.5%) while only 0.3% did not have WHO staging.

#### 4.3 Research results

## 4.3.1 Socio-demographic characteristics of pregnant women

Table 4.1 below presents the socio-demographics of the patients records which were retrieved in five clinics as stated above for a period of three years from 2019 to 2021. The mean age in the current study was  $36.1 \pm 13.36$  years and majority were females at 60.4%. Majority of the patients records were in the age group 18 - 34 years at 44.8% followed by age groups 35 - 44 years; 45 - 54 years; 55 - 64 years and 10 - 17 years at 25.2%; 17.5%; 7.1% and 2.3% respectively. Patients records between age group 0 - 9 years and greater or above 65 years had a share of 1.6%. Considering

marital status, majority of patient records were for those who were single at 71.5% followed by married at 25.5% while employment status revealed that majority of the patient records were for those who were unemployed or pensioners at 55.3% followed by those who were employed and scholars or minors at 40.7% and 3.9% respectively.

The analysis of CD4 counts revealed that majority of patents records were for those who had CD4 count of less than 200 cells/mm<sup>3</sup> at 26.3% followed by those with CD4 count between 200 and 349 cells/mm<sup>3</sup>; above 500 cells/mm<sup>3</sup>; and between 350 and 499 cells/mm<sup>3</sup> at 22.2%; 20.5% and 17.1% respectively. There were approximately 14% of the patients records with results of rejected or not done CD4 counts. Considering the viral load which is measured as number of copies/ml, majority of patients records were for those with viral load of less than 50 copies/ml at 37.6% followed by those with viral load of undetected at 20.4%. Approximately 26% of patients viral loads were not done while 2.5% patients records did not have any results for viral loads. The WHO staging revealed that majority of patients records were in stage 1 at 85.7% followed by stage 2; stage 3 and stage 4 at 9.3%; 4.5% and 0.2% respectively as presented in Table 4.1 below.

Table 4.1: Demographics of study participants

		No	(%)
Age in ye	ars		
	0 - 9	27	1.6
	10 – 17	39	2.3
	18 - 34	753	44.8
	35 - 44	423	25.2
	45 - 54	294	17.5
	55 - 64	119	7.1
	≥65	27	1.6
Marital st	atus		
	Single	1202	71.5
	Married	428	25.5
	Divorced	2	0.1
	Widowed	4	0.3
	Minor	45	2.7
	Not provided	1	0.1
Employm	ent status		
<u> </u>	Employed	685	40.7
	Unemployed/Pensioner	930	55.3
	Scholar/Learner/Minor	65	3.9
	N/A	2	0.1
CD4cat			
	>500	344	20.5
	350 - 499	287	17.1
	200 - 349	374	22.2
	<200	443	26.3
	Not done/Rejected	234	13.9
Viral load			
	<20	63	3.8
	20 -50	166	9.9
	>50	633	37.6
	Not done	435	25.9
	undetected	343	20.4
	Blank	42	2.5
WHO stag	ging		
	1	1442	85.7
	2	156	9.3
	3	76	4.5
	4	4	0.2
	Unknown	4	0.2

The current study reveals that there was a statistical significance difference (p<0.001) between gender, CD4 count and viral load (p=0.001) as presented in Table 4.2 below. Majority of females were in the age group 18 - 34 years at 55.7% while majority of males were in the age group 35 - 44 at 33%. Majority of patient records with low CD4 count of less than 200 cells/mm<sup>3</sup> were in age group 35 - 44 at 33.2% followed by age group 18 - 34 years; 45 - 54 years and 55 - 65 years at 29.1%; 26% and 6.6% respectively. Majority of patients records with normal CD4 count at above 500 cells/mm<sup>3</sup> were in the age group 18 - 34 years at 55.8% followed by age group 35 - 44 years; 45 - 54 years and 55 - 64 years at 17.1%; 14.2% and 5.5% respectively. The patients records with a high viral load were in the age group 18 - 34 years at 24.5%; 16.9% and 7.1% respectively as presented in Table 4.2 below.

		Age group in years							
		0 - 9	10 - 17.	18 - 34	35 - 44	45 - 54	55 - 64	≥65	P-value
Gender									
				556					
	Female	15 (1.5)	26 (2.6)	(55.7)	203 (20.0)	134 (13.2)	57 (5.6)	15 (1.5)	
				187					
	Male	12 (1.6)	13 (2.0)	(28.1)	220 (33.0)	160 (24.0)	62 (9.3)	12 (1.8)	<0.001
CD4 Count									
				192					
	>500	12 (3.5)	6 (1.7)	(55.8)	61 (17.7)	49 (14.2)	19 (5.5)	5 (1.5)	
			- ( )	139					_
	350 - 499	2 (0.7)	9 (3.1)	(48.4)	78 (27.2)	41 (14.3)	15 (5.2)	3 (1.1)	
				194					
	200 - 349	1 (0.3)	11 (2.9)	(51.9)	85 (22.7)	47 (12.6)	29 (7.8)	7 (1.9)	
				129					
	<200	6 (1.4)	8 (1.8)	(29.1)	147 (33.2)	115 (26.0)	29 (6.6)	9 (2.0)	
	Not								<0.001
	done/Rejected	6 (2.6)	5 (2.1)	99 (42.3)	52 (22.2)	42 (18.0)	27 (11.5)	3 (1.3)	
Viral load									
	<20	0 (0.0)	0 (0.0)	37 (58.7)	10 (15.9)	11 (17.5)	4 (6.4)	1 (1.6)	
	20 -50	0 (0.0)	4 (2.4)	55 (33.1)	56 (33.7)	31 (18.7)	16 (9.6)	4 (2.4)	
				293					
	>50	11 (1.7)	17 (2.7)	(46.3)	155 (24.5)	107 (16.9)	45 (7.1)	5 (0.8)	
				198					
	Not done	1 (0.2)	9 (2.1)	(45.5)	111 (25.5)	74 (17.0)	32 (7.4)	10 (2.3)	
				155					0.001
	undetected	15 (4.4)	9 (2.6)	(45.2)	77 (22.5)	59 (17.2)	21 (6.1)	7 (2.0)	

Table 4.2: Distribution of study participants by gender, CD4 count and viral load stratified by age group

# 4.3.2 Prevalence of opportunistic infections

The overall prevalence of opportunistic infections was found to be 7.4% for the period 2019 to 2022. as presented in Figure 4.1 below.

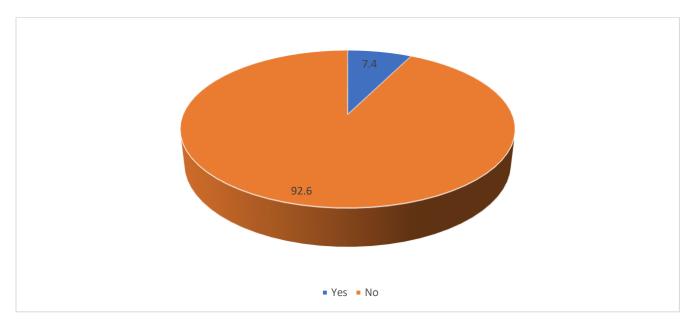


Figure 4.1: Overall prevalence of opportunistic infections

Table 4.3 below presents the prevalence of opportunistic infections stratified by year and it shows that the highest prevalence was in 2019 at 11.4% followed by 2020 and 2021 at 6.3% and 4.3% respectively.

Opportunistic	Opportunistic Period in years			
infections	2019	2020	2021	
No	504 (88.6)	540 (93.8)	513 (95.7)	<0.001
Yes	65 (11.4)	36 (6.3)	23 (4.3)	<0.001

 Table 4.3: Prevalence of opportunistic infections stratified by year

Figure 4.2 below presents the prevalence of opportunistic infections by gender stratified by age groups and it shows that the prevalence of opportunistic infections increased with increasing age from 0.8% in age group 10 - 17 years to 35.5% in age group 35 - 44 years then decreased to 6.5% in age group  $\le 65$  years. A similar trend has been seen in both

males and females which is a bell shaped curve. The highest prevalence in females was reported in age group 18 - 34 years at 37.7% while in males the highest prevalence was reported in age group 35 - 44 years at 35.2%.

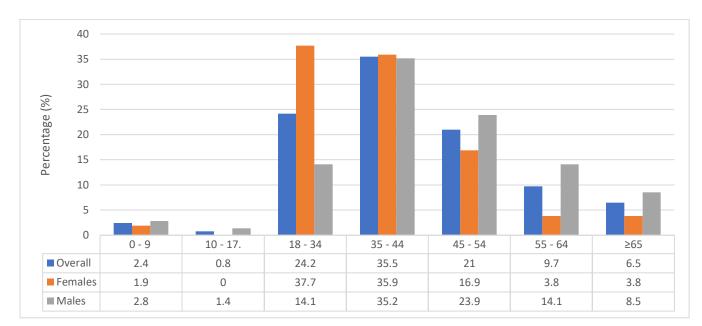


Figure 4.2: Prevalence of opportunistic infections by gender stratified by age groups

Figure 4.3 below presents the prevalence of opportunistic infections by CD4 count and it shows that the prevalence of opportunistic infections increased with decreasing CD4 count from 10.5% in patients with more than 500 cells/mm<sup>3</sup> to 12.1% in patients with CD4 count between 200 and 349 cells/mm<sup>3</sup>. The highest prevalence was recorded in patients with CD4 count of less than 200 at 37.1%.

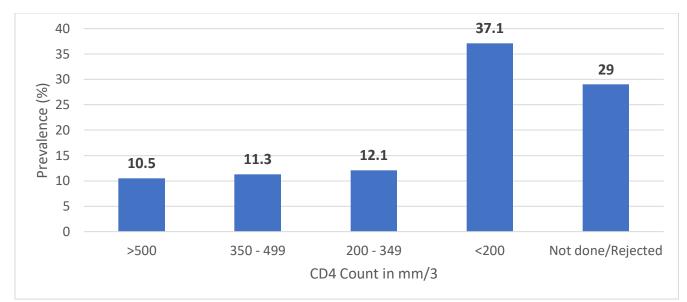


Figure 4.3: Prevalence of opportunistic infections by CD4 Count

Figure 4.4 below presents the categories of opportunistic infections reported in the current study and this shows that majority of the OIs were tuberculosis at 81.3% followed by hypertension and diabetes; sexually transmitted infections (STIs) or urinary tract infections (UTIs) and meningitis at 6.5%; 5.7% and 3.3% respectively.

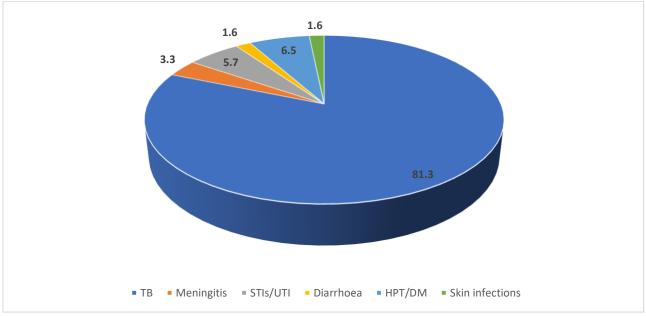


Figure 4.4: Categories of opportunistic infections

# 4.3.3 Association of association of socio-demographics opportunistic infections

In the univariate logistic regression, the association of socio-demographics opportunistic infections revealed that there was significant association of age, gender, CD4 count and WHO clinical staging. Older patients at age 18 years and above were 2.7 times more likely to have opportunistic infections at p<0.001 while patients aged 65 years and above were 6.5 times more likely to have opportunistic infections at p=0.005. Male patients were found to be 2.1 times more likely to have opportunistic infections at p=0.000. Patients with low CD4 count were 1.1 times more likely to have opportunistic infections at p=0.001 while patients with CD4 count not done or rejected were 4.6 times more likely to have opportunistic infections at p=0.001. Patients who were not categorized as WHO clinical stage 1 were 13.4 times more likely to have opportunistic infections at p=0.001. Patients who were not categorized as WHO clinical stage 1 were 13.4 times more likely to have opportunistic infections at p=0.001 as presented in Table 4.2 below.

Age in years	Odds ratio	p-value	95% CI
	OR(95%CI)		
< 18	Ref		
Older	2.7	0.000	1.8 – 4.0
Age group in years			
< 0 - 9	Ref		
18 – 34	0.6	0.421	0.2 – 1.9
35 – 44	1.8	0.274	0.6 – 5.2
45 – 54	1.5	0.463	0.5 – 4.5
55 – 64	1.7	0.356	0.5 – 5.6
≥65	6.5	0.005	1.8 – 24.1
Gender			
Females	Ref		
Males	2.1	0.000	1.5 – 3.1
Marital status			
Married	Ref		
Single	-	-	-
Divorced	-	-	-
Widowed	-	-	-
Employment status			
Employed	Ref		
Unemployed	1.1	0.469	0.8 –1.6
CD4 Count			
High	Ref		
Low	1.5 (1.3 – 1.8)	0.000	1.3 – 1.8
CD4 Count categories			

# Table 4.2 Association of socio-demographics and opportunistic infections Univariate Logistic Regression

>500	Ref		
350 – 499	1.3	0.498	0.6 – 2.8
200 - 349	1.1	0.867	0.5 - 2.3
> 200	2.9	0.001	1.6 – 5.6
Not done/rejected	4.6	0.000	2.4 - 8.9
WHO Staging			
1	Ref		
Other	13.4	0.000	9.7 – 18.5
WHO Staging category			
1	Ref		
2	6.3	0.445	1.9 – 20.8
3	9.7	0.000	2.3 – 17.9
4	6.4	0.000	1.4 – 8.9

# **4.4** Overview of research findings

The prevalence of opportunistic infections in the current study was found to 7.4% which is low however, this increased with increasing age. Occurrence of opportunistic infections were significantly associated with age and CD4 count.

# 4.5 Conclusion

In this chapter, the results of the study were presented and interpreted accordingly. The next chapter discusses these findings and compares the findings of this study to the relevant scientific literature.

# 5 CHAPTER 5: DISCUSSION AND RECOMMENDATIONS

### 5.1 Introduction

In the previous chapter, the findings of this study were presented and interpreted as per the objectives of the study. In this Chapter 5, the results of the current study are discussed and compared to the relevant scientific literature. The chapter is therefore, divided into the following sub-sections:

- Introduction;
- Characteristics of study population;
- The prevalence of opportunistic infections;
- Factors associated with opportunistic infections
- Study limitations;
- Conclusion and
- Recommendations.

# 5.2 Characteristics of study population

The current study revealed that patients who were HIV positive and their records retrieved the  $36.1 \pm 13.36$  years which is below the study conducted in East China (Luo, Sun, Cai, Shen, Liu, Wang & Zhang et al., 2016) and also lower than a study conducted in Uganda (Rubaihayo, Tumwesigye & Konde-Lule, 2015) but similar to a study conducted in Ethiopia (Mitiku, Weldegebreal & Teklemariam, 2015). Majority of patients in the current study were females which concurs with a study conducted in Ethiopia (Weldearegawi, Gerensea, Berihu, Gidey & Welearegay, 2020). Majority of patients in the current study were in the age group 18 - 34 years in the current study which concurs with studies conducted in Ethiopia (Dereje, Moges, Nigatu & Holland, 2019.; Weldearegawi et al., 2020) and also a study conducted in Cameroon (Kouanfack, Kouanfack, Billong, Cumber, Nkfusai, Bede & Wepngong et al., 2019).

The analysis of CD4 counts in the current study revealed that majority of patents records were for those who had CD4 count of <200/mm<sup>3</sup> which concurs with a study conducted in Cameroon (Kouanfack et al., 2019). Majority of the patients in the current

study were in WHO clinical stage I while least number of study subjects were WHO clinical stage IV which concurs with study findings from Damtie et al., (2013) conducted in Northwest Ethiopia and also supported by study findings from Gujarat, India by Basida et al., (2021).

#### **5.3 Prevalence of opportunistic infections**

Opportunistic infections (OIs) are the most significant complication of human immunodeficiency virus (HIV) infection and their prevalence differs among various countries in part due to different climates and socio-economic conditions (Pang, Shang, Li, Xu, Bi, Zhong & Pei, 2018). In the current study, the overall prevalence of opportunistic infections was found to be very low as compared to studies conducted in Ethiopia (Dereje et al., 2019; Weldearegawi et al., 2020). However, the study findings concurs with findings from a study conducted in Japan (Katano, Hishima, Mochizuki, Kodama, Oyaizu, Ota, Mine & Igari et al., 2014) as the prevalence of opportunistic infections were found to be significantly very low.

HIV-infected people are often co-infected with other, often "opportunistic" viruses, especially if living under conditions of poverty, crowding, and poor hygiene. Such coinfections may influence the outcome of ART (Rabenau, Lennemann, Kircher, Gürtler, Staszewski, Preiser & McPherson et al., 2010). In the current study, considering the prevalence of opportunistic infections by age, it was found to be consistently higher in older age groups which concurs with findings from a study conducted in Uganda (Rubaihayo, Tumwesigye, Konde-Lule, Wamani, Nakku-Joloba & Makumbi, 2016).

HIV infection is characterized by progressive and continuous impairment of the immune system function, with varying rates of progression among patients. HAART has been shown to be effective in arresting immune system impairment and prevention of disease progression, yet the incidence of OIs doesn't seem to cease. Opportunistic infections can occur in about 40% of people living with HIV, with a CD4 count less than 250 cells/mm<sup>3</sup> (Shenoy, Ramapuram, Shenoy, Ahmed & Srikant,

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2017). In the current study, the prevalence of opportunistic infections by CD4 count was found to be increasing with decreasing CD4 count which concurs with findings from a study conducted in Nairobi, Kenya (Chepkondol, Jolly, Yatich, Mbowe & Jaoko, 2020) and a study conducted in Indonesia (Fitri, Rambe & Fitri, 2018). Pulmonary tuberculosis was the most common opportunistic infection observed in which concurs with study by Dereje et al., (2019).

# 5.4 Factors associated with opportunistic infections

Opportunistic infection among HIV/AIDS continues to be a significant public health concern in African health care setting (Dagnaw Tegegne, Cherie, Tadesse, Tilahun, Kassaw & Biset, 2022). In the current study, using univariate logistic regression, age, gender, CD4 count and WHO clinical staging were found to be associated with development of opportunistic infections. This is supported by a study conducted by Prasitsuebsai et al., (2014) in Asia. In the current study there was a significant relationship between the male gender and the development of OIs with older age significantly associated with development of OIs and CD4 count of <200/mm<sup>3</sup> was also associated with the risk of developing an OIs (Kouanfack et al., 2019; Chepkondol, Jolly, Yatich, Mbowe & Jaoko, 2020). Being in the WHO clinical Stage III or Stage IV were independent predictors for the development of opportunistic infections in the current study which concurs with study findings by Dereje et al., (2019).

#### 5.5 Limitations of the study

The present study had several limitations. First, the quality of medical records was variable and some key information was often not recorded, so this made it difficult for some questions to be answered. Therefore, confounder information has been lacking and there might be missing information on data quality. The information related to factors contributing to opportunistic infections were not fully recorded and it was not possible to fully determine the contributory factors to opportunistic infections like the socioeconomic status and onset of ART, compliance to ART and duration on ART or the type of treatment patients given.

#### 5.6 Conclusions and Relevance

The study revealed that more females gets tested and put on treatment than males. Also the age 18-35 years is the group that is likely to get infected with opportunistic infections. Many of these people who had OIs were unemployed while only a few numbers of them were married and employed.

## **5.7 RECOMMENDATIONS**

#### Health facilities

The current study revealed that there is low prevalence of bacterial opportunistic infection in HIV infected patients but with the least prevalence Tuberculosis remained the number 1 OIs found in these patients and therefore, a significant concern that should be explored is the intervention that can reduce the burden of bacterial opportunistic infection with major focus on Tuberculosis. The prevalence of bacterial opportunistic infection in HIV infected patients was very low which could be due to lack of resources to do early and proper diagnosis Therefore, it is recommended that clinics in Moses Kotane sub-district be provided with trained staff on screening and diagnose bacterial opportunistic infections early and correct to prevent misdiagnosis.

#### 5.7.1 Research

High rate of infection amongst youth in this current study was significantly associated with unemployed and stability, and this may become important in future studies.

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# Appendix 1: REQUEST FOR PERMISSION TO CONDUCT RESEARCH



University of Limpopo

Department of Public health

Private Bag X1106, Sovenga, 0727, South Africa

To: University of Limpopo

Date:

Dear MS/Mr.

# REQUEST FOR PERMISSION TO CONDUCT RESEARCH

I am a registered Master's student in the Department of Public Health at the University of Limpopo. My supervisor is Prof E. Maimela. I would like to request permission to conduct a research study in the University Health Centre in Limpopo South Africa.

The proposed topic of my research is: PREVALENCE OF BACTERIAL **OPPORTUNISTIC** INFECTIONS AND ASSOCIATED SOCIO-DEMOGRAPHIC FACTORS IN PATIENT STARTING ANTI-RETROVIRAL THERAPY IN MOGWASE CLUSTER, MOSES KOTANE SUB-DISTRICT, NORTH-WEST PROVINCE. Should you require any further information, please do not hesitate to contact my supervisor or me. Our contact details are follows: mangaliongezwa@gmail.com as or ericmaimela@ul.ac.za). Upon completion of the study, I undertake to provide you with a copy of the dissertation.

Your permission to conduct this study will be greatly appreciated.

Yours sincerely

MANGALI .O

DATE

# Appendix 2: PERMISSION TO CONDUCT STUDY AT MOSES KOTANE SUB-DISTRICT

Moses Kotane Sub-district

Office of the sub-district Manager

Private Bag X1045, Sun City, 0316, South Africa

TITLE: PREVALENCE OF BACTERIAL OPPORTUNISTIC INFECTIONS IN PATIENTS TAKING ANTI-RETROVIRAL THERAPY IN MOGWASE CLUSTER, MOSES KOTANE SUB-DISTRICT, NORTH-WEST ROVINCE

Dear .Mr. L.E Mokotedi – SUB-DISTRICT MANAGER

By signing this form, I am allowing the researcher to conduct her research study in this institution.

I Lekgotla Ezrom Mokotedi; the sub-district manager of Moses Kotane sub-district hereby consent for the research study to be conducted in this institution.

Thank you,

Place:	
Signed:	Date:
Researcher:	Signed:

# Appendix 3: DATA COLLECTION TOOL

NB: There will be no interaction with patients however these are the list of questions the researcher (O MANGALI) will seek to answer while reviewing individual patient files

Date of HIV diagnosis:

Demographics:

Gender				Male		Fem	ale
Age in years							
Marital status	Widov	ved	Div	vorced	Married		Single
Occupation					1		
Section B:							
						-	
Baseline: CD4 Count		<100		100-350	350-50	00	>500
(cells per cubic milliliter of blood	)						
Baseline WHO Clinical staging		Stage 1		Stage 2	Stage	3	Stage 4
WHO clinical staging at tin diagnosis of opportunistic infecti		Stage1		Stage 2	Stage	3	Stage 4
Viral load at initiation				1	I		

Number of co-morbid	None	1	2	3	<3
diseases					
Co-morbid diseases					
	1				
Tuberculosis (specify)					
Diarrhea					
Syphilis					
Hypertension					
Diabetes Mellitus					
Other (specify)					

# Appendix 4: Ethical Clearance

	University of Limpopo
Departm F Tel: (015) 268	Oniversity of Employe nent of Research Administration and Development Private Bag X1106, Sovenga, 0727, South Africa 3935, Fax: (015) 268 2306, Email: anastasia.ngobe@ul.ac.za
	TURFLOOP RESEARCH ETHICS COMMITTEE
	ETHICS CLEARANCE CERTIFICATE
MEETING:	29 November 2022
PROJECT NUMBER:	TREC/600/2022: PG
PROJECT:	
Title: Researcher: Supervisor: Co-Supervisor/s: School:	Prevalence of bacterial opportunistic infections and associated socio- demographic factors in HIV infected patients initiated on antiretroviral treatment in Moses Kotane Sub-District, North West Province. O Mangali Prof E Maimela N/A Health Care Sciences
Degree:	Masters in Public Health
PROF D MAPOSA	
	P RESEARCH ETHICS COMMITTEE hics Committee (TREC) is registered with the National Health Research Ethics ber: REC-0310111-031
date. Applicati month before ii) Should any de researcher(s) r Amendment fr	arance Certificate will be valid for one (1) year, as from the abovemention on for annual renewal (or annual review) need to be received by TREC one lapse of this period. parture be contemplated from the research procedure as approved, the nust re-submit the protocol to the committee, together with the Applicat orm. E THE PROTOCOL NUMBER IN ALL ENQUIRIES.
iii) PLEASE QUOT	Finding solutions for Africa

#### **Appendix 5: District Department of Health Approval**

ealth Department Health North West Provincial Government **REPUBLIC OF SOUTH AFRICA** Stand No 00004 Lekwadi Sect Ledig 0338 Private BagX1045 Monwase Tel: 0664791301 Email.mmakgobatlou@nwpg MOSES KOTANE SUB DISTRICT CORPORATE SERVICES Eng L Makgoballou TO **MS MANGALI ONGEZWA** FROM ML MAKGOBATLOU AD CORPORATE SERVICES DATE 14 DECEMBER 2022 SUBJECT : ACKNOWLEDGEMENT AND APPROVAL We kindly acknowledge that we have received your request to collect data information for your master's degree in MKSD facilities. In response to your request we would like to let you know that it has been approved We kindly look forward to working with you MR KL Modisane Mr ML Makgobatlou Acting HRD Officer Assistant Director: Corporate Services 11 Date: 77 Date Submitted By Recommended/Not Recommended/Amended Mr. ND Magoro Acting Sub District Manager 12.2022 Date Approved/Not Approved/Amended Let's Grow North West Together

#### Appendix 6: Certificate from language editor

#### Tiyiselani & Rapetsoa scientific services

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Date: 12 June 2023

#### To Whom it May Concern

I hereby confirm that I have proof-read the document entitled: "Prevalence of bacterial opportunistic infections and associated socio-demographic factors in human immunodeficiency virus infected patients initiated on antiretroviral treatment in Moses Kotane Sub-District, North West Province" authored by O Mangali TK with student number 202176426 from University of Limpopo. The document has been edited and proofread for grammar, spelling, punctuation, overall style and logical flow. Considering the suggested changes that the author may or may not accept, at her discretion, each of us has our own unique voice as far as both spoken and written language is concerned. In my role as proof-reader I try not to let my own "written voice" overshadow the voice of the author, while at the same time attempting to ensure a Please referany queries to me. readable document.

Rapetsoa DB

