UNIVERSITY OF THE WESTERN CAPE

Faculty of Community and Health Sciences

RESEARCH MINI THESIS

Prevalence and patterns of comorbidities in adult HIV-related admissions in a public regional hospital in KwaZulu-Natal

A mini thesis written in partial fulfilment of the qualification of Master's in Public Health in the School of Public Health of the University of the Western Cape.

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Declaration

I declare that "*Prevalence and patterns of comorbidities in adult HIV-related admissions in a public regional hospital in KwaZulu-Natal*" is my own work and that it has not been submitted for any degree or examination in any other university and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Dr. Yejna Narain

Signed:

Date: 24 August 2021

Dedication

This mini thesis is written in memory of, and dedicated to my dear elder brother, Dr and Captain Dheeraj Narain. You always believed in me and in your passing, I find the strength to overcome the challenges faced and continue to make you proud.

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With God all things are possible. I firstly thank the Almighty for allowing the completion of this Master's qualification.

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ABSTRACT

Background: South Africa has the largest burden of HIV in the world with 7.9 million people living with HIV and 4.4 million registered on antiretroviral therapy (ART) in 2017. KwaZulu-Natal is hardest hit by the HIV epidemic with a prevalence of 27% among adults aged 15 to 49 years old. With the widespread ART uptake, the spectrum of HIV related admissions in hospitals has changed over the last decade. Hypertension, diabetes, cardiovascular disease, and renal failure have become significant reasons for inpatient care. Increased life expectancy, rising non-communicable diseases (NCDs) and easier access to ART have played a significant change in the landscape of inpatients as compared to the pre-ART era. To provide integrated healthcare to the patient, it is necessary to understand the prevalence and patterns of HIV comorbidities for efficient and effective service delivery to HIV patients at facility-level.

Aim: The current study aimed to describe the prevalence and patterns of HIV-related comorbidities in adult hospital admissions in iLembe, KwaZulu-Natal.

Methodology: A retrospective, cross-sectional survey was conducted of all adult HIV-related admissions between 1st October and 31st December 2019. Clinical and demographic characteristics were extracted from admission and discharge records, and laboratory data was collected via the National Health Laboratory Services using Labtrack. Summative and inferential analyses were done using SPSS v.23.

Ethics clearance was obtained from the Biomedical Research Ethics Committee of the University of the Western Cape, and permission to access patient data from the hospital management as well as the KwaZulu-Natal Department of Health's Health Research and Knowledge Management Department and National Health Research Committee.

Results: There were 1 269 admissions during the study period; of which 301 cases fulfilled the study inclusion criteria and 289 (96.0%) full medical records could be traced and entered analysis. The median age of participating patients was 38 years (IQR =18.5). It was found that 219 (75.8%) knew their HIV [positive] status upon admission; of which 76.7% (n=168) were on ART; and of the last-mentioned 65.8% (n=144) were virally suppressed. Hypertension (20%, n=59), chronic kidney disease (10.4%, n=30), dyslipidaemia (9.3%, n=27), diabetes (8%, n=23) and cardiovascular disease (5.6%, n=16) were the most prevalent health conditions. Just under a third (31.8%; n=92) of the participants reported a history of TB. Patients admitted

with a new or existing NCD had a significantly shorter in-hospital stay than patients admitted for an infectious cause (Median: 6.5 vs 9 days; *p*=0.037).

Conclusions

As South Africa aims to reach the 90-90-90 targets, HIV comorbidity with NCDs like hypertension, diabetes, dyslipidaemia, and chronic kidney disease is a growing problem in people living with HIV (PLWH). This new paradigm of an old disease warrants an integrated approach, that is holistic in nature. Increased community testing, improving linkage to health care and addressing adherence will play a key role in this next phase of the HIV pandemic.

Keywords: HIV, Anti-retroviral Therapy, Mortality, Admission, Hypertension, Diabetes, Chronic renal failure, Cardiovascular disease, Malignancy, Comorbidity, AIDS, Non-communicable disease

LIST OF ACRONYMS

Acronym	Description
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
BMI	Body mass index
CCM	Cryptococcal meningitis
CVD	Cardiovascular disease
CEO	Chief executive officer
CKD	Chronic kidney disease
GJGMRH	General Justice Gizenga Mpanza regional hospital
HIV	Human immunodeficiency virus
HCW	Health care worker
HSRC	Human Science Research Council
IQR	Interquartile Range
KZN	KwaZulu-Natal
KS	Kaposi sarcoma
LOS	Length of stay
NCD	Non-communicable disease
PLWH	People living with HIV
PCP	Pneumocystis carinii pneumonia
SANDOH	South African National Department of Health
TB	Tuberculosis
UWC	University of Western Cape
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organisation

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CHAPTER 1. INTRODUCTION

1.1 BACKGROUND

South Africa has one of the largest burdens of HIV and AIDS in the world, with 7.9 million people living with HIV in 2017 (HSRC, 2019; SANDOH, 2019). Since 2004, the South African public sector antiretroviral therapy (ART) programme has evolved and developed into one of the largest in the world, with 4.4 million people registered on ART as of 2017 (HSRC, 2019). ART has proved to be highly effective in the management of HIV. ART interrupts viral replication, enabling immune recovery, thus improving survival and quality of life for people living with HIV (Bor, Herbst, Newell & Barnighausen, 2014). The success of ART is demonstrated by an increase in the life expectancy of HIV patients on ART. It is estimated that HIV patients on ART reach between 70-86% of life expectancy in comparison to the HIV negative population (Bor et al., 2014; Johnson et al., 2013). South Africa's ART programme aimed to achieve the ambitious Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets by 2020 but these had been reached at the time of this study (Meyer-Rath et al., 2017; UNAIDS, 2014).

1.2 HIV EPIDEMIC IN SOUTH AFRICA AND KWAZULU-NATAL

The province of KwaZulu-Natal (KZN) is hardest hit by the HIV epidemic with a prevalence of 27% in all age groups (HSRC, 2019). KZN also has the highest ART exposure rate in the country with 69.8% of all people with HIV on ART, but is still short of UNAIDS 90-90-90 target (HSRC, 2019). The South African national average for virological suppression is 92% whilst KZN only achieved a virological suppression of 67.5% at the end of 2017 (HSRC, 2019; UNAIDS, 2020). South Africa achieved the other 90-90-90 targets: with 92% of people living with HIV in South Africa who know their status; but falling short on the number of people with HIV being on treatment (75%) (UNAIDS, 2020). HIV related admissions accounted for up to 66% and 54% of all admissions in district hospitals and tertiary hospitals in KZN in 2013, respectively (Meintjes et al., 2015).

1.3 IMPACT OF ANTIRETROVIRAL THERAPY

Sixteen years since the widespread uptake of ART, two-thirds of hospital admissions in public hospitals are HIV-related (Ford et al., 2015; Ford et al., 2016; Meintjes et al., 2015; SANDOH, 2019). It is reported that hospital admissions due to opportunistic infections and AIDS-related

illnesses decreased, and a new spectrum of HIV-related admissions has emerged. For example, in Johannesburg, South Africa, HIV-related admissions accounted for only 45% of all admissions (Long et al., 2016), which is a reduction from the 68% documented at the same facility in 2007 (Thomas et al., 2007). This reduction is attributed to the increase in availability in ART. In Harare, Zimbabwe, HIV related admissions accounted for 46% of admissions to urban/peri-urban hospitals and 66.8% in Lusaka, Zambia (Chihota et al., 2019; Ferrand et al., 2010). The reason for the lower non-HIV related admissions in South Africa as compared to Zambia and Zimbabwe could be attributed to a better level of virological suppressions amongst HIV infected individuals (UNAIDS, 2017).

Hypertension, diabetes, cardiovascular disease and renal failure are noted to be the most prevalent reasons for inpatient care in Sub-Saharan Africa (Gouda et al., 2019). This increasing trend can be attributed to an aging population especially due to the effect of ART (Bor et al., 2014; Gouda et al., 2019; Johnson et al., 2013). This change in the spectrum of inpatient cases is contributed to the increased life expectancy of HIV patients on ART - to approximate the life expectancy of the general population - and the increasing prevalence of non-communicable diseases (Bor et al., 2014; Gouda et al., 2019; Johnson et al., 2013). The abovementioned change in reasons for admission brings to light new challenges for treating HIV patients in hospitals.

1.4 HIV AND COMORBIDITIES

An aging population on ART places patients living with HIV infection at higher risk of developing multimorbidity (Kim et al., 2012). This demographic shift is affecting the landscape of non-communicable diseases (NCDs) in patients on ART (Boyd & Lucas, 2014). A multidisciplinary team is recommended to manage HIV infected individuals with multimorbidity. It is advocated that a patient-centred approach at the primary health level may improve patient outcomes in this changing landscape (Boyd & Lucas, 2014). The integrated HIV and TB treatment centre is the current standard in models of HIV care delivery in South Africa in keeping with the World Health Organisation's (WHO) 2012 recommendations (SANDOH, 2020; WHO, 2012). However, Broom et al. (2012) and Chu and Selwyn (2011) both suggested that a chronic disease model for the aging population with HIV infection is beneficial due to the high prevalence of comorbid conditions that are associated with non-AIDS events. This model focuses on managing comorbid conditions and screening for risk factors of

NCD in patients with HIV infection (Broom et al., 2012). With the spectrum of HIV-related diseases changing, a change in the approach to HIV infected individuals is required. Njuguna et al. (2018) described multiple nodes of services that integrated HIV and NCD care in Southern Africa which were feasible and could be implemented using existing infrastructure. These nodes or modalities include, amongst others, community-based integrated HIV and NCD screening and referral; screening for NCD in people living with HIV; integrated HIV/NCD care at facilities; differential care for stable patients with NCD and HIV infection (Njuguna et al., 2018).

1.5 PROBLEM STATEMENT

It is expected that KZN, as well as the rest of South Africa, will experience an evolution in the type of hospital admissions for HIV patients. Levitt, Steyn, Dave and Bradshaw (2011) postulated that HIV patients will present as inpatient admissions with non-infectious conditions to a greater proportion compared to HIV-related opportunistic infections, as also observed by Oni et al. (2015) in the Western Cape province. Case management of HIV patients has thus changed from mostly treating opportunistic infections towards the holistic management of comorbidities, NCDs. It is, therefore, argued that an integrated health model is required in the new era of HIV treatment that is characterised by an ever-increasing comorbid burden. This presents a departure from the historical specialised ART clinics and services towards comprehensive health care at the primary level. A whole-patient, integrated approach to the management of a patient with chronic conditions is required to replace the current disease-specific approach (Tinetti, Naik & Dodson, 2016). It is, therefore, imperative to determine the prevalence and patterns of comorbidities in HIV patients as they present in local settings so that the health service delivery for HIV patients can be reoriented to be more efficient and effective.

1.6 AIMS AND OBJECTIVES

The aim of the current study was to determine the prevalence and profile of comorbidities in adult HIV related admissions to General Justice Gizenga Mpanza Regional Hospital (GJGMRH) in KwaZulu-Natal between 1 October and 31 December 2019.

The objectives of the proposed study were:

- To describe the demographic and clinical profiles of HIV patients admitted to medical wards in GJGMRH.

- To describe the reasons for admission of HIV patients.
- To describe the pattern of admissions with respect to non-communicable diseases and infectious diseases.
- To describe the prevalence and patterns of comorbidities in admitted HIV patients.

1.7 OUTLINE OF MINI-THESIS

The current chapter elaborated on the introduction to and outline of the mini thesis.

In **Chapter 2** the literature on admissions to medical wards in patients with HIV infection, in South Africa is reviewed. The literature review primarily focuses on HIV/AIDS, the effects of ART on inpatient admissions and the effects of non-communicable diseases on admissions in an era of widespread ART usage.

Chapter 3 describes the methodology used in the current study and the study setting. The study design, data collection and analysis methods are described and motivated.

In **Chapter 4** the study results are presented. An analysis of the results is presented using tables and graphs to allow interpretations, inferences, and conclusions from them.

Chapter 5 presents a discussion of the results in relation to relevant current literature.

In **Chapter 6**, conclusions are drawn based on the main research findings and recommendations are offered for research, policy, and practice.

CHAPTER 2. LITERATURE REVIEW

This literature review covers the impact that ART has had on the disease profile of patients with HIV infection, including the impact ART has had on the profile of inpatient admissions to hospitals in South Africa since 2004. The recent literature on HIV comorbidities and the epidemiological changes that have occurred due to widespread ART usage are also reviewed and synthesised.

2.1 IMPACT OF ART EXPOSURE ON DISEASE PROFILE OF HIV INFECTED PATIENTS

Cohort studies in high-income countries have shown that people living with HIV (PLWH) have a higher prevalence of comorbidities compared to those that did not have HIV (Goulet et al., 2007) and that they tend to present with multiple comorbidities (De Francesco et al., 2018).

The roll-out of ART in South Africa has improved the life expectancy and survival of HIV patients (Bor et al, 2014), as also observed in other parts of the world (UNAIDS, 2017). Palella et al. (2006) found that patients retained on ART lived longer and had higher CD4 cell counts at death compared to those who were not on ART. They also tended to die due to non-HIV related illnesses. Patients with advanced HIV infection (CD4 cell counts < 200 cells/mm^3) on ART had predominantly renal, vascular and pulmonary disease whilst hypertension was associated with patients with CD4 cell counts of more than 200 cells/mm^3 (Goulet et al., 2007).

Another study showed lower mortality in HIV patients on ART. In their retrospective chart review of hospitalized HIV infected patients between 2004 to 2008 in New York City, people on ART had lower mortality and most of the in-hospital deaths of HIV infected patients were related to non-HIV related illnesses (Kim et al., 2013). The study also identified poor prognostic factors for death in hospitalized HIV infected individuals as low CD4 cell count, female sex, and poor adherence to ART.

2.2 PROFILE OF HOSPITAL ADMISSIONS

Overall, hypertension and diabetes are the main reason for adult patients seeking primary health care in South Africa (Mash et al., 2012). However, Long et al. (2016) found that the most common reasons for admissions in a regional urban hospital in South Africa were TB, bacterial infections and cardiovascular disease - in both HIV infected and non-infected patients. Meintjes

et al. (2015) confirmed TB and bacterial infections as the most common diagnosis of HIV infected patients at admission, and that deaths in HIV infected patients were due to TB and AIDS-defining illnesses.

HIV still accounts for almost two-thirds of the medical admissions in South African hospitals (Meintjes et al., 2015). In the study in New York City by Kim et al. (2013), admissions to hospitals for HIV infected individuals were mainly for non-HIV related conditions (hypertension and diabetes) and sepsis. This is in contrast to South Africa, where TB and bacterial infections were the main reasons for admissions amongst HIV patients (Long et al., 2016; Meintjes et al., 2015).

Van Heerden et al. (2017) found the prevalence of HIV and NCDs in peri-urban KZN was high. This could signal a change in the expected patterns of admissions in South Africa to resemble first world countries (Kim et al., 2013). The setting in which the study by Van Heerden et al. (2017) was conducted, resembled the iLembe District in its peri-urban setting with high unemployment, low income, and high HIV prevalence. Massyn, Barron, Day, Ndlovu and Padarath (2020) confirmed a high prevalence of diabetes, obesity, and hypertension in the iLembe District.

2.3 HIV COMORBIDITIES

With the advent of widespread ART uptake in South Africa, patterns of comorbidities have changed when compared to the pre-ART era (Badri, Wilson & Wood, 2002). Hypertension has been shown to have a higher prevalence in HIV infected individuals than HIV uninfected individuals (Schouten et al., 2014). Not only are NCDs more common in HIV affected individuals, but they also occur about 10 years earlier than HIV uninfected individuals (Guaraldi et al., 2011). Although infectious diseases were the predominant reason for admission in the pre-ART era, cardiovascular diseases have shown an increase due to multiple factors relating to the effects of the virus and the effects of ART (Long et al., 2016). AIDS-defining illnesses together with NCDs hypertension, diabetes, cardiovascular, renal disease, and malignancies will be discussed further.

2.3.1 INFECTIOUS DISEASES ASSOCIATED WITH HIV

Tuberculosis (TB) and other AIDS-defining illnesses such as cryptococcal meningitis (CCM) and pneumocystis carinii pneumonia (PCP) are the most common diseases in HIV infected individuals (Ghate et al., 2009). These conditions are very prevalent and account for a considerable number of admissions to South African hospitals (Cichowitz et al., 2018; Long et al., 2016).

2.3.1.1 Tuberculosis

Ten million people globally were affected by TB in 2018 (World Health Organization, 2019). In South Africa and the world, TB has been a leading cause of death (Massyn et al., 2020; Padayatchi , Daftary, Naidu, Naidoo and Pai, 2019). In SA, in 2017, 59.9% of TB cases had co-infection with HIV, the highest in the world (Padayatchi et al., 2019). The TB epidemic in South Africa is driven by the convergence of the HIV epidemic (Karim, Churhyard, Karim & Lawn, 2010). Newly diagnosed TB was the leading cause of hospital admissions in HIV infected individuals in South Africa and worldwide (Ford et al., 2016; Meintjes et al., 2015). Despite the use of widespread ART, the incidence of TB is still on the rise as compared to other opportunistic infections (Peer et al., 2019).

2.3.1.2 AIDS-defining illnesses

The Centre for Disease Control and Prevention classified 23 conditions as AIDS-defining illnesses in 1993 (Mocroft et al., 2009). These conditions are generally regarded as signalling advanced HIV infection. These conditions include oesophageal candida, extrapulmonary cryptococcosis, pneumocystis carinii pneumonia (PCP) and extrapulmonary tuberculosis (Castro et al., 1993). Globally, AIDS-defining illnesses account for a large proportion of admissions and deaths in HIV positive patients (Ford et al., 2015; Kim et al., 2013; Long et al., 2016). Badri, Maartens, Baker and Wood (2005) showed that patients with low CD4 cell counts, and not initiated on ART in South Africa were at a higher risk of developing AIDS-defining illnesses as compared to those on ART. Besides tuberculosis, cryptococcal meningitis, PCP and toxoplasmosis have shown the highest prevalence in patients with low CD4 cell counts (Fenner et al., 2013; Low et al., 2016).

The burden of fungal disease in South Africa is largely due to the impact of a large HIV infected population. CCM and PCP are the most prevalent fungal infections in the HIV infected population (Wills, Lawrence, Botsile, Tenforde & Jarvis , 2021). Despite the widespread use

of ART in Africa, the incidence of PCP in HIV infected individuals in patients with respiratory symptoms was 19% (Wills et al., 2021). The cost of PCP infection is high, due to a reduced life expectancy from diagnosis (39 months) and a lifetime cost of $40 288 (Freedberg et al., 1998).

Since the introduction of ART, AIDS-defining illnesses have shown a significant reduction, particularly in incidents of PCP and Kaposi sarcoma (Ives, Gazzard & Easterbrook, 2001). A systematic review of autopsy findings in Sub-Saharan Africa showed a similar reduction in AIDS-defining illnesses like PCP in the post-ART era (Peer et al., 2019).

2.3.2 NON-COMMUNICABLE DISEASES

Hypertension, dyslipidaemia, diabetes and cardiovascular disease are very prevalent amongst people living with HIV (Patel et al., 2018). Along with the above, the impact of HIV on renal failure and malignancies will be discussed below.

2.3.2.1 Hypertension

Hypertension is a leading cause of hospitalization and death globally, and the relationship between metabolic abnormalities and HIV has been well described (Fahme, Bloomfield & Peck, 2018). Young adults with HIV infection have a higher risk of developing hypertension when compared to adults without HIV infection (Ryscavage, Still, Nyemba & Stafford, 2019). The mechanism for the development of hypertension in HIV infected individuals is multifactorial. ART induced endothelial dysfunction may be a significant contributor to hypertension in patients who are now living longer because of ART (Fahme et al., 2018; Nduka, Stranges, Sarki, Kimani & Uthman, 2016). The longer the duration of ART exposure, the higher the risk of developing hypertension (Baekken, Os, Sandvik & Oektedalen, 2008). HIV causes an increase in lipopolysaccharides and inflammation which causes arterial stiffness leading to hypertension (Fahme et al., 2018) These factors and the chronic immune activation despite viral suppression result in patients with HIV infection having an almost two-fold risk in cardiovascular disease as compared to HIV uninfected individuals (Temu et al., 2020). Osetinsky et al. (2019) observed the growing impact of hypertension in the HIV population and extended two rural HIV treatment centres to include monitoring and treatment of hypertension. This was in keeping with comprehensive primary health care delivery.

A multi-disease model can be integrated into existing infrastructure to anticipate future health needs (Osetinsky et al., 2019). The South African Department of Health piloted an integrated chronic disease management model at selected primary health clinics that showed an effect in controlling hypertension and HIV (Ameh et al., 2016).

2.3.2.2 Diabetes

In patients with HIV, diabetes was more common in the post-ART era than in the pre-ART era. Diabetes is currently a significant reason for primary health care visits (Butt et al., 2004; Mash et al., 2012). Diabetes is an increasing concern in South Africa due to the complications that result in in-hospital care (Gouda et al., 2019). The incidence of diabetes increases with the rise in body mass index (BMI), irrespective of exposure to ART (Koethe, Grome, Jenkins, Spyros & Sterling, 2017). Butt et al. (2009) showed that hospitalizations for renal failure and CVD will increase due to an increase in the use of ART. This is due to the following factors: increased life expectancy because of ART; increased BMI associated with ART use and metabolic complications associated with ART use (Butt et al., 2004). The use of ART has also lead to other metabolic abnormalities like dyslipidaemia and lipodystrophy (Noubissi, Katte & Sobngwi, 2018). Lipodystrophy secondary to ART has been associated with increased abdominal fat which has been associated with insulin resistance and the development of type 2 diabetes mellitus (Young, Critchley, Johnstone & Unwin, 2009).

2.3.2.3 Cardiovascular disease and dyslipidaemia

HIV infection, even in the presence of virologic suppression, is an independent risk factor for myocardial infarction and other CVD events (Freiberg et al., 2016; Womack et al., 2014). Cardiovascular disease has been linked to adverse effects on lipid profiles, platelet activation, inflammation, and endothelial function. These factors predispose to coronary artery disease and cerebrovascular disease (Koethe et al., 2017). Higher total cholesterol, low-density lipoprotein (LDL) and triglycerides, and lower high-density lipoprotein (HDL) are observed in obese HIV-infected patients as compared to HIV- uninfected people (Koethe et al., 2017). In patients with HIV infection, advanced immune senescence may also contribute to higher CVD despite the use of ART (Castilho et al., 2016). The development of CVD increases the demand for inpatient care for both HIV infected and non-infected individuals (Koethe et al., 2017).

2.3.2.4 Renal Disease

An escalated burden of HIV associated end-stage renal disease is anticipated in Sub-Saharan Africa due to an increase in life expectancy of patients on ART, nephrotoxicity of ART and direct HIV associated nephropathy (Han, Naicker, Ramdial & Assounga, 2006; Naicker, 2013). Islam, Wu, Jansson and Wilson(2012) conducted a systemic review and meta-analysis of the relative risk of developing renal disease in patients with HIV infection and found that patients with advanced HIV and advanced age were more likely to have renal disease. The study also concluded that ART reduced the risk of renal disease. A 10-year review conducted in Cape Town showed a significant four-fold increase in renal failure in patients with HIV infection between 2000 to 2009 (Okpechi et al., 2011). Renal disease-related admission was noted by Long et al. (2016) to have generated the most expensive admission stays. This places a huge financial and resource strain on the public health system (Guaraldi et al., 2013).

2.3.2.5 Malignancies

AIDS-defining malignancies are decreasing due to the use of ART, but non-AIDS-related malignancies are rising (Patel et al., 2008; Shiels & Engels, 2017). In South Africa, Sitas et al. (1997) found that HIV-infected patients tend to have a higher incidence of malignancies linked to infective aetiology such as Kaposi sarcoma (KS). KS is an endothelial cell malignancy that is commonly associated with AIDS in Sub-Saharan Africa (Cesarman et al., 2019; Wagner, Ravi, Menter & Sood, 2017). Thomas (2001) and Sasco et al. (2010) made similar observations in sub-Saharan Africa (South Africa, Uganda and Zimbabwe) regarding the increased number of patients with KS.

A retrospective study at a tertiary centre in Johannesburg, South Africa, showed an increase in non-Hodgkin lymphoma in HIV infected individuals (Wiggill, Mantina, Willem, Perner & Stevens, 2011) similar to the findings of Patel et al. (2008) in the United States. High levels of HIV viremia 10 years prior to the diagnosis of malignancy or high viral loads at the time of diagnosis were most commonly associated with anal or Hodgkin's lymphoma (Riedel, Rositch & Redfield, 2015). A large observational study in the United States showed anal, vaginal, Hodgkin lymphoma, melanoma, liver, lung, colorectal and renal malignancy all showed a higher incidence in HIV infected individuals as compared to HIV negative individuals (Patel et al., 2008). These findings were confirmed in a Swiss HIV cohort that concluded that the ageing population was most likely the cause of the increase in non-AIDS-related malignancies

(Franceschi et al., 2010). A recent review of malignancies in Sub-Saharan Africa showed an increase in malignancy-related deaths due to non-HIV related malignancies compared to HIV related malignancies due to the increase in life expectancy amongst ART users (Chinula, Moses & Gopal, 2017).

2.4 SUMMARY

Non-communicable diseases and HIV infection have been major contributors to inpatient care in South Africa. The use of widespread ART has affected the profile and pattern of patients who are admitted to hospitals. NCDs carry a large disability burden and premature mortality rate and therefore should be a focus for primary health care initiatives. The growing burden of diabetes, hypertension and renal failure have raised questions on prioritisation and integration of NCD and HIV management. The growing burden of multimorbidity in the South African peri-urban population needs a restructuring of the health model and policy intervention (Oni et al., 2015) in order to match the evolving patterns of HIV admissions.

CHAPTER 3. METHODOLOGY

3.1 STUDY SETTING

The iLembe District is located on the eastern coast of KwaZulu-Natal. With a growing population of 678 048 people, it is the smallest of all districts in KwaZulu-Natal (Cooperative Governance and Traditional Affairs, 2020). The iLembe District is plagued by high unemployment and high poverty rates (iLembe District Municipality, 2017). The district also has a higher prevalence rate of HIV infection when compared to the national average at 19.4% versus 14% (HSRC, 2019). The district failed to reach any of the 90-90-90 targets in 2017. According to the South African National HIV prevalence, incidence and behaviour and communication survey, 72.1% of people with HIV who infected people in the iLembe District are aware of their status (HSRC, 2019). This is below the expected 90% expected by the UNAIDS strategy. Amongst those who were HIV positive in the district, 82.7% were on ART (HSRC, 2019). The biggest improvement in the district from 2017 to 2018 was in the third 90 of the UNAIDS 90-90-90 strategies, where virological suppression rates improved from 80.8% to 91.5% (HSRC, 2019; Massyn et al., 2020).

General Justice Gizenga Mpanza Reginal Hospital (GJGMRH) in the iLembe region serves a community of over 650 000 people.

3.2 STUDY DESIGN

A retrospective cross-sectional analysis was conducted for all HIV positive admissions to the inpatient medical wards at GJGMRH. Retrospective record reviews allow the investigator to look at pre-recorded, patient-centred information to answer research questions and assess factors contributing to different outcomes of interest (Hess, 2004). The study identified a cohort of adults who are HIV positive and were admitted to the inpatient medical wards at GJGMRH during the period: 1 October 2019 to 31 December 2019. The study described their demographic characteristics and clinical profile. It also looked at reasons for admission and determined prevalence and patterns of comorbidities in HIV positive admitted patients.

The survey design allows for the assessment of patients that have been admitted during this study period (Hess, 2004). Information was collected at a cross-section which limited loss to

follow-up. This study design was ideal as a first step to generate further hypotheses relating to the research problem that could be studied in the future.

3.3. STUDY POPULATION AND SAMPLING

All consecutive admissions into the medical ward during the study period were selected for analysis. According to the Department of Internal Medicine GJGMRH statistics for 2019, the average admission per month is 450 patients; 150 of those admitted were HIV positive.

3.3.1 INCLUSION CRITERIA

All documented HIV positive adult patients (18 years and over) who were admitted to the medical wards at GJGMRH during the study period were included. The HIV status was verified by laboratory tests and hospital records. If no confirmatory HIV test result appeared in the laboratory results for the current or prior admission, the study investigator attempted to obtain the patient's hospital record. The hospital record was assessed to check if a confirmed HIV test result from current or previous visits were documented in the medical notes and results flow chart. If no evidence of HIV testing was found in the laboratory results or medical notes, then the HIV status was recorded as HIV-unknown, and the hospital record was not used. If the hospital file could not be located, the status remained classified as HIV-unknown. Thus, the HIV prevalence was calculated using both laboratory data and hospital record review. The hospital records of all confirmed HIV-infected adults (confirmed using the procedures described above) were obtained from the records department and then selected data was captured on a standardized study tool by the study investigator.

3.3.2 EXCLUSION CRITERIA

Any patient who was admitted to a non-medical ward, specifically surgical, orthopaedic, obstetrics/gynaecology and paediatric wards.

3.3.3 SAMPLE SIZE CALCULATION

A minimum of 272 patients was required to achieve a confidence level of 95%, with a 5% margin of error. This is based on an estimated study population at 1350 (3-month estimate of admissions) and an assumed HIV prevalence of 33% (estimate of HIV infected as per previous year statistics).

3.4 DATA COLLECTION

A pro-forma standardized study tool was developed to ensure ease of data extraction, coding for simplified analysis and gathered mainly closed-ended quantitative data (Appendix 1). A computerised database of admission records exists. However, the records are often incomplete. A pilot assessment determined the variables that could be collected that would ensure the highest level of complete data. Patients' hospital files were located/retrieved in the GJGMRH Records Department, and missing data was filled in. The following information was extracted for each participant:

- Demographic characteristics: age, gender, race;
- HIV clinical characteristics: HIV testing (whether newly diagnosed in this admission); ART treatment history: current treatment, need for ART, duration of ART;
- HIV Staging: WHO stage and clinical criteria for staging;
- Immunological indices: CD4 count and viral load;
- Primary diagnosis or reason for hospital admission: one primary and two secondary diagnoses could be recorded;
- Comorbidities: all co-morbidities were recorded;
- Duration of hospital stay.

3.5 DATA ANALYSIS

The study investigator entered data into SPSS Version 23. Data quality and accuracy were checked by performing frequencies on categorical variables such as HIV status and by checking the ranges of continuous variables to identify outliers and those out of bounds, to eliminate and correct data capturing errors where possible. Data was first assessed to classify prevalence distribution, using descriptive statistics. Frequencies and percentages were calculated for categorical data and illustrated in tabular form.

Medians and interquartile ranges were used for data not amenable to the parametric description. Pearson's Chi-square test or Fisher's exact test was utilized for comparison between subgroups specifically, virologically suppressed versus unsuppressed; CD4 cell count: >200 vs <200; Age >40 vs <40 years. All *p*-values were 2-tailed and considered significant if below 0.05.

3.6 VALIDITY AND RELIABILITY

The validity of the proposed study was enhanced by reducing measurement and selection bias, increasing reliability, and controlling variables (Quintão, Andrade & Almeida, 2020).

The study was designed to have high construct validity because the information that was collected was based and designed according to existing theory and knowledge with regards to HIV related admissions. It may lack in areas of content validity only because of the possibility of lack of information from the files given the retrospective nature of the study. To overcome this, the pilot assessment determined the variables that could be collected that would ensure the highest level of complete data.

To ensure the highest level of validity and reliability, this study was designed to ensure that appropriate methods of measurement and sampling are used. Many of the conditions were standardised so that the methods may be applied consistently.

Due to the nature of the above study, the results were accurately captured because it was taken from patient's medical records and NHLS information. Thus test-retest reliability was not a major issue because the information was fixed and defined. Selection bias was reduced as only patients who met the inclusion criteria were included. The researcher had no direct influence on the selection process because the study was retrospective. The study was over-sampled to overcome selection bias that may occur.

To minimize measurement bias, there was only one data collector, and the data was verified by the researcher. The laboratory results were taken from the NHLS database, which was calibrated and complied with SANAS accreditation (ISO 15189:2007).

All the data that was captured was verified and randomly checked by the researcher. This ensured accurate capturing of the data.

3.7 ETHICS CONSIDERATIONS

Ethical issues were minimized as this was a retrospective record review and there was no interaction with patients. Therefore, informed consent from the patients was not required, but permission from relevant regulating bodies was sought.

After approval of the research proposal by the UWC Senate Higher Degrees committee and ethics clearance from the UWC Biomedical Research Ethics Committee (BM20/10/11), an application for permission to use data sources was made to the National Health Research

committee through their online application process. Permission to access hospital records was obtained via the hospital CEO at GJGMRH.

Each patient's folder was given a study number and the patient's name was not reflected thereafter. All identification was then reflected by the study number. The master key with the name and study number was kept by the principal investigator in the Department of Medicine's computer that was access controlled only by the head of department. This was an existing database. The various data copies were saved using passwords that are known only to the principal investigator.

CHAPTER 4. RESULTS

4.1 REALIZATION OF SAMPLE SIZE

As illustrated in Figure 1, there was a total of 1 269 medical admissions from 1 October 2019 to 31 December 2019. Patients that were admitted more than once during the study period were assessed as separate cases. Although 301 cases fulfilled the study inclusion criteria, medical details could only be traced for 96.0% (n=289) of admissions. Twelve admissions were excluded due to missing hospital files and department summaries. The crude prevalence of HIV in medical wards at GJGMRH was 23.7% (301/1269).

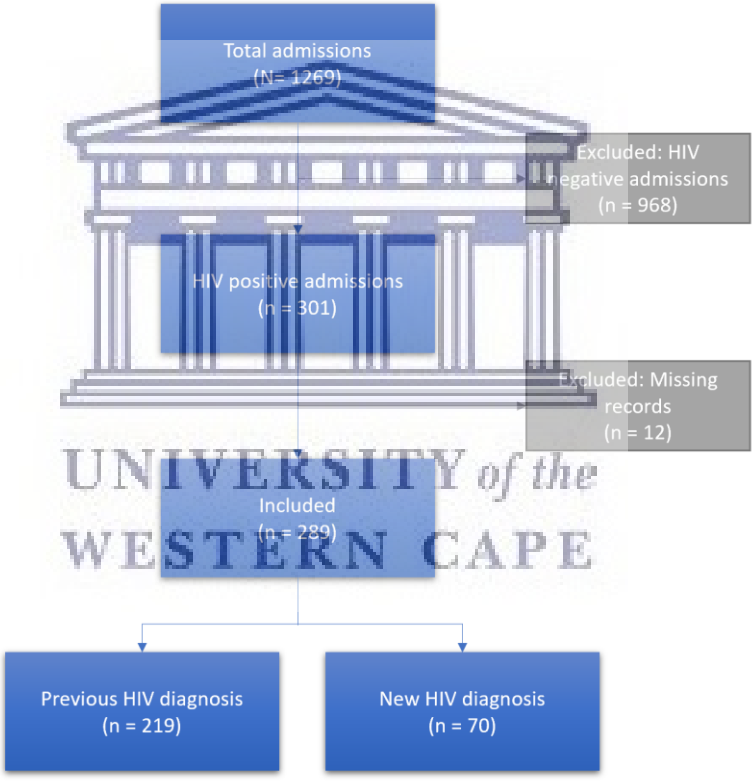

Figure 1: Breakdown of study participants admitted to the GJGMRH hospital during the period 1 October to 31 December 2019

4.2 SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF HIV PATIENTS AT ADMISSION

The median age of the patients was 38 years old with an IQR of 18. The sociodemographic and clinical characteristics of the study sample are shown in Table 1. Just over half of the participants were females (n=157; 52.6%), and most participants were Black South Africans (98.6%). Most patients (75.8%) knew their HIV status before admission.

Table 1: Sociodemographic and clinical characteristics of HIV patients at admission to GJGMRH (N = 289)

	Total n (%)	**Male n (%)**	**Female n (%)**	***p*-value***
Age in years				0.179
< 20	8 (2.8)	1 (0.7)	7 (4.6)	
20 – 29	57 (19.7)	23 (16.8)	34 (22.4)	
30 – 39	97 (33.6)	46 (33.6)	51 (33.6)	
40 – 49	61 (21.1)	35 (25.5)	26 (17.1)	
50 – 59	42 (14.5)	21 (15.3)	21 (13.8)	
60 and older	24 (8.3)	11 (8.0)	13 (8.6)	
Medical history				
Pre-existing HIV diagnosis	219 (75.8)	99 (72.3)	120 (78.9)	0.185
Hypertension	59 (20.4)	22 (16.1)	37 (24.3)	0.081
Established target organ injury	25 (42.4)	8 (36.4)	17 (45.9)	0.471
Diabetes Mellitus	23 (8.0)	15 (10.9)	8 (5.3)	0.075
Dyslipidemia	27 (9.3)	6 (4.4)	21 (13.8)	**0.006**
Chronic Kidney Disease	30 (10.4)	15 (10.9)	15 (9.9)	0.764
Cardiovascular Disease	16 (5.6)	5 (3.7)	11 (7.2)	0.364
Malignancy	9 (3.1)	6 (4.4)	3 (2.1)	0.094
Previous Tuberculosis	92 (31.8)	43 (31.4)	49 (32.2)	0.877

***** *Chi-square test for categorical data and one-way ANOVA for quantitative data*

Hypertension was the most prevalent pre-existing condition (20%, n=59), followed by chronic kidney disease (10.4%, n=30), dyslipidaemia (9.3%, n=27), diabetes (8%, n=23) and cardiovascular disease (5.6%, n=16). Among those with hypertension, 42.2% (25/59) reported major end-organ damage (myocardial infarction, cerebrovascular accident or renal failure). Micro and/or macrovascular complications were present in more than half (52.2%, 12/23) of the patients with previously diagnosed diabetes mellitus.

Nine patients had an established diagnosis of malignancy at admission: three with non-Hodgkin's lymphoma, four with Kaposi's sarcoma and two with hepatocellular carcinoma.

Ninety-two patients (31.8%) had history of previous TB; of which 31.4% (n=43) among males and 32.2% (n=49) among females.

There was no statistically significant difference in the prevalence of hypertension (16.1% vs 24.3%; p=0.081), diabetes mellitus (10.9% vs 5.3%; p=0.075), chronic kidney disease (10.9% vs 9.9%; p=0.764), cardiovascular complications (3.7% vs 7.2%; p=0.364), and malignancies (4.4% vs 2.1%; p=0.094) between males and females. Females were significantly more likely to develop dyslipidaemia compared to males (13.8% vs. 4.4%; p=0.006).

4.3 IMMUNOLOGICAL AND VIROLOGICAL PROFILE OF HIV PATIENTS

The immunological profile of admissions was compared by CD4 count in Table 2 since a low CD4 cell count is a poor predictor of disease progression (Goujard et al., 2006). Males (n=73; 57%) were more likely to have a CD4 cell count less than 200 cell/mm^3; whilst females (n=97; 60.2%) were more likely to have a CD4 cell count higher than 200 cell/mm^3 (p=0.003).

Patients with lower CD4 cell counts stayed significantly longer in hospitals (Median 9 days vs 7 days; p=0.020). Patients with CD4 cell counts higher than 200 cells/mm^3 were more likely to have cardiovascular (n=47; 76.6%), uro-renal (n=91; 44.1%), respiratory (n=28; 17.4%), endocrine (n=28; 14.9%), or haematological (n=34; 21.1%) systems affected (Table 2).

Patients with a CD4 count less than 200 cell/mm^3 were more likely to be admitted for an infectious disease (p<0.0001) (Table 2). Tuberculosis was more likely in patients with a CD4 cell count less than 200 cells/mm^3 (n=87; 62.5%) (p<0.0001). The respiratory (n=27; 17.2%), neurological (n=12; 9.4%) and gastrointestinal (n=40; 30.5%) systems were more commonly affected in patients with a lower CD4 cell count.

Table 2: Immunological profile by sociodemographic and clinical characteristics of HIV inpatients at GJGMRH

	Total n (%)	**CD4 cell count <200 n (%)**	**CD4 cell count ≥200 n (%)**	***p-value***
TOTAL	289	128	161	
Age in years (Median)(IQR)	38 (18.5)	37 (13)	37 (18)	*0.141*
<20	8 (2.8)	1 (0.8)	7 (4.3)	
20 – 29	57 (19.7)	24 (18.8)	33 (20.5)	
30 – 39	97 (33.6)	52 (40.6)	45 (28.0)	
40 – 49	61 (21.1)	30 (23.4)	31 (19.3)	
50 – 59	42 (14.5)	15 (11.7)	27 (16.8)	
60 and older	24 (8.3)	6 (4.7)	18 (11.2)	
Gender				***0.003***
Male	137 (47.4)	73 (57.0)	64 (39.8)	
Female	152 (52.6)	55 (39.8)	97 (60.2)	
Median Length of stay (in days) (IQR)	7 (8)	9 (8)	7 (9)	***0.020***
Admission Reason				***<0.0001***
Non-communicable disease	103 (35.6)	16 (12.5)	87 (54.0)	
Communicable disease	186 (64.4)	112 (87.5)	74 (46.0)	
Non-communicable disease*				
Cardiovascular	60 (18.7)	13 (10.2)	47 (76.6)	***0.002***
Uro-Renal system	151 (43.6)	60 (43.0)	91 (44.1)	***0.029***
Respiratory	36 (12.5)	8 (6.3)	28 (17.4)	***0.004***
Neoplastic	9 (3.1)	5 (3.9)	4 (2.5)	*0.489*
Hepatic and Gastrointestinal	9 (3.1)	5 (3.9)	4 (2.5)	*0.489*
Metabolic and Endocrine	32 (9.7)	4 (3.1)	28 (14.9)	***0.003***
Musculoskeletal	1 (0.3)	0 (0.0)	1 (0.3)	*0.372*
Haematological	87 (30.1)	53 (41.4)	34 (21.1)	***<0.0001***
Neurological	18 (6.2)	4 (3.1)	14 (8.7)	*0.052*
Social related±	26 (9.0)	9 (7.0)	17 (10.6)	*0.298*
Communicable disease*				
Tuberculosis (TB)	129 (41.9)	87 (62.5)	42 (25.4)	***<0.0001***
Uro-Renal	5 (1.7)	4 (3.1)	1 (0.6)	*0.105*
Respiratory	68 (21.8)	27 (17.2)	41 (25.5)	***0.002***
Neurological	15 (5.2)	12 (9.4)	3 (1.9)	***0.004***
Hepatic and gastrointestinal	59 (20.0)	40 (30.5)	19 (11.8)	***<0.0001***
Other sepsis	7 (2.4)	4 (3.1)	3 (1.9)	*0.488*

*Some patients had more than one type of NCD or CD

∞*Chi-square test for categorical data and one-way ANOVA for quantitative data*

± Parasuicide, substance abuse, herbal intoxication, abandoned in hospital.

Table 3 compares the different characteristics between admitted patients who were virologically suppressed (<1000 copies/mL) and those who were virologically unsuppressed (≥1000 copies/mL) (Fokam et al., 2019). Virologically suppressed patients have better long term outcomes as compared to virologically unsuppressed patients (Fox et al., 2012). Patients who were virologically suppressed were significantly more likely to be older (Median age 39.5 years; IQR 22) than patients who were unsuppressed (Median age 37 years; IQR 15; p<0.0001). Males were more likely to have an unsuppressed viral load than females (n=81 (55.9%) vs n=64 (44.1%); p=0.004).

Patients who were virologically unsuppressed tended to have longer in-hospital stays than those who were virologically suppressed (Median 8 days vs 7 days; p=0.116). Patients who were virologically suppressed on admission were more likely to be admitted for an NCD, whilst patients who were unsuppressed were more likely to be admitted for an infectious aetiology (n=66 (45.8%) vs n=108 (74.5%); p<0.0001).

Patients who were virologically suppressed were more likely to have a cardiovascular (n=45 (27.1%) vs n=15 (10.3%); p<0.0001) or respiratory disorder (n=29 (20.1%) vs n=7(4.8%); p<0.0001), as opposed to patients who were unsuppressed, who tended to have a haematological disorder (n=31(21.5%) vs n=56 (38.6%); p=0.002).

Tuberculosis (n=84 (53.8%) vs n=45 (29.9%); p<0.0001) was the most significant infectious aetiology for patients who were virologically unsuppressed. Neurological (n=12 (8.3%) vs n=3 (2.1%); p=0.018) and gastrointestinal systems (n=40 (26.9%) vs n=19 (13.2%); p=0.012) were significantly affected in patients with an unsuppressed viral load.

Table 3: Virological profile by sociodemographic and clinical characteristics of HIV inpatients at GJGMRH (N=289)

	Total	HIV Viral load		*p-value*
		Suppressed (n=144)	Unsuppressed (n=145)	
	n (%)	n (%)	n (%)	
Age in years (Median; IQR)	38 (8.5)	39.5 (22)	37 (15)	***<0.0001***
< 20	8 (2.8)	4 (2.8)	4 (2.8)	
20 – 29	57 (19.7)	23 (16.0)	34 (23.4)	
30 – 39	97 (33.6)	45 (31.3)	52 (35.9)	
40 – 49	61 (21.1)	22 (15.3)	39 (26.9)	
50 – 59	42 (14.5)	32 (22.2)	10 (6.9)	
60 and older	24 (8.3)	18 (12.5)	6 (4.1)	
Gender				***0.004***
Male	137 (47.4)	56 (38.9)	81 (55.9)	
Female	152 (52.6)	88 (61.1)	64 (44.1)	
Length of stay (Median; IQR)	7 (8)	7 (8)	8 (9)	*0.116*
Reason for Admission				***<0.0001***
Non-communicable disease	103 (35.6)	66 (45.8)	37 (25.5)	
Communicable disease	186 (64.4)	78 (54.2)	108 (74.5)	
Non-communicable disease*	103 (35.6)	66 (45.8)	37 (25.5)	
Cardiovascular	60 (18.7)	45 (27.1)	15 (10.3)	***<0.0001***
Uro-Renal system	151 (43.6)	79 (43.1)	72 (44.1)	*0.109*
Respiratory	36 (12.5)	29 (20.1)	7 (4.8)	***<0.0001***
Neoplastic	9 (3.1)	6 (4.2)	3 (2.1)	*0.305*
Hepatic and Gastrointestinal	9 (3.1)	4 (2.8)	5 (3.4)	*0.743*
Metabolic and Endocrine	32 (9.7)	22 (13.2)	10 (6.2)	*0.127*
Musculoskeletal	1 (0.3)	1 (0.7)	0 (0.0)	*0.315*
Haematological	87 (30.1)	31 (21.5)	56 (38.6)	***0.002***
Neurological	18 (6.2)	8 (5.6)	10 (6.9)	*0.637*
Social related±	26 (9.0)	10 (6.9)	16 (11.0)	*0.224*
Communicable disease*				
Tuberculosis	129 (41.9)	45 (29.9)	84 (53.8)	***<0.0001***
Uro-Renal	5 (1.7)	3 (2.1)	2 (1.4)	*0.646*
Respiratory	68 (21.8)	42 (27.1)	26 (16.6)	*0.095*
Neurological	15 (5.2)	3 (2.1)	12 (8.3)	***0.018***
Hepatic and gastrointestinal	59 (20.0)	19 (13.2)	40 (26.9)	***0.012***
Other sepsis	7 (2.4)	4 (2.8)	3 (2.1)	*0.695*

*Some patients had more than one type of NCD or CD

Chi-square test for categorical data and one-way ANOVA for quantitative data

± Parasuicide, substance abuse, herbal intoxication, abandoned in hospital.

Table 4 compares GJGMRH 90-90-90 targets with district and WHO targets. The 90-90-90 targets for the study population were not achieved (Table 4). Admissions to the hospital showed that 75.6% of people with HIV infection knew their status. This was better than the district levels of 72.1%. Of those patients admitted to GJGMRH that were aware of their HIV status, 76.7% of admissions had been on sustained ART but only 65.8% had reached virological suppression.

Table 4: Report on 90-90-90 targets at GJGMRH vs district

	Known HIV status	**On ART**	**Virally suppressed**
WHO/UNAIDS[+] Targets	90%	90%	90%
South Africa[*]	**92%**	75%	**92%**
KwaZulu-Natal[&]	**95%**	77%	**95%**
iLembe District [#]	72.1%	82.7%	**91.5%**
GJGMRH	75.6%	76.7%	65.8%

+ (UNAIDS, 2014)
***** (UNAIDS, 2019)
& (Pillay & Johnson, 2021)
(Human Science Research Council, 2019)

4.4 COMPARISON OF NEW AND PRE-EXISTING NON-COMMUNICABLE DISEASE

Hypertension (34.6% vs 9.3%; $p<0.0001$), diabetes mellitus (15.7% vs 1.9%; $p<0.0001$) and dyslipidaemia (15.0% vs 4.9%; $p=0.004$) were significantly more common pre-existing conditions in patients older than 40 years compared to patients younger than 40 years old (Table 5). Uro-renal (n=86; 52.8%) and endocrinopathies (n=26; 16.7%) were the main reason for new NCD admissions in patients over the 40 years ($p<0.0001$). Older patients developed acute kidney injury more than younger patients (33.9% vs 8.7%; $p<0.0001$) as a new NCD.

In patients younger than 40 years, hypertension (30.1% vs 10.2%; $p<0.0001$) and chronic kidney disease (21.4% vs 2.7%; $p<0.0001$) was more prevalent as new NCD admissions than in older patients over 40 years. Diabetes mellitus (10.7% vs 3.2%; $p=0.010$) and dyslipidaemia (5.8% vs 1.1%; $p=0.018$) were significantly more common as new NCD presentations in younger patients than older patients.

Table 5: Prevalence of pre-existing NCDs and newly NCD diagnosed in HIV infected patients admitted to GJGMRH according to age

NCD conditions	Total n (%)	Age		*p*-value
		Under 40 years n (%)	40 years and older n (%)	
Pre-existing NCD				
Hypertension	59 (20.4)	15 (9.3)	44 (34.6)	<**0.0001**
Diabetes Mellitus	23 (8.0)	3 (1.9)	20 (15.7)	<**0.0001**
Dyslipidaemia	27 (9.3)	8 (4.9)	19 (15.0)	**0.004**
Renal Failure	30 (10.4)	12 (7.4)	18 (14.2)	0.061
Cardiovascular Disease	16 (5.6)	6 (3.8)	10 (3.4)	0.306
Malignancy	9 (3.1)	4 (2.5)	5 (3.9)	0.476
New NCD diagnosis				
Uro-Renal system	151 (43.6)	65 (36.4)	86 (52.8)	<**0.0001**
- Acute kidney injury	72 (24.9)	9 (8.7)	63 (33.9)	<**0.0001**
- Hypertension	51 (17.3)	32 (30.1)	19 (10.2)	<**0.0001**
- Chronic Kidney disease	27 (9.3)	22 (21.4)	5 (2.7)	<**0.0001**
- Prostatomegaly	1 (0.3)	1 (1.0)	0 (0.0)	0.178
Metabolic and Endocrine	32 (9.7)	6 (2.8)	26 (16.7)	<**0.0001**
- Diabetes mellitus	17 (5.9)	11 (10.7)	6 (3.2)	**0.010**
- Dyslipidemia	8 (2.8)	6 (5.8)	2 (1.1)	**0.018**
- Hypothyroidism	4 (1.4)	2 (1.9)	2 (1.1)	0.546
- Diabetic ketoacidosis	3 (1.0)	3 (2.9)	0 (0.0)	0.019
Cardiovascular Disease	60 (18.7)	32 (17.9)	28 (19.7)	0.911
Malignancy	9 (3.1)	4 (2.5)	5 (3.9)	0.476
Respiratory	36 (12.5)	20 (12.3)	16 (12.6)	0.949
Hepatic and Gastrointestinal	9 (3.1)	5 (3.1)	4 (3.1)	0.976
Musculoskeletal	1 (0.3)	0 (0.0)	1 (0.8)	0.258
Haematological[+]	87 (30.1)	54 (33.3)	33 (26.0)	0.176
Neurological[#]	18 (6.2)	8 (4.9)	10 (7.9)	0.305
Social related*	26 (9.0)	19 (11.7)	7 (5.5)	0.067

+ Haematological - diseases include deep vein thrombosis; anaemia

Neurological – diseases include epilepsy, delirium, meningitis, cerebral toxoplasmosis, neurocysticercosis

* Social related – Parasuicide, Substance abuse, herbal intoxication, abandoned in hospital.

4.5 REASONS FOR ADMISSIONS

Infectious diseases were the most common reasons for admission (n=186, 64%); with NCD admissions at 36% (n=103) (Figure 2).

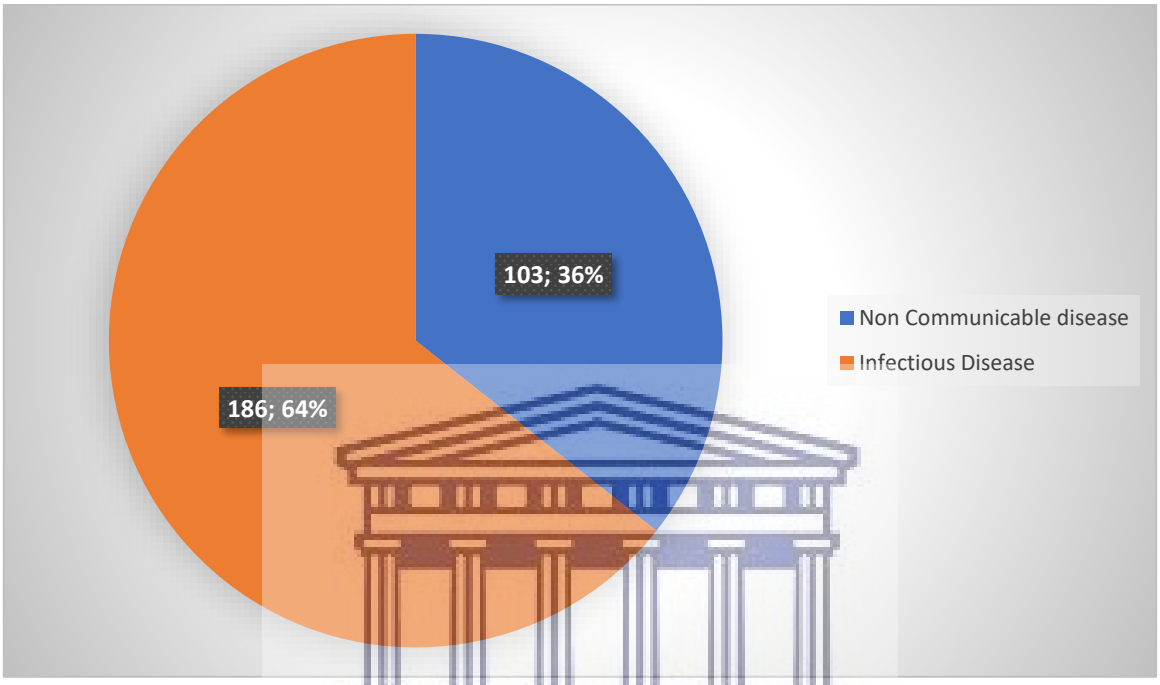

Figure 2: Distribution of admissions for study period

Figures 3 and 4 illustrate the breakdown of admissions between NCDs and infectious aetiology. Uro-renal, (n=151; 35%), haematological (n=87; 20%) and cardiovascular disease (n=60; 14%) were the main contributors to NCD admissions. Tuberculosis (n=129; 46%) was the main aetiology of infectious admissions.

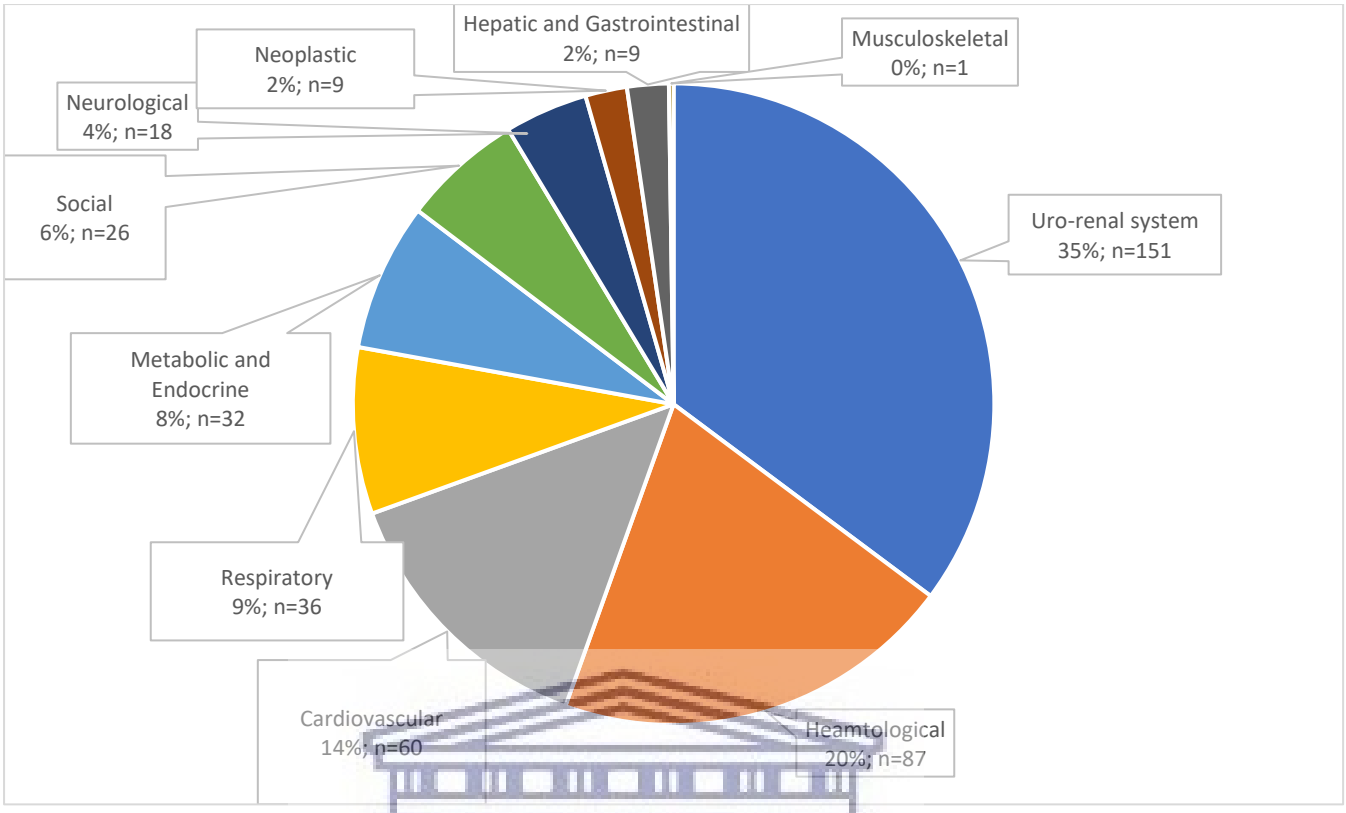

Figure 3: A breakdown of non-communicable disease admissions per organ system involved.

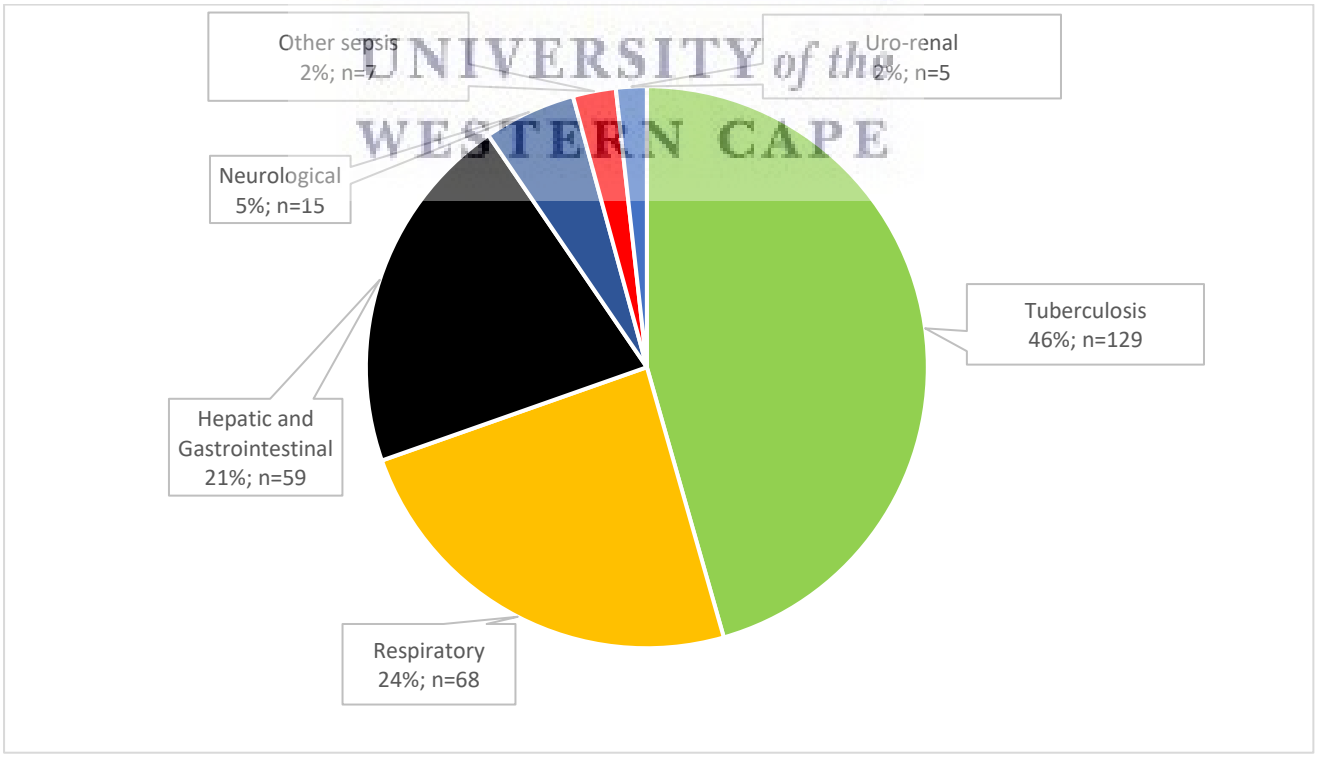

Figure 4: A breakdown of infectious disease admissions by organ system/aetiology

Table 6 shows the descriptive characteristics between patients admitted with NCD versus infectious aetiology. Patients admitted with NCDs were slightly older (median age 38 years; IQR 18) than patients admitted with infectious diseases (median age 37 years; IQR 14); although there was no statistical significance between both groups (p=0.102). There was also no statistical significance difference between the genders and the reason for admission (p=0.235).

Patients who were admitted with an NCD were more likely to have a prior history of an NCD than those who were admitted for an infectious cause. Hypertension (35.9% vs 11.8%; p<0.0001), diabetes mellitus (14.6% vs 4.3%; p=0.002), dyslipidaemia (19.4% vs 3.8%; p<0.0001), renal failure (23.3% vs 3.2%; p<0.0001) and malignancies (35.9% vs 11.8%; p<0.0001) were significant prior NCDs in the NCD cohort compared to the infective cause/aetiology cohort.

Of the 219 (75.8%) patients admitted with a known HIV status, 23.3% (n=53) had defaulted on treatment. The median viral load of patients admitted for an NCD were significantly lower than those admitted for an infectious disease (33,043 vs 142,870 copies/mm^3; p=0.037). Patients admitted for NCDs had higher CD4 cell counts than patients with an infectious reason for admission (477 vs 239 cells/mm^3; p<0.0001). The lower the CD4 count, admission was more likely related to an infectious aetiology.

Patients with NCD reasons for admission were more likely to have WHO clinical stage 2 (n=46; 44.7% vs n=28; 15.1%) in contrast to stage 3 (n=30; 29.1% vs n=94; 50.5%) in infectious disease (p<0.0001). Of the 70 patients with WHO stage 4 disease, 64 patients (34.4%) were admitted for an infectious aetiology. No patients with WHO stage 1 disease were admitted for an infectious cause.

Patients admitted for NCDs had a significantly shorter duration of admission than patients admitted for an infectious cause (Median 6.5 days vs. 9 days; p=0.037).

Table 6: Demographic characteristics of study population according to NCD vs infectious cause for admission

Characteristics	Total N=289	NCD n=103	CD n=186	*p-value*
Age in years (Median; IQR)	38 (18.5)	38 (18)	37 (14)	*0.102*
Gender				*0.235*
Male	137 (47.4)	44 (42.7)	93 (50.0)	
Female	152 (52.6)	59 (57.3)	93 (50.0)	
Pre-existing medical illness				
Hypertension	59 (20.4)	37 (35.9)	22 (11.8)	***<0.0001***
Diabetes Mellitus	23 (8.0)	15 (14.6)	8 (4.3)	***0.002***
Dyslipidaemia	27 (9.3)	20 (19.4)	7 (3.8)	***<0.0001***
Renal Failure	30 (10.4)	24 (23.3)	6 (3.2)	***<0.0001***
Malignancy	9 (3.1)	6 (5.8)	3 (1.6)	***0.048***
HIV staging				
HIV Viral load (Mean; ±SD)	108839 (356636)	33043 (133550)	142870 (415911)	***0.037***
CD 4 Cell Count (Mean; ±SD)	323.67 (369.5)	476.62 (289.1)	238.98 (382.4)	***<0.0001***
WHO clinical stage (Mean; ±SD)	2.84 (0.87)	2.20 (0.83)	3.19 (0.68)	***<0.0001***
WHO Clinical stage category				***<0.0001***
WHO Clinical stage 1	21 (7.3)	21 (20.4)	0 (0.0)	
WHO Clinical stage 2	74 (25.6)	46 (44.7)	28 (15.1)	
WHO Clinical stage 3	124 (42.9)	30 (29.1)	94 (50.5)	
WHO Clinical stage 4	70 (24.2)	6 (5.8)	64 (34.4)	
Length of stay in days Median (IQR)	7 (8)	6.5 (8)	9 (8)	***0.037***

Chi-square test for categorical data and one-way ANOVA for quantitative data

4.6 CLINICAL PRESENTATION OF PATIENTS ADMITTED TO HOSPITAL

Figure 5 gives a graphical comparison of a clinical presentation of NCD vs infectious/communicable disease (CD). Cough, diarrhoea and vomiting were more likely associated with patients admitted for an infectious aetiology (p<0.0001) whereas chest pain, body swelling, and symptoms of hyperglycaemia were associated with NCD admissions (p<0.0001).

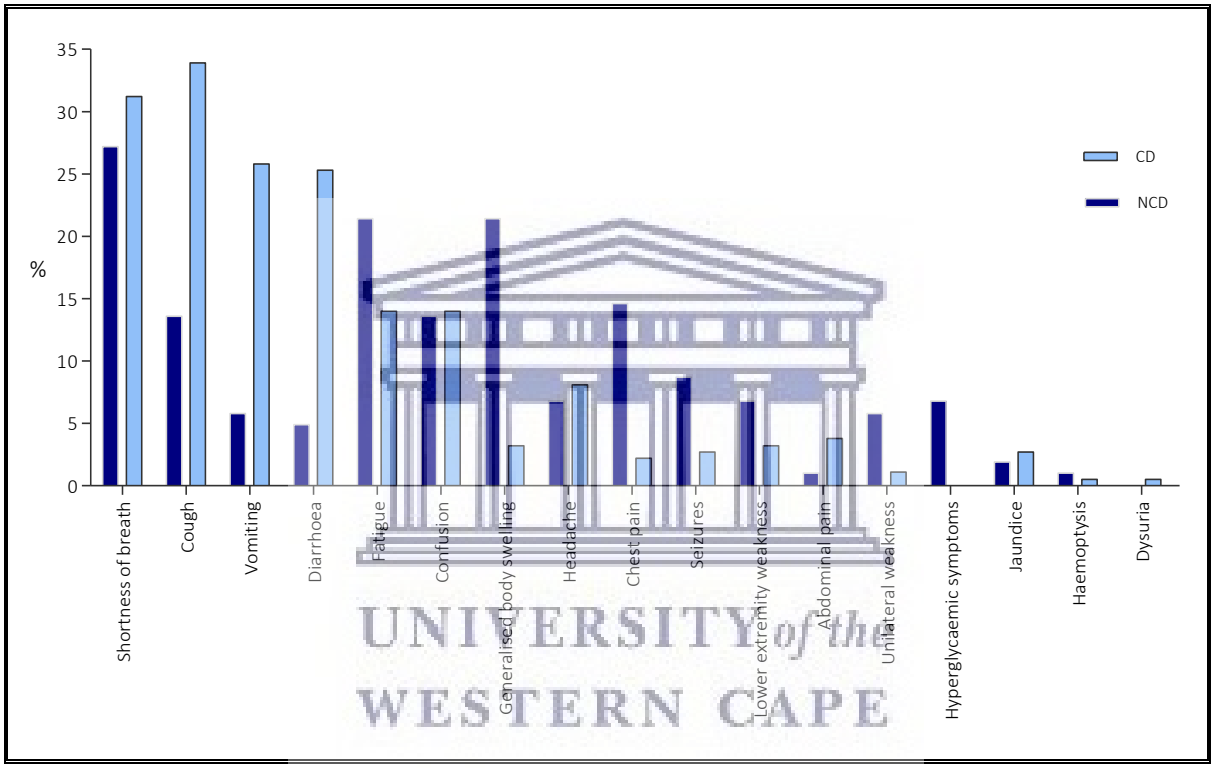

Figure 5: Comparison of presenting symptoms in NCD vs infective admissions

4.7 SUMMARY OF RESULTS

There were 1 269 admissions during the study period. Although 301 cases fulfilled the study inclusion criteria, medical details could only be traced for 96.0% (n=289) of admissions The median age of participating patients was 38 years (IQR =18.5). Of the total patients, 219 (75.8%) were known to have HIV infection before admission; 76.7% (n=168) were on ART, and 65.8% (n=144) were virally suppressed. Hypertension was the highest prevalent condition (20%, n=59), followed by chronic kidney disease (10.4%, n=30), dyslipidaemia (9.3%, n=27), diabetes (8%, n=23) and cardiovascular disease (5.6%, n=16). Nine patients had an established

diagnosis of malignancy at admission. Just under a third (31.8%; n=92) of participants reported a history of TB.

Patients with higher CD4 cell counts were more likely to be admitted for an NCD than patients with a lower CD4 cell count. Patients admitted with an NCD were more likely to be classified at WHO clinical stage 2; while patients admitted with infectious diseases were WHO stage 3 and stage 4 diseases. Uro-renal and endocrinopathies were the main reasons for new NCD admissions in participants over the age of 40 years. Patients admitted with a new or existing NCD had a significantly shorter in hospital stay than patients admitted for an infectious cause (Median: 6.5 vs 9 days; p=0.037).

CHAPTER 5. DISCUSSION

5.1 CHARACTERISTICS OF HIV PATIENTS ADMITTED TO HOSPITAL

In our study, there was no statistically significant difference in the prevalence of hospital admissions between females and males (52.6% vs. 47.4%, respectively). Generally, females in Southern Africa have a 2.5 times more likely chance of having HIV infection compared to males (UNAIDS, 2020). Meintjes et al. (2015) found a higher prevalence of female HIV inpatients (n=338; 57.8%) in their study in a district hospital in the Western Cape. This may be due to the difference in health-seeking behaviours of males and females.

In this study, males (n=73; 57%) were more likely to have a CD4 cell count less than 200 cell/mm^3; whilst females (n=97; 60.2%) were more likely to have a CD4 cell count higher than 200 cell/mm^3 (p=0.003). This suggests males seek HIV treatment at more advanced stages of HIV infection than females or when they become symptomatic. Females may routinely test during pregnancy or as part of family planning and be otherwise asymptomatic. Studies confirmed that females tend to have higher CD4 cell counts than males at the initiation of ART and at the time of presentation of illness (Loupa et al., 2006; Means et al., 2016; Prins et al., 1999).

Patients in the study were on average older (38 years old) than described by Meintjes et al. (2015) (Median 35.3 years). This variation may be due to improvement in ART coverage over the 6 years between both studies. Multiple studies have shown a similar age group for PLWH who were admitted into hospital (Álvarez et al., 2017; Crowell et al., 2016; Lakoh et al., 2019; Raberahona et al., 2018); thus showing little significance in the age of admitted patients with HIV infection.

5.2 REPORT ON 90-90-90 TARGETS

This study reports that only 75.8% of HIV patients knew their status upon admission to the hospital. This is below UNAIDS' target of 90%, but higher than the 72.1% reported in the iLembe District (HSRC, 2019). The provincial and national uptake of HIV testing was 95% and 92%. This reflects a success in the national testing campaigns which may not be successful at district levels.

The key of the first 90 target is a move to an active approach to ending HIV by 2030 (UNAIDS, 2014). With more people knowing their HIV status, there is a move from morbidity and mortality gains to therapeutic and preventative benefits of ART (UNAIDS, 2014). Knowledge of HIV status has been consistently increasing in Southern Africa since 2000 and is currently 84% in the region (Giguère et al., 2021). This is due to effective and efficient HIV testing programs, like the South African universal test and treat program (Bessong et al., 2021). In 2016 the South African Department of Health introduced the National HIV Testing Service policy which focussed on patient-initiated counselling and testing and client-initiated counselling and testing. This goal of the policy was to timeously identify PLWH through testing services and effectively link them to appropriate care and treatment (South African National Department of Health, 2016). By achieving the first 90-90-90 target South Africa has shown the success of an effective testing campaign.

Our study showed that 76.7% of inpatients were on ART, which is less than the expected target of 90% (UNAIDS, 2014). According to the 2017 South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, the iLembe District had an ART sustained rate of 82.7%, whilst and KZN and national rates were 77% and 75% respectively (HSRC, 2019; Pillay & Johnson, 2021; UNAIDS, 2019).

The second 90-90-90 indicator gives an impression of linkage to ART amongst those that test positive for HIV (Marinda et al., 2020). The inpatient sustained ART rate may be understandably lower than the district rate. This reflects the positive effect that ART usage has on viral load suppression and better health and reduced hospitalizations.

Virological suppression was observed as 65.8% of the study population that was on ART at the time of admission to GJGMRH. Virological suppression is an indicator of the success of the ART role out program. The iLembe District had achieved virological suppression in 91.5% of patients according to the 2017 South African National HIV Prevalence, Incidence, Behaviour and Communication Survey (HSRC, 2019). National and provincial rates of virological suppression were 92% and 95% respectively. A total of 186 (64.4%) admissions in the cohort were for infectious diseases. The impaired immunological state (low CD4 cell count and unsuppressed viral load) predisposes patients to infectious diseases.

South Africa has difficulty in reaching the 90-90-90 targets, particularly in the 15 to 24-year old population (Lake et al., 2019). This may be for multiple reasons. Poor uptake of testing in

the communities, poor linkage of care to health systems and poor adherence to therapy are the key factors that hamper achieving the 90-90-90 targets. Poverty, limited access to viral load testing, lack of support services, privacy and stigma are amongst the other reasons for failure in achieving the 90-90-90 targets. The rate of defaulting ART in our study population was 23.3% (n=51) (data not shown). This reflects the poor knowledge of the importance of ART in the community. Distance from health facilities, limited food sources, mental health, discordant relationships, patients whose partner's HIV status was unknown or not tested and patients who fear stigma were the main reasons for defaulting ART in Southern Africa (Asefa et al., 2013).

5.3 REASONS FOR HOSPITAL ADMISSIONS OF PEOPLE WITH HIV

In KwaZulu-Natal, the incidence of tuberculosis according to the 2019/20 Annual Report was 442 per 100 000 and the national incidence of TB was 615 per 100 000 (KwaZulu Natal Department of Health, 2020; World Health Organization, 2019). Tuberculosis was the most prevalent infectious disease present in the HIV inpatient population (41.9%).

In the current study, infectious diseases were the most common reasons for admissions (64%), compared to 36% for new NCDs. Meintjes et al. (2015) reported a much lower prevalence of new NCD (3.8%) when compared to our study (36%). The higher NCD prevalence (36%) in our population may be attributed to the older age of our study sample. Our study showed that the most prevalent newly diagnosed NCDs among HIV inpatients were hypertension (37%), chronic kidney disease (10.4%), dyslipidaemia (9.3%) and diabetes (8.3%).

WHO estimates the prevalence of hypertension, dyslipidaemia and diabetes in South Africa at 42%, 32% and 11% respectively (WHO, 2018). Compared to our findings, Van Heerden et al. (2017) reported the prevalence of hypertension at 33.3% (vs 20%), dyslipidaemia 20% (vs 9.4%) and diabetes 3.9% (vs 8%) in a rural KZN community. Our study also showed a lower prevalence of hypertension, chronic kidney disease, dyslipidemia and diabetes compared to the national estimates (WHO, 2018).

Patients admitted for NCDs had a significantly shorter duration of admission than patients admitted for an infectious cause (Median 6.5 days vs. 9 days; p=0.037). These findings were similar to the findings of Long et al. (2016).

5.4 HIV COMORBIDITIES

Our study found the prevalence of hypertension in our sample to be 37%. The South Africa Demographic and Health Survey (SADHS) 2016 found hypertension to be 44% in males and 46% in females in the general population. Globally, 35% of PLWH on ART have hypertension (Fahme et al., 2018). Hypertension in Africa is a growing problem amongst the older population, and with the extended life expectancy because of ART, the prevalence of hypertension is expected to increase (Lloyd-Sherlock et al., 2014; Manne-Goehler et al., 2017). A large prospective study (n=77 696) of South Africans found that 22% of patients were hypertensive at the initiation of ART while a further 13% developed hypertension while on ART (Brennan et al., 2018). This study closely resembles our findings.

Chronic kidney disease (CKD) had a prevalence of 10.4% in our study population. South African CKD estimates range between 6% to 17% (Jardine & Davids, 2020). HIV associated CKD accounted for 27.6% of all causes of CKD in South Africa (Halle et al., 2019). Tenofovir, a backbone of first-line ART, is associated with a 1-2% prevalence of nephrotoxicity (Islam et al., 2012; Seo et al., 2020). Madala, Thusi, Assounga and Naicker (2014) conducted a study in Northern KwaZulu-Natal, 100km from GJGMRH in 2011, and found the prevalence of HIV in patients with CKD was 28.5%. Our study had a lower prevalence of CKD as compared to the study by Madala et al. (2014) because our study period was considerably shorter at 3 months as compared to 36 months.

Dyslipidaemia was present in 9.3% of patients admitted with HIV at GJGMRH. The prevalence of dyslipidemia in Africa is estimated between 13% to 70% (Husain et al., 2017). Dyslipidemia in PLWH is common in both ART naïve and treated patients in Southern Africa (Dave et al., 2016). South African estimates of dyslipidemia prevalence in PLWH is 32.2% (Husain et al., 2017).

HIV-infected persons in South Africa showed an increased risk of dysglycaemia prevalence (impaired fasting glucose, impaired glucose tolerance, or diabetes) (Levitt et al., 2016). African estimates for diabetes prevalence in PLWH ranges from 2.1% to 26.5% (Husain et al., 2017). A systematic review and meta-analysis by Prioreschi et al. (2017) showed an incidence of diabetes in PWLH of 17.4% in Africa. Diabetes in our study had a prevalence of 8.3% (n=24). The reason for the lower prevalence in our settings may be multifactorial.

5.5 REASON FOR LOWER PREVALENCE OF NCD IN STUDY POPULATION

Our study had a lower prevalence of NCDs as compared to national and international studies (Frigati, et al., 2015; Maimela et al., 2016; Miszkurka et al., 2012). This could be due to the reasons described below. In our study there was a fairly even distribution between males (n=137; 47.4%) and females (n=152; 52.6%). In large African and South African studies, females tend to be over-represented (Maimela et al., 2016; Meintjes et al., 2015; Miszkurka et al., 2012; Van Heerden et al., 2017). Females also tend to have higher levels of NCDs than males (Miszkurka et al., 2012). The fairly even spread of the gender in this study may have resulted in a low prevalence of NCDs. Females tend to have more postive health seeking behaviours than males; while men are more likely to present with severe illness compared to females (Edwards, 2016). Given that the study is hospital based, the even distribution may be attributed to these factors.

Patients with NCDs with lower socioeconomic status were associated with shorter life expectancies and more disabilities (Stringhini et al., 2018). Low socioeconomic status has been associated with an increase in NCDs (Allen et al., 2017; Hosseinpoor et al., 2012; Schneider, Bradshaw, Steyn, Norman & Laubscher, 2009; Stringhini et al., 2018).

The primary NCDs associated with low-income households were related to smoking and alcohol use as compared to high-income households that had predominantly diabetes and metabolic complications (Allen et al., 2017; Schneider et al., 2009). Schneider et al. (2009) concluded that within the South African context, lifestyle illness and NCDs are prevalent amongst the poor and the treatment for chronic disease is lacking. Our study is set in a peri-urban hospital that largely services a low socioeconomic community. The study design looked largely at the medically related illness (e.g hypertension, CKD, diabetes and dyslipidemia) amongst PLWH, and not specifically related to smoking and alcohol use. This information could not be obtained from the records that were assessed. The study also looked at the prevalence of NCDs in the PLWH population without access to private health care. This may again skew the true prevalence of NCDs in the HIV population in the drainage area of the hospital and not on NCDs in all patients admitted.

The prevalence of undiagnosed NCDs in South Africa is significant, especially for hypertension (Govindasamy et al., 2013; Rheeder et al., 2017). Internationally, approximately 50-62% of diabetes is undiagnosed in low- and middle-income countries (Pheiffer et al., 2018). During screening programs done as part of research studies, the prevalence of undiagnosed

hypertension in KwaZulu-Natal ranged from 32% to 58.1% and for diabetes it ranged from 0.8% to 9% (Govindasamy et al., 2013; Kushitor et al., 2021). Achwoka et al. (2019) assessed the prevalence of NCDs in sub-Saharan Africa at 11.5% in PWLH. The study, however, concluded that the NCD burden may be underestimated because of a reduction in health-seeking behaviour by PLWH. Kachimanga et al. (2017) showed that with a well-planned screening program for NCDs, there can be an increase in the number of patients diagnosed with NCDs. In their study, Kachimanga et al. (2017) showed a three-fold increase in the diagnosis of hypertension and diabetes by implementing a screening program at existing health facilities including HIV clinics. Kachimanga et al. (2017) and Achwoka et al. (2019) both emphasise the importance of properly structured screening programs for NCDs within existing HIV care and treatment centres. The KZN Department of Health is committed to screening for NCDs at all health facilities, but community screening is still lacking (KZN Provincial Health Summit, 2011). The low levels of screening in KZN may be the reason that index presentations to the hospital may be for a complication of an NCD, rather than the primary aetiology.

Healthcare workers and patients in developing countries have a disadvantage because of the lack of access to information (Pakenham-Walsh & Bukachi, 2009). This leads to a reduced understanding of the diagnosis and management of NCDs. A study in Uganda by Musoke et al. (2021) showed that healthcare workers had little knowledge on NCDs although more than half were responsible for NCD activities. The same study also found that patients confidence in healthcare workers treating NCDs were low and therefore rarely consulted them (Musoke et al., 2021). Locally, in the Western Cape, Onagbiye et al. (2020), found that healthcare workers with low educational levels had poor knowledge of NCDs risk factors. The lack of knowledge on NCDs diagnosis by HCWs may contribute to the lower levels of NCDs in the study population.

South Africa has a history of poor record-keeping and data collection (Mphatswe et al., 2012). In a study in KZN by Garrib et al. (2008), data collection was 2.5% incomplete and 25% was inaccurate. The inaccuracy of data collection could be responsible for the lower prevalence of NCDs in our study population (Haque et al., 2005).

There is under-utilization of health care facilities in South Africa due to low expectations for consistent and high-quality care. There is also a general mistrust in the medical system in South Africa (Ibanez-Gonzalez et al., 2014). Availability and affordability were other barriers to

healthcare utilization, especially amongst females (Department of Health & South African Medical Research Council, 2007). These factors may account for the lower levels of NCDs in our population due to patients not attending healthcare facilities.

5.6 IMMUNOLOGICAL AND VIROLOGICAL PROFILE OF HOSPITAL INPATIENTS WITH HIV

The CD4 cell count is a significant marker of the immunological health of a person's immune system. In PLWH, a CD4 cell count that is lower than 200 cells/mm^3 is associated with a higher incidence of opportunistic infections. This is highlighted in our study which showed a significant relationship between a low CD4 cell count and an infectious disease.

There is a paucity of studies on the relationship between CD4 cell count and NCDs. A Kenyan study by Achwoka et al. (2019) showed no relationship between CD4 cell counts and NCDs. A Brazilian study, however, did show that a low CD4 nadir (<100cells/mm^3) was associated with multimorbidity especially dyslipidaemia (Castilho et al., 2019). Our study has shown that patients with a CD4 cell count of more than 200 cells/mm^3 were more likely to be admitted with an NCD (n=87; 54% p<0.0001). This is a significant finding that shows the relationship between a failing immune system and infectious aetiology.

An HIV viral load is a measure of HIV genetic particles within a patient's blood. The aim of ART is to reduce the HIV viral load to undetectable levels. An undetectable viral load is a marker of therapeutic success. If a patient's viral load is still detectable while on ART, non-compliance or treatment failure are the main considerations. Study patients admitted with infectious diseases were more likely to have an unsuppressed viral load (n=108 vs n=78; p<0.0001) than patients with a suppressed viral load. Slightly over half of the patients with unsuppressed viral loads were diagnosed with tuberculosis (53.8%). Fenner et al. (2017) had similar findings in a South African study, which showed that ongoing viral load replication was an independent risk factor for the development of tuberculosis.

George, McGrath and Oni (2019) also showed no association between NCDs and an unsuppressed HIV viral load in their study in the Western Cape. In our study, however, we were able to show a significant relationship between NCDs and a suppressed viral load as compared to unsuppressed viral loads (n=66 (45.8) vs 37 (25.5%); p<0.0001). This could indicate future growth in NCDs as we achieve 90-90-90 targets.

International trends have shown a decline in the length of stay over the last 20 years due to widespread ART usage (Coelho, Ribeiro, Veloso, Grinzstejn & Luz, 2017; Falana et al., 2018; Shaaban & Martins, 2019). Long et al. (2016) assessed the length of stay (LOS) of HIV infected patients at a Johannesburg hospital. They found that patients with HIV infection had an average length of stay of 9.3 days as compared to 7.3 days for people without HIV infection. Our study showed that PLWH tended to have a longer length of stay if the CD4 cell count was lower (median 9 days) and were virologically unsuppressed (median 8 days).

5.7 WHO CLINICAL STAGING OF INPATIENTS ADMITTED TO GJGMRH

WHO clinical stage was a good predictor of the reason for admission. Patients who were clinically Stage 1 or 2, normally considered to be healthier, tended to be admitted for NCDs rather than infectious diseases (Stage 1: n=21 vs n=0; $p<0.0001$ and Stage 2: n=46 vs n=28; $p<0.0001$). Patients who were clinically Stage 3 and 4 were more likely to be admitted for infectious diseases than NCD, namely tuberculosis (Stage 3: n=94 vs n=30; $p<0.0001$ and Stage 4: n=64 vs n=6; $p<0.0001$). This indicates that clinical staging is a good marker to determine whether a patient has an NCD or infectious aetiology.

5.8 LIMITATIONS OF THE STUDY

The study only considered medical records for patients admitted within the period of three months due to time constraints (1st October to 31st December 2019). The study was self-funded and had no sponsorships. The seasonal variations encountered in hospital admissions will not be captured in this snapshot assessment because of the short duration of the study. The annual spike in influenza infection was not captured, which could have resulted in lower infectious disease admissions.

Twelve patients' records (4%) could not be retrieved and resulted in their exclusion from the study.

The study period was prior to the first South African COVID-19 case, thus minimising the effect of the pandemic on the study population.

The study relied on patient records that were made by different clinicians during the study period. This may of lead to inconsistencies in the reporting style, and may therefore, affect the outcomes of the study. These inconsistencies may be minimal due to all medical reports being reviewed by a senior physician before being placed in the patient's file.

CHAPTER 6. CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

This study aimed to highlight the prevalence and patterns of NCDs in patients living with HIV who are admitted to hospital. Hypertension, diabetes, dyslipidaemia, and chronic kidney disease were the most common NCDs. Our study confirms the high prevalence of NCD comorbidities in the HIV population that is virologically suppressed; albeit at a younger age than the general population. This points to the premature aging effect that HIV infection has, and that the future of HIV treatment programs should integrate NCD care in the HIV care package for treatment experienced patients in addition to ongoing adherence support and keeping ART patients engaged in care.

Infectious aetiologies, like tuberculosis, were more common in patients with a CD4 cell count of less than 200 cells/mm and/or patients who were virologically unsuppressed. A failure to achieve the 90-90-90 targets will perpetuate the ever-growing TB endemic in the country.

The study highlights severe challenges to the South African health system in meeting 90-90-90 targets. This hospital-based study showed poor uptake of testing in the communities (75.6%), poor linkage of care to health systems (76.7%) and poor adherence to therapy (65.8%) are the key factors that hamper achieving the 90-90-90 targets. These findings are mirrored by the poor performance of the district (72.1%, 82.7% and 91.5%) in achieving the 90-90-90 targets.

6.2 RECOMMENDATIONS

Health centres that treat PLWH need to adapt to screen and treat NCDs. South Africa can attempt to reach the WHO 25 x 25 goals of a 25% reduction in premature mortality from NCDs by 2025 with the use of existing resources (WHO, 2013).

NCDs is a growing problem in PLWH, irrespective if virological suppression is achieved. PLWH under the age of 40 years old were at-risk population for developing NCDs especially hypertension (n=32; 30.1%); chronic kidney disease (n=22; 21.4%); diabetes mellitus (n=11; 10.7%) and dyslipidaemia (n=6; 5.8%). Improved screening programs at health facilities and

community levels could prevent a new health crisis. An integrated health system with NCD and HIV treatment and screening could provide more holistic care for patients.

Economic and health burdens with regards to NCDs could be obviated by a two-pronged approach. In the short-term, low-cost screening for early detection of NCDs in whom early interventions effectively alter the natural history of the disease. The use of several low cost, high impact interventions for secondary prevention and clinical care are the key to the short-term plan. In the long-term, population-based prevention strategies are needed to prevent the acquisition or augmentation of NCDs in low-risk populations and reduction of risk in populations already affected by health transition.

Increased community testing, improving linkage to health care and addressing adherence will play a key role in this next phase of the HIV pandemic in order to reach the 90-90-90 targets.

According to the Adherence Guidelines published by the National Department of Health South Africa (2016), shortfalls to adherence were:

a) Lack of knowledge and understanding of disease and treatment
b) Perceptions of disease
c) Depression and anxiety
d) Behavioural factors
e) Treatment burden, treatment fatigue and adverse drug events
f) Socioeconomic and demographic factors
g) Poor social support
h) Poor health care provider skills and attitude
i) Organisational barriers like prolonged waiting time

The guidelines recommend universal, multiphase screening programs to improve linkage to care. This, however, does not translate into real-world screening programs due to the poor integration and compartmentalisation of care in primary health facilities. The knowledge between HCWs and patients need to be improved if adherence is to be improved. Specialised adherence councillors need to focus on integrating NCD and HIV counselling.

To address the future syndrome of HIV and NCDs within South Africa, an integrated chronic disease model is required (Knight, Schatz & Mukumbang, 2018). This model may be feasible within the South African primary health system if systemic challenges and change management are addressed during the implementation phase (Mahomed & Asmall, 2015).

The COVID pandemic has created a problem with adherence and the effects of which may still be in its infancy. The expected rise in advanced tuberculosis and delayed diagnosis of NCDs may contribute to increased hospitalisation in PLWH. The effects of COVID on the South African health system still need further evaluation.

A longer study focusing on mental health, smoking and effects of alcohol in addition to NCDs would provide more insight into the burden of NCDs within the PLWH population. A multicentre study would account for variations between rural, peri-urban and urban populations and the effects of HIV and NCD multimorbidity.

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APPENDICES

Appendix I: A breakdown of infectious disease admissions by organ system/aetiology

Study Number	
Hospital Number	

Demographics

Age	
Race	
Sex	

Date of admission	
Date of discharge	

Presenting problem	

Diagnosis	

Length of stay(days)		

HIV details

HIV status	Positive	1
	Negative	2
	Refused testing	3

CD4	
Viral load	

On ART	Yes	1
	No	2

Compliance	Yes	1
	No	2

WHO clinical staging	stage 1	1
	stage 2	2
	stage3	3
	stage 4	4

Tuberculosis

Previous TB	yes	1
	No	2

current TB	Yes	1
	No	2

Site of TB	Pulmonary	1
	Pleural TB	2
	Abdomen TB	3
	TB Meningitis	4
	Genitourinary TB	5

Hypertesions

Hypertension	Yes	1
	No	2

Number of Agents	One	1
	Two	2
	Three	3

Four	4
Five	5

Target organ damage	Yes	1
	No	2

Diabetes

Diabetes	Yes	1
	No	2

HbA1C	

Medication	Insulin	1
	Oral agents	2
	Both	3

Target organ damage	Yes	1
	No	2

Dyslipidemia

Dyslipidaemia	Yes	1
	No	2

Renal Failure

Renal failure	Yes	1
	No	2

Dialysis requiring	Yes	1
	No	2

Urea	
eGFR	

Patient on TDF	Yes	1
	No	2

CVS complications

Myocardial Infarction	Yes	1
	No	2

Stroke	Yes	1
	No	2

Malignancy

Malignancy	Hodgkins lymphoma	1	Lung ca	6
	Non Hodgkins lymphoma	2	Liver ca	7
	Karposi Sarcoma	3		
	Cervix Ca	4		
	Prostrate ca	5		

Appendix 2: GJGMRH permission to conduct study

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

GJGM REGIONAL HOSPITAL
Postal Address: Private Bag x10609, Stanger 4450

Tel: 0324376015 Fax. 0867567812
Email.gustavo.lopez@kznhealth.gov.za
www.kznhealth.gov.za

OFFICE OF THE SENIOR MANAGER: MEDICAL SERVICES

Enquiries: Dr. G. Lopez
EXT: 6015
DATE: /07/2021

Dr Yejna Narain
Medical Officer
Department of Internal Medicine
GJGMR Hospital

RE: PERMISSION TO CONDUCT RESEARCH AT STANGER HOSPITAL.

Dear Dr Y Narain;

I have pleasure in informing you that permission has been granted to you by Stanger Hospital to conduct research on: **PREVALENCE AND PATTERNS OF COMORBIDITIES IN ADULT HIV-RELATED ADMISSIONS IN A PUBLIC REGIONAL HOSPITAL IN KWAZULU NATAL**

Please note the following:

1. Please ensure that you adhere to all policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Please ensure this office is informed before you commence your research.
4. Stanger Hospital will not provide any resources for this research.
5. You will be expected to provide feedback on your findings to GJGMR Hospital.

Thanking you;

Senior Manager: Medical Services
Stanger Hospital

Appendix 3: Health Research Development Council Ethics Clearance letter

UNIVERSITY of the WESTERN CAPE

60 YEARS of hope, action & knowledge

11 December 2020

Dr Y Narain
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM20/10/11

Project Title: Prevalence and patterns of comorbidities in adult HIV-related admissions in a public regional hospital in KwaZulu Natal

Approval Period: 11 December 2020 – 11 December 2023

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

Permission to conduct the study must be submitted to BMREC for record-keeping.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

Director: Research Development
University of the Western Cape
Private Bag X 17
Bellville 7535
Republic of South Africa
Tel: +27 21 959 4111
Email: research-ethics@uwc.ac.za

NHREC Registration Number: BMREC-130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

Appendix 4: Health Research Committee KwaZulu-Natal

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
Email: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management

NHRD Ref: KZ_202106_006

Dear Dr Y. Narain
(University of the Western Cape)

Approval of research

1. The research proposal titled **'Prevalence and patterns of comorbidities in adult HIV-related admissions in a public regional hospital in KwaZulu Natal'** was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby **approved** for research to be undertaken at General Justice Gizenga Mpanza Hospital.

2. You are requested to take note of the following:
   a. *All research conducted in KwaZulu-Natal must comply with government regulations relating to Covid-19. These include but are not limited to: regulations concerning social distancing, the wearing of personal protective equipment, and limitations on meetings and social gatherings.*
   b. *Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.*
   c. *Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.*
   d. *Provide an interim progress report and final report (electronic and hard copies) when your research is complete to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za*
   e. *Please note that the Department of Health shall not be held liable for any injury that occurs as a result of this study.*

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee
Date: 21 July 2021

Fighting Disease, Fighting Poverty, Giving Hope