Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in City of Cape Town Primary Health Care facilities.

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A mini-thesis submitted in partial fulfilment of the requirements for the degree of Master in Public Health at the School of Public Health, University of the Western Cape

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KEY WORDS

HIV

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Co-morbidity

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Service integration

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HbA1c

Glycaemic control

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Non-communicable disease

ABSTRACT

Background: In the Eastern and Southern African regions, 16 million people living with HIV (PLHIV) are accessing treatment for HIV and are therefore linked to care. Many of these access points occur within vertical HIV care programmes. The challenge for health services at the primary level is integrating the care and treatment of conditions such as diabetes and hypertension within existing programmes to address the growing non-communicable disease epidemic in Sub–Saharan Africa.

Aim: The study aimed to determine the factors associated with glycaemic control in people living with HIV and Diabetes co-morbidity within integrated care models in the Khayelitsha sub-district.

Methods: A retrospective cohort analysis of people living with HIV and Diabetes was used in this study. Patient data were extracted from the Patient Electronic Health Management Information System (PREHMIS), paper-based records and data obtained from the Provincial Health Data Centre. Bivariate and multivariate analyses were conducted to determine factors associated with glycaemic control as defined by an HbA1c less than or equal to 8% as described by local guidelines applied in the sub-district. The data were analysed using SPSS Statistics version: 28.0.0.0 (190) software.

Results: In this study, females were 0.4 times as likely as males (crude OR = 0.4 [CI 0.19 – 0.84] $p = 0.01$) to obtain glycaemic control. This association remained statistically significant at the multivariate analysis level (aOR = 0.35 [0.14 – 0.85] $p = 0.02$). Patients not on insulin were 6.5 times as likely as those on insulin to obtain glycaemic control (crude OR = 6.5 [3.1 – 13.9] $p < 0.01$) and 8.6 times as likely after adjusting for other variables in the model (aOR = 8.6 [3.65 – 20.4] $p < 0.001$). The univariate associations, which were shown for the antiretroviral treatment regime and the duration of antiretroviral treatment with glycaemic control, did not persist in the multivariate analysis.

Conclusions: In this study, the integrated management of diabetes in the PLHIV population in primary care services revealed that 33.3% of HIV-positive patients on treatment for diabetes reached glycaemic control, below the target of 50% set by the National Department of Health. Females were less likely to achieve glycaemic control. The majority of patients in this study had insulin included in their treatment regime, yet people on insulin were less likely to obtain glycaemic control. This highlights the need for clinical services in primary

care to refocus staff training to combat clinical inertia and increase efforts in the areas of the education of patients, which will enable patients to become active managers in their healthcare.

DECLARATION:

I declare that *Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in City of Cape Town Primary Health Care facilities* is my work, has not been submitted for any degree or examination at any other university, and that all the sources I have used have been indicated and acknowledged in the references section.

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Signature

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ABBREVIATIONS AND ACRONYMS

3TC	Lamivudine
AC	Adherence Club
ART	Antiretroviral treatment
ATV	Atazanavir
AZT	Zidovudine
BMI	Body Mass Index
CDC	Centres of Disease Control
CIDRZ	Centre for Infectious Disease Research Zambia
CRP	C-Reactive Protein
D4T	Stavudine
DMOC	Differentiated Model of Care
DTG	Dolutegravir
EFV	Efavirenz
FPG	Fasting Plasma Glucose
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HIV	Human Immunodeficiency Virus
ICSM	Integrated Clinical Service Management
IDV	Indinavir
INSTI	Integrase inhibitor
ITS	Interrupted Time Series
LMIC	Low and Middle Income Country
LPV	Lopinavir

MCV	Mean Cell Volume
MSF	Medecins Sans Frontieres
NCD	Non-Communicable Disease
NFV	Nelfinavir
NHLS	National Health Laboratory Service
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
OGTT	Oral Glucose Tolerance Testing
OTMC	Omnibus Test of Model Co-efficiencies
PA	Physical activity
PG	Plasma glucose
PLHIV	People living with HIV
PREHMIS	Patient Record and Electronic Health Management Information System
RCT	Randomised Control Trial
RTV	Ritonavir
SANAS	South African National Accreditation System
SBP	Systolic Blood Pressure
SEMDSA	Society of Endocrinology, Metabolism and Diabetes South Africa
SQV	Saquinavir
TB	Tuberculosis
TDF	Tenofavir
WHO	World Health Organisation

CHAPTER 1: INTRODUCTION

1.1. Background

The global statistics for Human Immuno-deficiency Virus (HIV) show that 38.4 million [33.9 – 43.8 million] adults were living with HIV in 2021, and 76% of adults aged 15 years and older living with HIV had access to antiretroviral therapy (ART) (UNAIDS, 2022). As a result of the global response to the HIV–epidemic, AIDS-related deaths have reduced by 68% since 2004 (UNAIDS, 2022). This has resulted in an ageing HIV population with four times greater odds of having a comorbid condition compared to younger HIV-positive adults (Roomaney, Van Wyk & Pillay-Van Wyk, 2022). Other factors which increase the risk of the development of metabolic disorders within this population are factors related to the combination anti-retroviral treatment (ART). These factors include the older generation Protease inhibitors (PIs) (Samaras *et al.,* 2007) and Nucleoside reverse transcriptase inhibitors (NRTIs), which are associated with the development of lipodystrophy (Carr & Cooper, 2000) as well as obesity and the increase of weight after the initiation of ART (Sakar & Brown, 2019).

Obesity is one of the risk factors for numerous non-communicable diseases (NCDs), including diabetes. Rapid unplanned urbanization in low- and middle-income countries is associated with health inequity. The nutrition transition combined with lifestyle changes increases the risk of obesity and the development of NCDs (Smit *et al*., 2010). There is a shortage of epidemiologic studies on the relationship between diabetes and infectious disease in Sub-Saharan Africa (Tamuhla *et al*., 2021). Yet, uncontrolled diabetes in the HIV population increases the risk of developing Tuberculosis (TB) (Pillay, Aldous & Mahomed, 2016) and could fuel the TB epidemic in this region.

Within this population of co-infected individuals, different subgroups of patients with diabetes and HIV can be identified. Patients can present with a pre-existing history of diabetes and subsequently contract HIV, or patients are diagnosed with diabetes at the onset of HIV infection. Lastly, patients can develop hyperglycaemia after the start of ART. The management of diabetes in HIV-positive individuals in an integrated care setting requires that the clinician considers the cause and subsequent development of the disease, as the mechanism of metabolic dysregulation may vary. Patients with pre-existing diabetes at the time of HIV diagnosis may experience metabolic deterioration and the complication of drug-

drug interaction with oral anti-diabetic treatment and ART. Patients diagnosed with diabetes at the onset of ART or later may benefit more from an insulin-containing regime (Kalra *et al.*, 2011).

The estimated adult (15 to 49-year-old) HIV prevalence in South Africa is 20.4% (WHO, 2019), with 72% of all people living with HIV (PLHIV) on antiretroviral treatment (ART) (AVERT, 2022) and therefore linked to care. NCDs are overtaking Group 1 diseases (communicable diseases, maternal and child conditions and nutritional conditions) as the leading cause of mortality in South Africa (National Department of Health [NDOH], 2022). In South Africa, the leading cause of natural death from 2015 – 2017 was TB. During the same period, Diabetes Mellitus ranked second in this category (Department of Statistics South Africa, [Stats SA], 2017). This requires the health system to consider the management of multiple morbidities within a population already linked to care (Oni *et al*., 2015) to prevent losing the advances gained in life expectancy and quality of life at a population level as a result of the roll-out of ART.

The South African National development plan: Vision 2030 (Department of the Presidency, 2011) advocates for "Complete health systems reform" (Department of the Presidency, 2011: 298) and Integrated Clinical Service Management (ICSM) was identified as a key focus within the Ideal Clinic Realisation Model (NDOH, 2015). Another model which has proven the success of integrated care within the HIV population in the Western Cape is the success of the Prevention of Mother to Child Transmission (PMTCT) programme in decreasing the vertical transmission of HIV during the antenatal period to 0.3% (Western Cape Department of Health [WCDOH], 2020a). In 2018, 40% of TB patients were HIV positive, with 82% starting antiretroviral therapy before being diagnosed with TB and therefore linked to care (WCDOH, 2020a).

1.2. Research Problem

Longitudinal health data from the Khayelitsha Sub-district shows that HIV-positive patients had diabetes determined at a younger age (46 years compared to 53 years in the HIV-negative group, $p < 0.001$) (Tamuhla *et al*., 2021). In the same study, HIV-positive individuals had poorer glycaemic control over time than the HIV-negative group. This study also showed only 24.5% of the participants had glycated haemoglobin (HbA1c) less than 7% at baseline despite 85% of the cohort being on treatment for diabetes (Tamuhla *et al*., 2021).

ART programmes have introduced interventions to improve treatment outcomes of PLHIV. The vertical antiretroviral adherence clubs (AC) is a differentiated mode of care (DMOC) model and programmatically aims to assist in achieving the WHO "90-90-90" target. In the Cape Town health district in 2017, "…32 000 ART patients were in an AC" (Tsondai *et al*., 2017: 51). This study showed retention in care levels of 95.2% (95% CI, 91 – 96.4) at 12 months from enrolment (Tsondai *et al*., 2017), and 97.2% of patients had suppressed HIV viral loads (HIV viral loads less than 400 copies/ml) (Tsondai *et al*., 2017). Therefore, within this population already linked to care, if comorbid conditions are diagnosed, the patient is removed from the vertical ART AC (Tamuhla *et al*., 2021; Oni *et al*., 2015). The re-absorption and retention of stable patients in the facility will lead to increased patient load, causing clinic congestion which may have an adverse effect on adherence to clinic appointments and treatment.

City of Cape Town's Primary Care (City Health) facilities, situated in the Khayelitsha sub-district, provide integrated NCD and HIV care, defined as clinical care at a single service point (personal communication with Dr Kay Joseph, Senior Medical officer, Area East; 20 July 2021). In an attempt to decongest facilities with stable patients and to draw on the success of the vertical HIV ART adherence club model (Tsondai *et al.,* 2017), comorbid clubs have been introduced at two facilities in the Khayelitsha sub-district to service HIV-positive patients with co-morbidities. By removing the obstacle of fragmented clinical care, this study aims to determine the factors associated with reaching glycaemic control at the primary level.

1.3 Rationale

The integrated care of multiple morbidities in the HIV population requires the redesign of health services with policies on integrated care, strengthening the capacity and expansion of the healthcare workforce, adequate health information systems and a monitoring and evaluation platform to ensure that the 90/60/50 cascading targets for managing NCDs are met (NDOH, 2022). The study will contribute to the knowledge and understanding of the current treatment and management of diabetes in the HIV population where clinical care has been integrated. It also seeks to identify potential areas of advancing the healthcare of PLHIV and diabetes comorbidity.

1.4. Study Aim

The study aimed to determine glycaemic control and the factors associated with glycaemic control in patients with HIV and diabetes mellitus (DM) receiving integrated care in the Khayelitsha sub-district.

1.4.1. Study Objectives:

- To determine levels of glycaemic control in patients with HIV and DM who had been on treatment for at least 18 months by 31 December 2019.
- To determine the socio-demographic characteristics associated with glycaemic control in patients with HIV and DM.
- To determine the association between clinical measures, namely BMI and HIV viral load (V/L) suppression with glycaemic control in patients with HIV and DM.
- To determine the association between medical treatment factors of the diabetic treatment and the combination of ART with glycaemic control in patients with HIV and DM comorbidity

1.5. Outline of the Mini-thesis

Chapter 2 explores the literature on integrated care and factors associated with glycaemic control in people living with HIV.

Chapter 3 describes the methodology of the study.

Chapter 4 describes the results of the study.

Chapter 5 presents a brief discussion of the results of the study

Chapter 6 presents the conclusion and recommendations of the study.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

Integrated care is an approach to overcome fragmented care (Goodwin, 2016), but different definitions are used to describe integrated care depending on the differing professional points of view (Goodwin, 2016). This chapter will review the available literature on integrated care models and their effects on health outcomes in Low- and Middle-Income Countries. The diagnoses and management of diabetes in the HIV-positive population are influenced by multiple factors, which include medication and the presence of medical conditions which may cause bone marrow suppression (Society for Endocrinology, Metabolism and Diabetes of South Africa [SEMDSA], 2017) as well as context-specific socio-cultural factors that may add to the risk factors for developing diabetes (Okop *et al.,* 2016).

2.2 Defining integrated care

The following descriptions of the various interpretations of integrated care have been published in a perspective paper in the International Journal of Integrated Care (Goodwin, 2016). A health system-based definition describes services that are delivered in a manner where patients receive a "… continuum of health promotion, disease prevention, diagnosis, treatment, disease management, rehabilitation and palliative care services, coordinated across the different levels and sites of care…" (Goodwin, 2016; 1). Secondly, a managerial definition of integrated care is the maintenance of a coordinated service between independent stakeholders on a collaborative project. A social science-based definition of integrated care could entail the integration of a coherent methodology, which include the financial, administrative and clinical levels of patient care. Lastly, person-centred coordinated care is based on the patient's perspective of integration. In this definition, the patient plans their care with stakeholders who work together and therefore allows the patient to collate services to achieve their treatment outcomes (Goodwin, 2016). For this study, the goal is to enhance "…quality of care and quality of life, consumer satisfaction and system efficiency …" (Goodwin, 2016; 1), which is descriptive of the social science-based definition.

2.3. ART use and the utilisation of healthcare services for NCDs

The Health and Aging in Africa Longitudinal Study (HAALSI) cohort aimed to assess the relationship between ART use and the utilisation of healthcare services for hypertension and

diabetes. The study reported that age, body mass index (BMI) and systolic blood pressure (SBP) were lower among the HIV-positive patients than the HIV-negative patients (Manne-Goehler *et al*., 2017). Multivariate logistic regression models of diagnosis and preventative counselling for hypertension and diabetes showed greater odds of receiving a blood pressure (BP) measurement (adjusted odds ratio [aOR] 1.27, 95% CI 1.04 – 1.55), blood glucose measurement (aOR 1.26, 95% CI 1.05 – 1.51) or counselling regarding exercise (aOR 1.57, 95% CI 1.11 – 2.22) among the HIV-positive individuals on ART compared to HIV-negative individuals. Similar relationships were found between ART use and the awareness of a diabetes diagnosis or treatment of diabetes, but due to the lower prevalence of diabetes diagnosis in this study, these were not statistically significant. The study's outcomes suggest that ART programmes may provide a system to strengthen other health programmes for chronic care (Manne-Goehler *et al*., 2017).

2.3.1 Models of HIV integrated care

A literature review and key informant interviews on integrated NCD and HIV programmes in Low-income countries (LIC) identified three service delivery models. These models include 1) NCD services integrated into centres which originally provided HIV care, 2) HIV care integrated into primary health care already offering NCD services and (3) simultaneous introduction of integrated HIV and NCD services (Duffy *et al*., 2017). All models included clinical training, the development of clinical protocols and adapted medical records.

NCD services integrated into centres providing HIV care

The AMPATH study was set in nine primary health care clinics in Kenya, originally providing HIV care and treatment. NCD services for hypertension, diabetes, chronic respiratory diseases and cervical cancer screening were integrated. Analysis between 2010 and 2013 revealed improved blood pressure from 161/94 mmHg to 147/87 mmHg, and average blood glucose were reduced after six months (Edwards *et al*., 2015, as cited by Duffy *et al.*, 2017). In Uganda, NCD care, sexual and reproductive health services and cervical cancer screening were integrated at a single site that traditionally offered HIV care and treatment. Of the 10 285 HIV-positive participants, 10,5% were diagnosed with hypertension and 8% with diabetes (Mukasa *et al*., 2014, as cited by Duffy *et al*., 2017). Partners in Health in Malawi integrated the delivery of HIV, TB, hypertension, diabetes as well as malnutrition

in 13 integrated chronic care clinics. Analysis during 2014 – 2015 showed that 6781 patients were on ART and that 721 patients had NCDs (Wroe *et al*., 2015). The study found that the integrated approach reduced barriers to care for patients (Wroe *et al*., 2015).

HIV care integrated into Primary health care already offering NCD services

Medecins San Frontieres (MSF) in Kenya integrated HIV care in two existing primary care clinics. Services offered were HIV care, hypertension as well as diabetes care. Findings were that the rate of defaulting NCD-care decreased from 37% to 30% (Edwards *et al*., 2015, as cited by Duffy *et al*., 2017). Centre for Infectious Disease Research in Zambia (CIDRZ) analysed 12 primary health care sites between 2008 – 2011. In this study, HIV care and treatment were integrated into primary health care clinics providing general outpatient services. The integration of services led to increased efficiencies in the use of resources such as clinic space as well as staff time, and the study yielded an increase in HIV case finding and a decrease in HIV-associated stigma but resulted in an increase in patient waiting time (Topp *et al*., 2012).

Simultaneous introduction of HIV and NCD services

MSF Cambodia offered integrated care for HIV, hypertension and diabetes at two rural clinics between 2002 -2005 and found that of the patients who initiated ART, 87% remained in care after 24 months; the median CD4 showed an increase from 53 at baseline to 316 at 24 months, and in people with diabetes, 71% were alive after 24 months of treatment (Janssens *et al*., 2007). The review concluded that regardless of the integration model, experience from HIV care models can be used to adapt existing systems to provide care and treatment for the increasing population of PLHIV and NCDs (Duffy *et al.,* 2017).

2.4. Defining glycaemic control

The diagnostic criteria for diabetes, according to WHO, is based on a fasting venous or capillary plasma glucose value greater than or equal to 7.0 mmol/L; a 2-hour post-load venous plasma glucose of greater than or equal to 11.1 mmol/L or a 2-hour post-load capillary plasma glucose of greater than or equal to 12.2 mmol/L. In addition, a random plasma glucose greater than or equal to 11.1 mmol/L in the presence of symptoms suggests diabetes or an HbA1c of 6.5% is recommended as the cut-off point for diagnosing diabetes

(WHO, 2020). However, the HEARTS-D technical package states that HbA1c can be inaccurate in some conditions (WHO, 2020). The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA), 2017 guidelines state that the same diagnostic criteria apply for PLHIV and HIV-negative patients. However, it recognises that the use of HbA1c for diagnoses may be affected by multiple variables, including medication, the presence of anaemia, or conditions which may cause bone marrow suppression. The SEMDSA recommends a glucose tolerance test for diagnoses in the presence of HIV (SEMDSA, 2017).

In the monitoring of glycaemic control, HbA1c is advocated, as this measure provides an average measurement of plasma glucose over the preceding eight to twelve weeks (WHO, 2020). In the event that HbA1c is not available, a fasting plasma glucose (FPG) value can be used to assess glycaemic control. Most informative is a glucose profile with several pre- and post-prandial measurements taken throughout the day, which can be used to inform treatment decisions (WHO, 2020). The HEARTS-D technical package (WHO, 2020) recognises that an individualised approach is preferred but states that most patients can be expected to aim for 7.0%. This HbA1c target can be relaxed to less than 8% in people with advanced complications and low life expectancy. If an absent HbA1c, an FPG of less than or equal to 7.0 mmol/L and a post-prandial PG of less than or equal to 9.0 mmol/L can be used (WHO, 2020). The SEMDSA guideline recommends that caution is needed in interpreting HbA1c due to the number of factors specific to HIV which may influence the HbA1c value (SEMDSA, 2017). An HbA1c of 7.1% to 8.5% is quoted in the recommendations to be "… acceptable for the elderly, the frail, those with limited life expectancy, multiple co-morbidities…" (SEMDSA, 2017: S34).

2.4.1 Studies on monitoring tests of glycaemic control in HIV – infected patients.

A cross-sectional study looking into the correlation between fasting glucose, oral glucose tolerance testing (OGTT) and HbA1c to determine the prevalence of diabetes and pre-diabetes in a population of 220 HIV-positive individuals on ART (Coelho *et al*., 2018) revealed that no patients were diagnosed with HbA1c. The study found a 5.9% prevalence when OGTT was used, and 3.2% prevalence was obtained when fasting glucose was used. The results indicated that HbA1c underestimated the levels of glycaemia in this population. The authors argue that using OGTT may allow for an earlier diagnosis of disturbances in glucose haemostasis. In this study, the diagnosis of DM was defined as fasting glucose greater than or equal to 126 mg/dl [7.0 mmol/L], HbA1c greater than or equal to 6.5 % or 120

min plasma glucose greater than or equal to 200 mg/dl [11.1 mmol/L] during the OGTT (Coelho *et al.*, 2018).

Low haemoglobin (Hb) values and situations which shorten erythrocyte lifespan have been associated with lower HbA1c values (Diop *et al*., 2006 as cited by Coelho *et al.*, 2018). Haemolysis had a higher prevalence in HIV-infected patients (Diop *et al*., 2006 as cited by Coelho *et al.*, 2018), and an increased mean cell volume (MCV) is a marker which is indicative of a greater proportion of younger erythrocytes. These younger erythrocytes have a shorter time to become glycated (Coelho *et al.*, 2018). The relationship between MCV and HbA1c-fasting glucose discordance has been observed (Coelho *et al.*, 2018). The study concludes that using OGTT may provide an earlier diagnosis of disturbances in glucose haemostasis (Coelho *et al.*, 2018).

In the monitoring of HIV-infected patients with diabetes (Kim *et al*., 2014), HbA1c values were compared to finger-prick glucose averaged over three months. The study was a retrospective chart review of 65 patients with DM and HIV during a calendar year. HbA1c estimated actual average glucose within the established range in 54% of cases, underestimated average glucose in 19% of patients and overestimated average glucose in 27%. All patients in this study were on ART, with no statistical differences between the classes of ARVs for underestimation, overestimation or accurate estimation. The study's findings suggest that HbA1c should be complemented with accurate finger-prick reporting in this patient population (Kim *et al.*, 2014).

2.5. Management of diabetes co-morbidity in Low- and Middle-income Countries (LMIC)

In a review article on the double burden of diabetes and global infection in LMICs, it was stated that 4 out of 5 people with diabetes live in LMICs (Dunachie & Chamnan, 2018). A systematic review and meta-analysis into the effects of integrated models of care for diabetes and hypertension in LMIC countries by Rohwer *et al*. (Rohwer *et al.*, 2021) included two interrupted time series studies (ITS) and three randomized control trials (RCTs). Three of these studies were from South Africa, one from Uganda/Kenya and one from India. The study included participants with diabetes and/or hypertension and other diseases. Grading of Recommendations, Assessment, Development and Evaluation (GRADE) were given for the outcomes of mortality, disease-specific morbidity, quality of life, HbA1c, systolic blood

pressure (SBP), cholesterol levels and access to care (Rohwer *et al.*, 2021). The size of the effect, as well as the certainty of the evidence, was taken into consideration. In disease-specific morbidity of HIV and NCD control with integrated care compared to usual care, 1 RCT (with very low certainty evidence) found that integrated care may result in a small increase in the number of PLHIV who achieve both viral suppression and NCD control with a prevalent NCD at follow-up (RR 1.24 [95% CI:1.1 – 1.4]). In access to care, one ITS reported no change in the trend found from pre-intervention to post-intervention for new diabetics on treatment at population-level, nor was there any change at clinic level for new diabetics on treatment. On HbA1c, the study found that "The mean change in HbA1c with integrated care was 0.11% higher (95% [CI:0.2 lower – 0.42 higher])" (Rohwer *et al.*, 2021: 14) and concluded that integrated care might have little or no effect on HbA1c (Rohwer *et al.*, 2021). A cohort study into the integrated care of HIV, hypertension and diabetes was conducted in Dar es Salaam and Kampala (Birungi *et al.*, 2021), with the primary outcome of retention in care and HIV plasma viral load. The study with 2273 patients enrolled in integrated care had 832 HIV-positive participants, 546 with hypertension, 313 with diabetes and 582 patients had multiple co-morbidities. The study found that eighty-two percent of the participants with HIV infection (82.5% [95% CI: 79.9% – 85.1%]) were retained in care; eighty-five percent (85.0% [95% CI: 81.1% - 89.0%] of diabetics were retained in care; approximately seventy-nine percent (78.8% [95% CI: 75.4%- 82.3%]) of hypertensive patients were retained in care, and approximately ninety-one percent (90.9% [95% CI: 88.6 – 93.3%]) of patients with multiple morbidities remained in care (Birungi *et al.*, 2021). The outcome for viral load less than 100 copies /mL was 88.5%. Although high rates of retention and viral suppression were achieved in this study, 67.1% of patients with diabetes co-morbidity had an HbA1c greater than 6.5% at the end of the study (Birungi et al., 2021).

A retrospective chart review of patients attending a diabetic clinic at a district-level hospital in KwaZulu-Natal included 653 first-patient visits, of which 22.82% self–reported that they were HIV-infected (Pillay, Aldous & Mahomed, 2016). Most of the HIV-infected patients (89.36%) were on ART. The HIV-infected patients ranged between 41 and 60 years, whereas the HIV-un-infected cohort's ages ranged between 51 – 70 years, and 67.76% of the HIV-infected patients were female. The mean HbA1c for the HIV-infected cohort was higher at 11.08% vs 10.14% ($p = 0.044$) compared to the HIV-uninfected cohort, with 85.23% of the HIV-infected patients displaying sub-optimal glycaemic control as defined by HbA1c less than or equal to 7%. The majority (55.91%) of the HIV-infected cohort had a BMI greater

than or equal to 30kg/m². Statistically significant differences were also found for nephropathy defined by proteinuria (25.66% vs 14.43%) and neuropathy (48.68% vs 42.10%) between the HIV-infected and HIV-uninfected patients. Insulin mono-therapy vs combination of insulin and oral anti-diabetic treatment showed no statistical significance on the mean HbA1c obtained in the HIV-infected cohort (Pillay, Aldous & Mohamed, 2016).

A study into the routinely collected health data of a virtual cohort of diabetics linked to care in the Khayelitsha Sub-district (Tamuhla *et al*., 2021) showed that 18 % of the total study population of 13 771 were HIV positive. The study found that 84.3 % of this population ever started diabetes treatment, with 16.7% recoding the last HbA1c less than 7 %. The study states that all HIV-positive individuals were on ART and that the chronic medication (ART) and natural course of disease progression may be a contributing factor to chronic hyperglycaemia, but the poor integration of services for HIV and DM at the primary level may lead to poor adherence as a result of multiple clinic visits required (Tamuhla *et al*., 2021).

2.5.1. Group-based care for HIV and co-morbid conditions

The outcomes of PLHIV and NCD multi-morbidity attending integrated care clubs in Cape Town were studied in a retrospective cohort analysis which recorded variables for optimal disease control at three time points, i.e. 12 months prior to club enrolment, at the point of club enrolment, and 12 months post club enrolment (Gausi *et al.,* 2021). A total of 247 patients were enrolled, of which 221 (89.5%) had hypertension, 4 (1.6%) had diabetes, and 22 (8.9%) had both hypertension and diabetes. HIV viral suppression rates (defined as having a viral load less than 1000 copies/ml) were 98.6% at 12 months prior to club enrolment, 99.5% at the time of enrolment and 99.4% at 12 months after club enrolment. Optimal blood pressure control (defined as BP less than 140/90) was achieved in 58.9% of the cohort at the point of enrolment and decreased to 49.4% at 12 months after enrolment. Similarly, optimal glycaemic control (defined as HbA1c less than 7.5%) was recorded in 87.5% of diabetics at the point of enrolment but decreased to 53.3% at 12 months after enrolment into the integrated clubs. In this study, retention in care was high, with only 6.9% lost to follow-up at 12 months, and viral suppression rates were high. However, the optimal control of the NCD had declined despite the adherence levels being 92.2% before club enrolment and 94.2% after club enrolment (Gausi *et al.,* 2021).

2.6. Antiretroviral therapy and glycaemic control

2.6.1. Hyperglycaemia in treatment-naive patients

Hyperglycaemia has been described in an Ethiopian cohort of ART-naïve HIV-positive patients (Faurholt-Jepsen *et al.*, 2019). A cross-sectional study of adult HIV-positive ART naïve patients showed that 16.0 % had impaired fasting glucose, 18.7% had impaired glucose tolerance, and 7.6% had diabetes. Counter-intuitively, the traditional risk factors for diabetes, like advanced age, anthropometry and increased waist circumference, were associated with lower 2-hour plasma glucose. Less than three percent (2.7%) of the study population had a BMI greater than 25 kg/m². In this study, opportunistic infections were not associated with HbA1C. A non-HIV-infected reference group was age and sex-matched to the last 100 recruited patients in order to compare and establish the prevalence of diabetes among HIV-negative patients from the same area. Within the HIV-negative group (n=100), diabetes was diagnosed in 2% using HbA1c and 0% using fasting plasma glucose. Insulin in serum was measured using a commercial ELISA kit, and C-reactive protein (CRP) was measured in serum. The authors concluded that HIV infection and malnutrition lead to low insulin production and insulin deficiency in that inflammation, measured by elevated CRP, was associated with reduced insulin secretion. The authors, therefore, argue that HIV is a potential inducer of insulin deficiency (Faurholt-Jepsen *et al.*, 2019).

2.6.2. ART-associated hyperglycaemia

A cross-sectional comparative study into ART-associated hyperglycaemia and dyslipidaemia in HIV-infected patients in Ethiopia revealed that the prevalence of hyperglycaemia was 7.9% in patients on ART compared to 5.6% in non-ART groups (Abebe *et al.*, 2014). In this study, it was found that ART initiation was not associated with increased serum glucose levels ($p = 0.45$). However, the ART group showed a higher mean glucose level than the non-ART group ($p = 0.019$). Within this cohort, first-line ART contained two nucleoside reverse transcriptase inhibitors (NRTIs) such as [Zidovudine (AZT), /Stavudine (D4T), Lamivudine (3TC) or Tenofavir (TDF)] with a non-nucleoside reverse transcriptase inhibitor (NNRTI) [either Nevirapine (NVP) or Efavirenz (EFV)]. Furthermore, 10.3% of the subjects were on ART for more than 45 months; 33.3% were on ART for 25-44 months, 34.1% were on ART for 13-24 months, and 22.2% on ART for 6-12 months (Abebe *et al.*, 2014).

A case study on a 30-year-old Chinese male showed that the patient developed diabetes

mellitus while on ART and with the subsequent discontinuation of Zidovudine (AZT), his hyperglycaemia improved to a point where diabetes medication was no longer required (Iwata & Ogawa, 2017).

Protease Inhibitors (PI) have different metabolic effects (Kalra *et al.*, 2011). Lopinavir (LPV) & Ritonavir (RTV) increase levels of fasting triglycerides and free fatty acids but do not affect insulin sensitivity, whereas Indinavir (IDV) & RTV induces insulin resistance but has no effect on lipid metabolism. IDV & RTV blocks GLUT-4-mediated glucose transport, but Atazanavir (ATV) and Amprenavir do not have this effect. Patients on treatment with Nelfinavir (NFV), IDV, LPV or Saquinavir (SQV) for more than 12 weeks showed changes to first-phase insulin release with a 25% reduction in ß-cell function (Kalra *et al.*, 2011).

The second generation integrase inhibitors (INSTIs), like Dolutegravir, are currently preferred in ART regimes due to their low toxicity, tolerability and high genetic barrier to virological resistance. The mechanism of action of INSTIs is believed to be that of chelating magnesium, which may lead to disorders of glucose metabolism. Magnesium serves as a co-factor in post-receptor insulin action (Hailu, Tesfaye, & Tadesse, 2021).

A case series on new-onset Diabetes Mellitus after Dolutegravir (DTG)–based ART use showed 3 cases of severe hyperglycaemia (plasma glucose level greater than 250 mg/dl [13.89 mmol/L] with or without ketonuria after 1-12 months of DTG-based ART regimes (Hailu, Tesfaye, & Tadesse, 2021). The SAILING, SPRING 2, SINGLE and VIKING 3 clinical trials recognized severe hyperglycaemia with or without life-threatening acute complications after INSTI use (Hailu, Tesfaye & Tadesse, 2021).

2.7. Socio-cultural factors influencing risk factors for diabetes

A descriptive qualitative study with 78 participants aged between 35 and 70 years from an urban African township in the Cape Town Metropolitan was conducted by Okop *et al*., in 2016, which showed the impact of cultural perceptions about body size and the "belief that overweight is 'normal' and not a disease…." (Okop *et al.,* 2016:1). Another qualitative study exploring the perceptions of acceptable body size of women and children by Mvo *et al*., (Mvo, Dick & Steyn, 1999), showed that the perception of being overweight has many positive associations in the African community in South Africa. The research was informed by in-depth interviews with ten overweight African residents of Khayelitsha and identified that being overweight and obese is perceived as a reflection of a husband's ability to care for

his family. Obesity is viewed as an indication that the person is healthy and without HIV/AIDS, TB or cancer. A thin individual is considered to be a person who is experiencing physical or emotional stress (Okop *et al.*, 2016). The perceptions around a bigger body size as a sign of happiness and wealth starts in adolescence and was reported in a qualitative study in black girls aged 10 -18 years in Cape Town (Puoane, Tsolekile & Steyn, 2010). These studies (Okop *et al.*, 2016; Puoane, Tsolekile & Steyn, 2010 & Mvo, Dick & Steyn, 1999) indicate that the cultural perceptions of obesity could present a challenge to interventions aimed at addressing obesity.

2.8. Individual factors which influence glycaemic control in people living with HIV and diabetes

Downstream factors which affect glycaemic control include biological and behavioural factors. A study into the association between family history and diabetes within the context of HIV was conducted in a specialised diabetes clinic in an HIV endemic area in Kwa-Zulu-Natal, South Africa (Chetty & Pillay, 2021). The retrospective cohort study utilised data from 957 diabetic patients. Within this cohort, 146 (15.3%) were HIV-infected, with 84 (57.5%) on a fixed-dose combination (FDC) ART. The study found that HIV-infected diabetics on an FDC with a positive family history of diabetes had higher HbA1c levels than those without a positive family history of diabetes (HbA1c of 9.52% vs 8.52%). In addition, a positive maternal family history of diabetes on an FDC showed increased HbA1c levels (HbA1c of 9.81% vs 8.55%, $p = 0.009$) (Chetty & Pillay, 2021).

A systematic review into the factors which determine dietary and physical activity behaviours in women of reproductive age in urban Sub-Saharan Africa (Yiga *et al.*, 2020) identified 9853 studies, of which 93 studies were selected for full-text review. From these 23 articles (13 investigated dietary behaviour & 10 investigated physical activity with 3 which investigated both dietary behaviour & physical activity) were included in the analysis. The study concluded that the notable factors which determined dietary behaviour included convenience, available finances, current food skills and knowledge gaps, as well as work environments in which it is difficult to buy good quality fresh food. In addition, the rapid changing of the transport environment influences physical activity. Intra-individual level factors which influenced physical activity (PA) include the lack of knowledge of the benefits

of physical activity, barriers such as lack of time and financial constraints and attitudes towards physical activity (Yiga *et al.,* 2020).

2.9. Summary of the Literature Review

ART programmes have innovative systems which include decentralized care, peer-counselling, community engagement, support for patients on treatment to improve adherence and task-shifting, which could be leveraged for the development of chronic NCD services (Adeyemi *et al.,* 2021). The potential benefits of service integration include the reduction of fragmented services with increased efficiency in resource usage and an increase in the number of patients remaining in care by reducing the cost and inconvenience for patients with multiple-morbidities (Adeyemi *et al.,* 2021). The disadvantages include increased workload for HIV-NCD staff, and therefore without adequate resourcing, integration of HIV-NCD services has the potential risk of reducing the quality of existing HIV services. The evidence on the effectiveness of integrating NCD and HIV services in LMIC is limited (Adeyemi *et al.,* 2021). Other upstream factors which place this study population at high risk are rapid urbanisation with the resultant poor planning of the build environment with decreased opportunity for exercise. Intermediate factors include the socio-cultural beliefs of obesity and being overweight. Individual risk factors for the development of most NCDs are high body mass index (BMI), lack of physical activity, poor dietary intake, aging, stress genetics and a family history of Diabetes Mellitus.

CHAPTER 3: METHODOLOGY

3.1. Introduction

This section describes the methodology of the study. It contains a description of the study setting, the study design, the study population, sampling procedures, data collection and analysis. The validity, reliability and generalizability of the study are described.

3.2 Description of the study setting

Khayelitsha is an informal settlement with a total population of 391 749 (Department of Statistics, South Africa [Stats SA], 2011), with 28.2% of the population younger than 14 years old and 70.2 % of the population between the ages of 15-64 years old. Approximately 34.6% of households have piped water inside their dwellings; 80.8% have electricity for lighting; 71.7% of households have flush toilets connected to a municipal sewerage line; and 80.9% of homes are serviced by weekly refuse removal (Stats SA, 2011). Antenatal HIV prevalence in the Cape Metro increased from 20.9% in 2017 to 22.0% in 2019 (Woldesenbert *et al*., 2021).

Primary Health Care in the Khayelitsha Sub-district is delivered via a district health system in partnership with the Western Cape's Provincial Department of Health via a Service Level Agreement (SLA) with the Cape Town Municipality's Community Services and Health Directorate: City Health Department (Community Services and Health Directorate City Health Department, 2020). The National Health Act, No.61 of 2003, assigns the responsibility of provision of Personal Primary Health Care Services to the Provincial Health Department, but Schedule 4A of the constitution allows for services to be allocated to the local government via a mutual agreement. In pursuing the vision of building a "Healthy City for All", the city delivers Comprehensive Primary Health Care services, including promotive and preventative health care to women, men and children (reproductive health, immunisation and well-baby clinics), treatment of sick children; HIV/AIDS, STI and TB programmes and limited adult curative and chronic care (Community Services and Health Directorate City Health Department, 2020).

The National Department of Health has introduced the "Ideal Clinic" realisation model (NDOH, 2015), which classifies clinics into "small", "medium", or "large" facilities based on the demographic profile, the disease burden of the facilities' drainage area and the social

determinants of health in the area. These factors are considered when determining the service package rendered as a healthcare facility (Community Services and Health Directorate City Health Department, 2020).

Table 1: Facility categorisation

Category	PPHC Services	Satellite	Pharmacy Services	HR requirement
TYPE A	All, including outreaches; No NCDs	Some	Medicine room; Pre-packed medication parcel (PMP) collection at some facilities	PN/ CNP Clinical Medical Officer (CMO) Support for Tuberculosis(TB) services
TYPE B	All, including outreaches; No NCDs	Some	Registered dispensary; PMP collection at some facilities	PN/ CNP Clinical Medical Officer (CMO) Support for Tuberculosis(TB) services Post Basic Pharmacy Assistant (PBPA)
TYPE C	All services and outreaches, including limited NCD care only to ART/TB clients	Yes	Registered dispensary; PMP collection at some facilities	PN/CNP PBPA CMO support/ sessional
TYPE D	All services and outreaches, including NCD care to all patients, limited to Essential Medicines List	Yes	Registered dispensary; PMP collection	PN/CNP PBPA CMO support/ sessional
Community Day Clinic CDC	All services and outreaches, including all NCD care to all clients	No	Licensed and registered pharmacy; PMP collection at selected clinics	PN/ CNP PBPA CMO RP

(Table adapted from Coetzee, 2021).

The Khayelitsha Sub-district has ten facilities, with four facilities classified as Community Day Centres (CDCs) and six facilities classified as “clinics”.

Of these, patients from 5 facilities were identified as receiving integrated HIV and NCD care during the timeframe identified by this study.

At the time of data collection, one facility was closing down due to a decision by City Health Management. Patients, as well as patient-related information, were transferred out to various facilities, which included provincial health services. These patients were therefore excluded from the sample (i.e. nine folders).

3.3 Study design

The study is a quantitative retrospective review of patient data retrieved from paper-based patient records of people living with HIV and diabetes at the City Health Primary Care facilities and from electronic medical records from the Provincial health data Centre. The study design allows for the collection of various outcomes as well as baseline or exposure variables (Beaglehole, Bonita & Kjellstrom, 1997). In this study, the odds of glycaemic control within integrated care settings will be the primary outcome. The retrospective study design was suitable as routine data was available from electronic patient monitoring systems, and patient records were easily accessible, which reduced the financial as well as human resources required (Ehrlich & Joubert, 2014).

3.4. Study population and sampling

3.4.1. Study population

The study population was people with HIV and diabetes enrolled in integrated care models in Primary Health Care services at the City Health facilities in the Khayelitsha Sub-district in the Western Cape. The information required for the study was available from patient records at the facility and electronic information systems.

3.4.2. Sampling

The electronic database of patients (PREHMIS) was used to identify study participants who had both an ART regime provided and a diabetes visit data element captured between October 2019 and December 2019. This sampling timeframe was chosen due to the multi-month dispensing of chronic medication in this patient category. The sample size of 110 was calculated by Epi-Info StatCalc for cohort studies with the assumptions of a 28% outcome of glycaemic control (Monanabela, Van Huyssteen & Coetzee, 2019), a power of 80% and a confidence level of 95%. Sub-district data from PREHMIS yielded 302 patients with HIV and DM enrolled in an integrated care model. As a result of the service de-escalation at the primary level which was brought about by the Covid-19 pandemic in 2020 (City Health, 2020), the sampling was done in 2019. Whole population sampling was conducted to account for exclusions as per the following criteria:

3.4.2.1 Inclusion criteria

- Adults on treatment for diabetes for at least 18 months by 31 December 2019
- Adults on ART for at least 18 months by 31 December 2019
- At least one documented HbA1c in the last 12 months
- Aged 18 or older on 1 July 2018.
- Receiving care for both HIV and DM in an integrated care model for at least 18 months by 31 December 2019.

3.4.2.2. Exclusion criteria

- PLHIV with gestational diabetes
- Individuals transferred in from other sub-districts within 18 months.
- Individuals transferred out to another facility by 1 July 2018.

The local guidelines prescribe annual HbA1c testing once HbA1c less than or equal to 8% is achieved with more frequent monitoring if HbA1c is found to be above 8% (Knowledge Translation Unit [KTU], 2020). Recruiting adults who have been on treatment for diabetes for at least 18 months will ensure that they have at least one recorded HbA1c result.

3.5 Data Collection

The primary source of data was paper-based patient records. In cases where blood results were missing from patient folders, these were obtained via a secondary data set which was

provided by the Provincial Health Data Centre (PHDC). The PHDC collates data from other health information systems like PREHMIS and the National Health Laboratory System (NHLS) via a unique patient identifier (WCDOH, 2020a). Data were extracted from the sources indicated in Table 1.

Table 2: Source of data

Variable	**Source**
Gender	Paper-based patient records
Age	Paper-based patient records
Body Mass Index (BMI)	Paper-based patient records
Current ARV Regime	Paper-based patient records
Duration in years on current ARV regime	Paper-based patient records
Viral load results	Paper-based records/ PHDC data set
Current Diabetes medication	Paper-based patient records
Treatment Duration for diabetes	Paper-based patient records
Last recorded HbA1c	Paper-based records/PHDC data set
Mode of care and the duration of mode of care	Paper-based Patient records

Extracted data were de-identified and captured on a password-protected Excel spreadsheet (see Appendix1), which will be stored for five years.

Age was collected as numerical data and re-classified as categorical data of age groups 18-39 years old; 40-49 years old; 50-59 years old; 60-69 years old; 70-79 years old; greater than 80 years old.

BMI was re-classified as categorical data of less than18.5 kg/m² as underweight; 18.5- 24.9 kg/m² as normal; 25.0 – 29.9 kg/m² as overweight and greater than 30 kg/m² as obese (WHO, 2021).

HIV Viral load was collected as numerical data and was re-classified as categorical data of VL less than 400 copies/ml as VL suppressed and VL greater than or equal to 400 copies/ml.

The current diabetes treatment regime in this study is defined by insulin included or insulin not included. This study does not distinguish between the type of insulin (basal or biphasic insulin), nor does it distinguish between the type of oral anti-glycaemic agents.
Diabetes medication was classified as categorical data as follows: insulin included in the regime and no insulin included in the regime.

ARV regime was classified as categorical data as follows: NRTI based further stratified as TDF/FTC, ABC/3TC or AZT/3TC; PI-based or Integrase inhibitor-based regime.

Duration on the current ARV regime was classified as categorical data of 0-2 years, 3-5 years, 6 – 10 years and greater than 10 years.

Mode of care was classified as categorical data as follows: Individualised, integrated care or group-based integrated care as of 31 December 2019. Duration enrolled in the mode of care was recorded in months. (See Appendix 2)

3.6. Data analysis

Data were analysed using IBM SPSS Statistics version: 28.0.0.0 (190) software. The study describes the levels of glycaemic control in the population of PLHIV and diabetes comorbidity. It further determines the association between glycaemic control and other variables, namely: 1) socio-demographic characteristics of this population, 2) ART therapy, 3) HIV viral load and 4) diabetes treatment.

Frequency tables were run to verify the adequacy of available data on the variables of interest. Data for certain variables (such as BMI and mode of care) had too much missing data as clinicians had poorly recorded BMI. The reasons for the removal of patients from the group-based integrated mode of care and for the missing BMI data were not included as part of this study.

To describe the study population, descriptive frequency tables were created for categorical variables indicating the number of participants in the various categories as well as the proportions (the percentage is presented in one decimal place).

Age as a continuous variable was presented and further stratified by gender. Means, medians and inter-quartile ranges were presented to one decimal place, while the standard deviation was presented to three decimal places.

The outcome variable (dependent variable) of HbA1c was stratified as a dichotomous

variable with HbA1c less than or equal to 8 % and HbA1c greater than 8% in quarter 4 (October to December of 2019).

To determine the statistical significance of predictors of glycaemic control, chi-square tests and binary logistic regression analysis were conducted between categorical independent variables and the dependent variable with the *p*-value set at 0.05, and for odds ratios, a 95% confidence interval was provided (odds ratios and 95 % confidence intervals are reported to 2 decimal places).

To determine the "goodness of fit" the Omnibus test of model coefficients (OTMC) was used to determine significance, and the chi-square value for the model was 44.388 on 7 degrees of freedom and a *p*-value less than 0.001.

3.7. Validity and Reliability

3.7.1 Validity

Clear definitions of inclusion criteria were set to ensure the study's validity. Variables were known before data collection. The variables were described as follows:

- Viral load was measured by the National Health Laboratory System (NHLS) in copies per ml (copies/ml). The programmatic definition of viral load suppression at the time of the study was defined as a viral load of less than 400 copies/ml (Western Cape Department of Health, 2018a). In this study, viral load suppression was measured in the preceding 12 months.
- HbAlc was measured by the National Health Laboratory System (NHLS) in percentage (%). The target for glycaemic control in the Western Cape Province is less than or equal to 8% (KTU, 2020). In this study, HbA1c was measured in the preceding 12 months.
- Age at the last birthday was measured in years.
- Body Mass Index as measured by the formula: $\frac{weight\ (kg)}{height\ (m)^2}$.
- Integrated care: The integration of clinical care for both HIV as well as Diabetes Mellitus at one service point

This ensured that the comparison was valid using data from paper-based records and information systems for blood monitoring results via secondary data sources. Missing data were cross-checked with data from the PHDC, and this was indicated on the Excel datasheet. Analysis was conducted based on the totals with complete records.

3.7.2. Reliability

One person collected all data in the same manner for the study.

Selection bias was averted by enrolling all adults in the sample who met the inclusion criteria.

Measurement error was minimised as blood results from the NHLS were extracted from the paper-based records and secondary data set from PHDC. NHLS laboratories are accredited by the SA National Accreditation System (SANAS) for compliance with international standards.

BMI measurement may have been influenced by inter-observer variation as different measuring instruments for height and weight were used between facilities. These measures were taken directly from folder reviews, and no observer bias was expected.

Researcher Bias: Folder numbers were changed to study participant numbers; therefore, patient details were anonymised to ensure the distance between the researcher and the participants was maintained during the analysis. This ensured objectivity and reduced bias.

Participant error and participant bias: the retrospective study design ensured the distance between the participant and the researcher.

3.8. Generalisability

The adults in this study are presumed to be representative of adults across the sub-district. Thus, the findings can be generalisable within models of integrated clinical care in the sub-district and other high-burden areas within the province with similar epidemic patterns and incidences of NCD among PLHIV. However, the study may not be generalisable to adults with HIV in other regions of the country with different prevalences of Diabetes Mellitus and participants living in various social, cultural and economic environments and settings that use another measure of HbA1c for glycaemic control.

3.9. Ethics Consideration

Ethics approval for conducting this research was obtained from the University of Western Cape's Biomedical Ethics and Research Committee. Further approval to conduct research at health facilities and data was obtained from the City of Cape Town's Community Services and Health Department. Secondary data from the Provincial Health Research Committee was required to access missing data from the patient folders. No harm was expected in the course of the research as the study was non-experimental and was in the form of a record review

rather than engagement with patients. The dataset from the PHDC is a secondary data source, and care was taken to match anonymised data by using unique study numbers instead of patient names during analysis. The allocation of a unique study number ensured that study participants were not re-identifiable following the outcome of the analysis. No information or consent forms were required. The study did not directly benefit patients from whom data were collected. However, the study's findings may be used to recommend future models of integrated care and service delivery to people living with HIV.

The selection of patients was fair in that the criteria were based on the medical conditions of interest in the study. Ethnicity and race were not considered in the selection of participants.

3.10. Conflict of interest

I am currently employed as the Senior Medical Officer: Area North in the City Health Department. Area North includes the Western and the Northern Sub-districts where integrated care has been implemented. I am directly involved in delivering care to patients in an integrated setting. However, the study was conducted in the Khayelitsha Sub-district and did not pose a conflict of interest. Data was drawn from patient records and health information systems, which ensured distance between the researcher and the study participants.

CHAPTER 4: RESULTS

4.1 Introduction

This chapter will report on the results of the study. It will outline the realisation of the study sample, the description of the study sample, the clinical characteristics as well as the duration of treatment of both ART and diabetes treatment. The bivariate and multivariate analysis to determine factors associated with glycaemic control as defined by HbA1c less than or equal to 8 % will be presented.

4.2 Realisation of sample

In total, 302 PLHIV with a diabetes visit were identified via the PREHMIS system. These patients were identified across six facilities in the Khayelitsha Sub-district.

Table 3: Number of patients records identified per facility

Name of Facility	**Number of patient files**
Facility 1	9
Facility 2	114
Facility 3	5
Facility 4	38
Facility 5	106
Facility 6	30
Total	**302**

Of the 302 folders identified initially for inclusion in the study, 51 folders could not be found at the respective facilities. As a result, 251 folders were reviewed. Of the 251 folders, 58 patients were excluded because they were not on both ART and DM-treatment for 18 months by 31 December 2019 and did not meet the inclusion criteria.

Diagnostic information from 20 patients was incorrectly captured as the folder review revealed no evidence of a diabetes diagnosis recorded in the folder, and one patient was a

known diabetic with no evidence of HIV recorded in the folder.

Five patients had HIV and DM co-morbidity but were not in integrated care as they received treatment for either DM or HIV at a different facility. A total of 6 patient folders were excluded as duplicate folders were opened, and no information relating to the period under investigation was available from the folders. Two patients were transferred-in from outside the district 18 months prior to 31 December 2019.

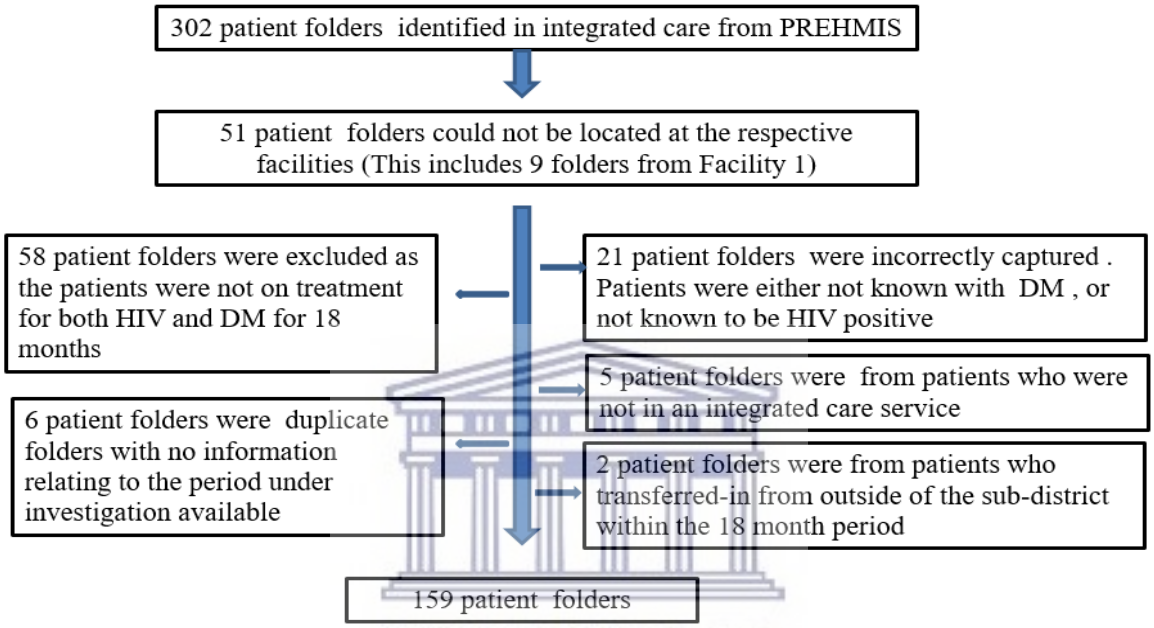

Figure 1: Realisation of Sample

4.3 Characteristics of the study participants

4.3.1. Demographic characteristics

4.3.1.1. Age

The median age of the study participants was 51 years (IQR = 45 - 56), with the youngest aged 24 years and the oldest aged 72 years. The mode for this population was 47 years. A total of 44% (n=70) of the participants were 50 – 59 years old.

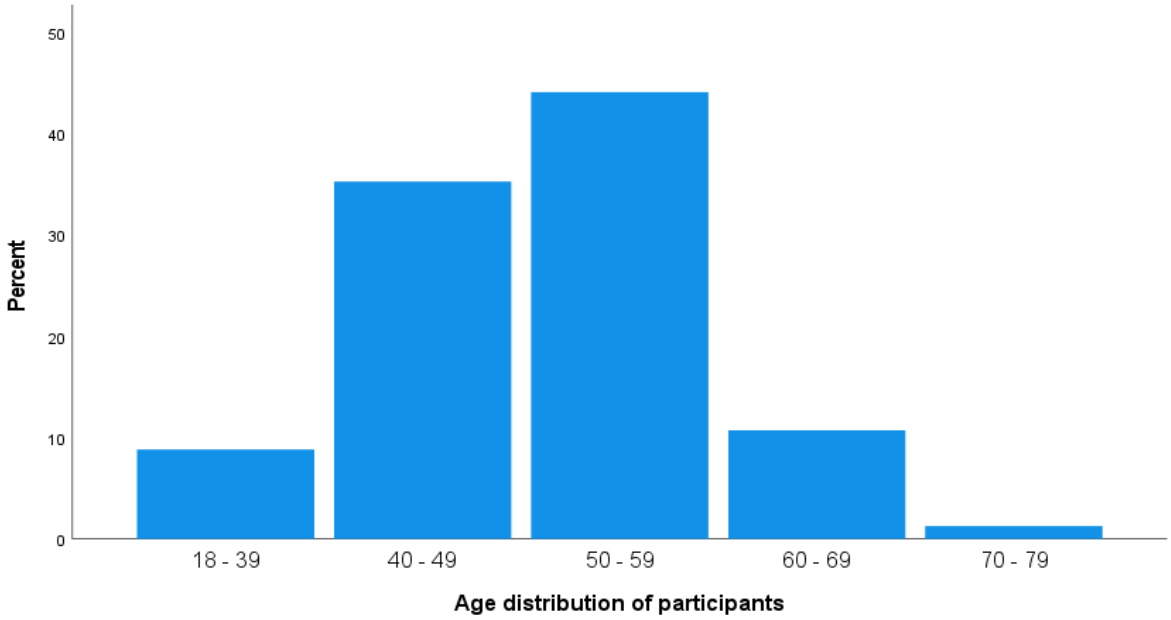

Figure 2: Age distribution of participants

4.3.1.2. Gender

In this study, 72.3% (n = 115) were female, and 27.7% (n=44) were male. The median age for females was 49 years, while the median age for males was 54 years, as shown in Table 4.

Table 4: Distribution of participants by age and gender

Age								
Gender	**N**	**Mean**	**Median**	**Std. Deviation**	**Minimum**	**Maximum**	**Range**	**Skewness**
Female	115	49.01	49.00	8.564	24	70	46	-.403
Male	44	54.18	54.00	7.444	37	72	35	-.043
Total	159	50.44	51.00	8.567	24	72	48	-.370

Table 5: Demographic characteristics of the study participants

Variable	Frequency (n)	Percentage (%)
Gender		
Male	44	27.7
Female	115	72.3
Age Group		
18 – 39	14	8.8
40 – 49	56	35.2
50 – 59	70	44.0
60 – 69	17	10.7
70 – 79	2	1.3
> 80	0	0

4.3.2. Clinical characteristics of the study participants

4.3.2.1. Body Mass Index

Body Mass Index (BMI) was poorly recorded in patient files. In 60.7 % of cases, an annual BMI was not recorded by December 2019. In cases where BMI was recorded, 87.7% (n=50) were obese as measured greater than 30 kg/m²; 5.3% (n=3) were overweight as recorded between 25 – 29.9 kg/m² and 7% (n=4) were normal at 18.6 – 24.9 kg/m².

4.3.2.2. Viral load Suppression

The HIV viral load monitoring showed that 83 % (n=132) of this study population had a suppressed viral load. HIV viral load was not suppressed in 12 (7.5%) participants, while the viral load was not measured in 9.4% (n=15) of this study population.

Table 6: Clinical characteristics of the study participants

Variable	Frequency (n)	Percentage (%)
BMI		
< 18.5	0	0
18.5 – 24.9	4	7
25 – 29.9	3	5.3
> 30	50	87.7
Viral Load		
< 400	132	83
>400	12	7.5

4.3.3. Medical treatment of the study participants

4.3.3.1 ART treatment regime

All participants in this study had been on ART and Diabetes Mellitus treatment for a minimum of 18 months, as set out by the inclusion criteria for this study. The combination ART consisted of 2 NRTIs with either an NNRTI or a protease inhibitor (PI), with one patient on an integrase inhibitor. The majority of the participants in this study (76.1%) were on a TDF/FTC, NRTI regime (n=121), followed by 13.2% (n=21) on ABC/3TC and 10.7% (n=17) on AZT/3TC.

In this cohort, 89.9% of participants were not on a PI-based regime, inferring that most of this study population was on the first-line ART regime.

Of the participants on a PI-based regime, 5.7% were on an ATZ/RTV regime (n=9), and 4.4% (n=7) were on an LPV/RTV-based regime. One person was on an integrase inhibitor regime. See Table 7.

Table *7*: ART treatment information of the study participants

Variable	Frequency (n)	Percentage %
Current ART regime		
TDF/FTC	121	76.1
ABC/3TC	21	13.2
AZT/3TC	17	10.7
LPV/RTV	7	4.4
ATZ/RTV	9	5.7
Integrase inhibitor	1	0.6
Duration on current ART regime		
0 - 2 years	59	37.1
3 - 5 years	58	36.5
6 - 10 years	38	23.9
> 10 years	4	2.5

4.3.3.2 ART regime duration

In this study, 59 (37.1%) participants were on their current ART regime for 0-2 years, followed by 58 (36.5%) participants who were on their current regime between 3-5 years; 38 (23.9%) had been on their current regime 6-10 years with 4 participants (2.5%) on ART regime longer than ten years.

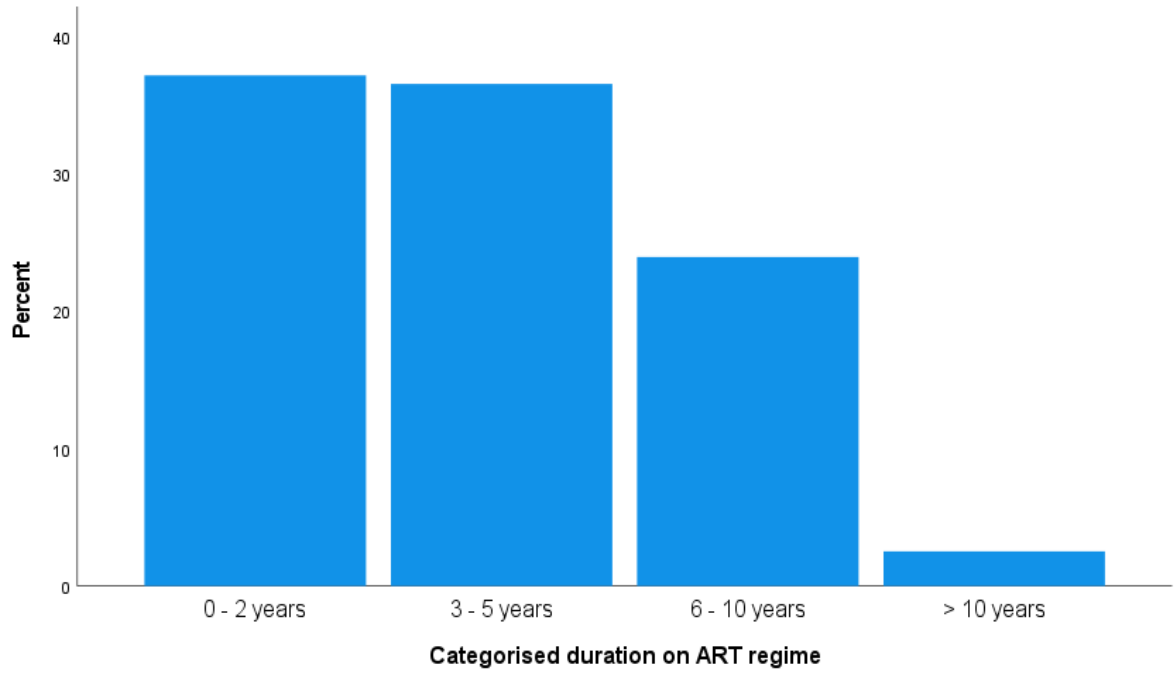

Figure 3: Duration on ART regime

4.3.3.3 Diabetic treatment

All participants in this study had been on treatment for diabetes for a minimum of 18 months as set out by the inclusion criteria for this study, with 60.4 % (n= 96) of study participants having insulin included in their diabetic treatment regime.

The current regime in this study is defined by insulin included or insulin not included. This study does not distinguish between the type of insulin (basal or biphasic insulin), nor does it distinguish between the type of oral anti-glycaemic agents.

The mean treatment duration in months was 37.76 months, with a median of 31 months on treatment.

Table 8: Diabetes treatment information of the study participants

Variable	Frequency	Percentage
	(n)	(%)
Diabetes treatment		
Insulin included in the regime	96	60.4
Insulin not included in the regime	63	39.6
Duration on treatment for diabetes		
0 - 2 years	93	58.5
3 - 5 years	47	29.6
6- 10 years	17	10.7
> 10years	2	1.3

Categorised, 58.5 % (n=93) of participants were on their current DM treatment regime for 0-2 years; 29.6 % (47) were on their current DM treatment regime for 3- 5 years; 10.7% (n=17) were on their current regime between 6-10 years; and 2 participants (1.3%) had been on their current regime for longer than ten years.

4.3.3.4. Mode of Integrated care

In this cohort, 96.2% accessed care for both HIV and diabetes outside the group-based care setting, with only 6 participants (3.8%) enrolled in group-based care by December 2019. Apart from the 6 participants enrolled in group-based care, an additional 22 participants had previously been in group-based care but were removed from integrated group care to allow for more frequent monitoring.

Table 9: Mode of integrated care of the study participants

Variable	Frequency	Percentage
	(n)	(%)
Mode of Care		
Individualised Integrated care	153	96.2
Group-based Integrated care	6	3.8

4.4 Glycaemic control

The mean HbA1c was 9.1%, with a minimum and maximum of 5.0 % and 12.8 %, respectively. About 13 (8.2%) participants did not have a representative HbA1c measurement by quarter 4, 2019. Of the remaining 145 participants, the glycaemic control was described as follows.

Glycaemic control is defined as HbA1c less than or equal to 8%, revealed that 58.5% (n=93) did not reach glycaemic control, while 33.3% (n=53) had a glycaemic index equal to or less than 8%.

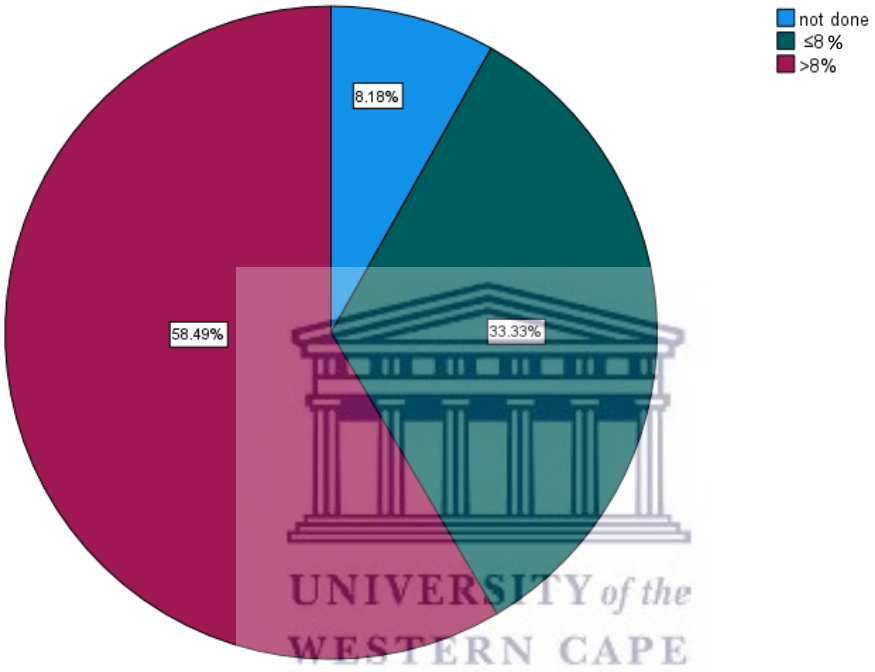

Figure 4: Percentage of study participants reaching glycaemic control

4.5 Factors Associated with Glycaemic Control

The factors associated with glycaemic control are summarized in Table 10.

4.5.1. Socio-demographic characteristics associated with glycaemic control:

Age group categorised as age 40 – 49 years old (p = 0.93), 50-59 years old (p = 0.77), 60 – 69 years old (p = 0.82) and 70 – 79 years old (p = 0.63) was not significantly associated with glycaemic control at a p-value of 0.05 in this study.

Gender was associated with glycaemic control (p = 0.01). In this study, females were 0.4 times as likely to reach glycaemic control as males (crude odds ratio = 0.4 [95% confidence interval (CI) (0.19 – 0.84)]. This association was statistically significant.

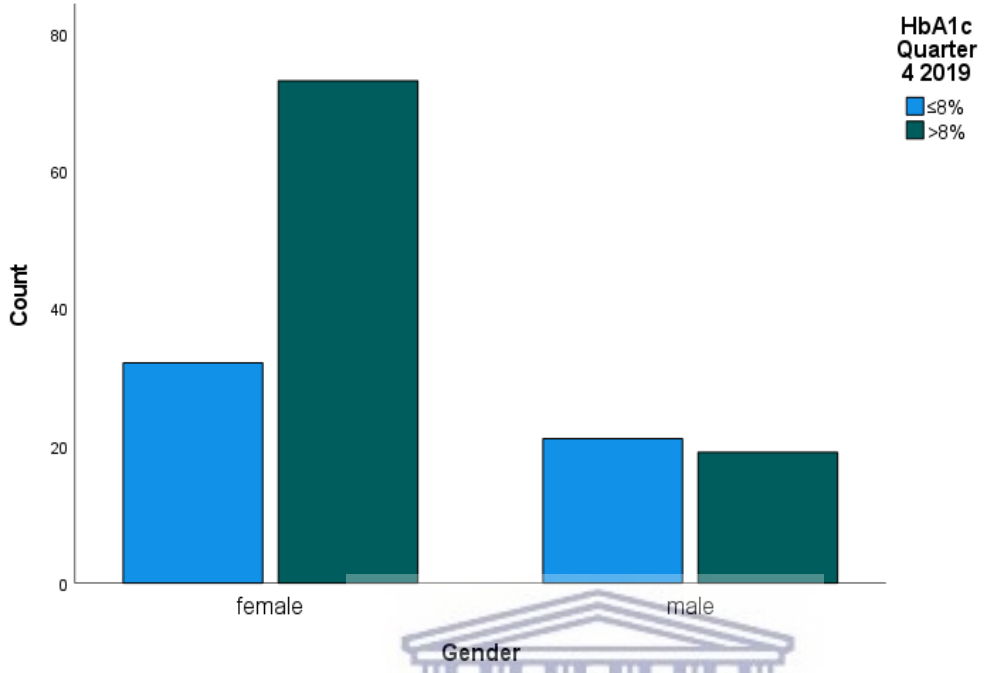

Figure 5: Association of gender with glycaemic control

4.5.2. Clinical factors and glycaemic control

BMI was poorly recorded in this study, with 88 participants not having an annual BMI recorded by quarter 4, 2019. The association of BMI and glycaemic control could not be computed due to insufficient data.

Viral load suppression was not significantly associated with glycaemic control at a p-value of 0.05 in this study (p = 0.59).

4.5.3. Medical treatment factors and glycaemic control

4.5.3.1 ART Regime

Participants on the NRTI combination of ABC/3TC were 0.38 times as likely to achieve glycaemic control (odds ratio = 0.38 [95% CI 0.15 – 0.97] p = 0.04) than patients on the TDF/FTC NRTI combination in this study cohort.

Patients who had been on ART for 6 to 10 years were 3.9 times as likely to achieve glycaemic control than patients on ART for 0 – 2 years (odds ratio = 3.9 [CI 1.5-10.35]; *p* = 0.01) in this study cohort. The ART treatment factors were statistically significant in univariate analysis.

4.5.3.2 Diabetes regime

Study participants with no insulin included in the regime were 6.5 times as likely to achieve glycaemic control in this study than participants who did have insulin included in their current regime (crude odds ratio = 6.5 [CI (3.1 – 13.9)]). The association was statistically significant (*p* = < 0.01).

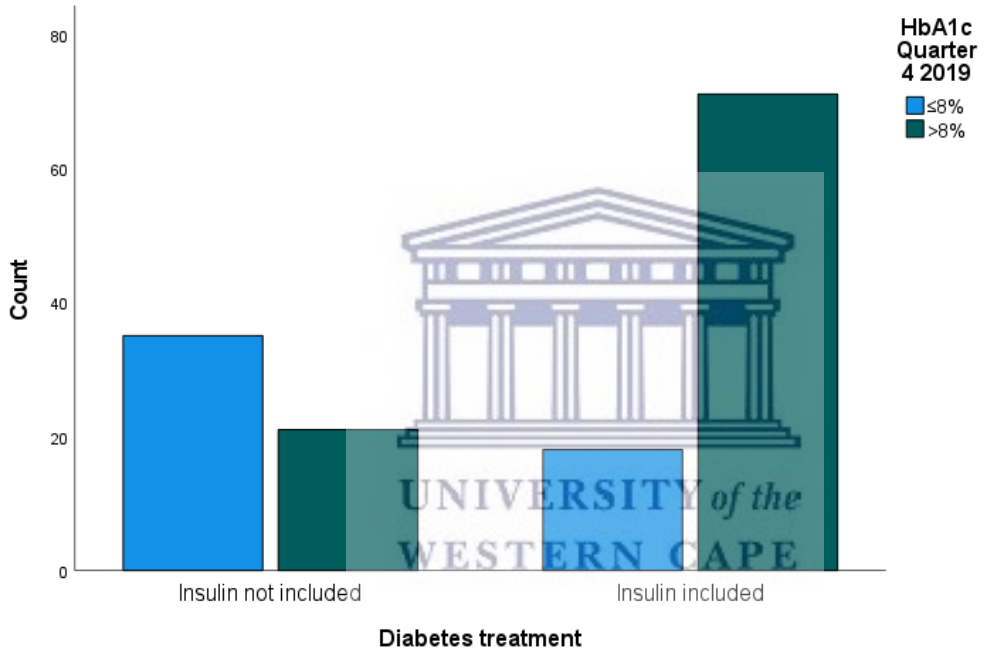

Figure 6: Association of insulin included in diabetes regime with glycaemic control

The duration of treatment for diabetes was not significantly associated with glycaemic control in this study; 3-5 years (*p* = 0.71); 6-10 years (*p* = 0.52); greater than 10 years (*p* = 0.99).

The association of mode of care and glycaemic control was not included as insufficient participants were enrolled in group-based integrated care for 18 months.

4.5.4. Multivariate Analysis

The variables which showed statistical significance at the univariate level were included in the multivariate analysis. These included gender, ART regime, duration on ART regime and

the diabetes treatment. At multivariate analysis level, the association between gender remained statistically significant ($p = 0.02$) in that females were 0.35 times as likely to achieve glycaemic control with an adjusted odds ratio (aOR = 0.35 [CI 0.14 – 0.85]). The diabetes treatment regime of insulin not included in the regime maintained statistical significance ($p < 0.001$). The odds of patients with no insulin included in the regime were 8.6 times as likely to achieve glycaemic control (aOR = 8.6 [CI 3.65 – 20.461]).

Both the ART duration and the ART regime did not maintain statistical significance for the multivariate analysis. See Table 10 on the following pages.

Table 10: Factors associated with glycaemic control						
Factor	**Characteristic**	**n (% Glycaemic Control)**	**Crude OR (95%CI)**	***p-value***	**Adjusted odds ratio**	***p-value***
Gender	Male	21 (52.5%)	1		1	
	Female	32 (30.5)	0.4 (0.19 – 0.84)	0.01*	0.35 (0.14 – 0.85)	0.02*
Age Group	18 – 39	4 (33.3%)	1			
	40 – 49	17 (34.7%)	0.93 (0.25 - 3.58)	0.93		
	50 – 59	25 (37.9%)	0.82 (0 .22 - 3.0)	0.77		
	60 – 69	6 (37.5%)	0.83 (0.17 - 4.0)	0.82		
	70 – 79	1 (50%)	0.5 (0.02 - 10.25)	0.63		
	> 80	0	0	0		
Viral Load	<400	47 (37.3%)	0.71 (0.21 – 0.47)	0.59		
	≥400	5 (45.5%)	1			
Current ART Regime	NRTI: TDF/FTC	36 (33.3%)	1		1	
	NRTI: ABC/3TC	12 (57.1%)	0.38 (0.15 -0.97)	0.04*	0.34 (0.12 – 1.1)	0.07
	NRTI: AZT/3TC	5 (31.3%)	1.1 (0.35 - 3.4)	0.87		

	PI	6 (37.5%)	0.96 (0.5 - 1.9)	0.93		
	Integrase inhibitor	0	0	0		
Duration on current ART regime	0-2 years	25 (52.1%)	1		1	
	3 - 5 years	19 (33.9%)	2.1 (0.96 - 4.67)	0.06	1.81 (0.71 – 4.6)	0.22
	6 - 10 years	8 (21.6%)	3.9 (1.5 - 10.35)	0.01*	2.88 (0.93 – 8.8)	0.07
	> 10 years	1 (25%)	3.2 (0.32 - 33.6)	0.32		
Diabetes treatment	Insulin included in regime	18 (20.2%)	1			
	Insulin not included in regime	35 (62.5%)	6.5 (3.1 – 13.9)	<0.01*	8.6 (3.65 – 20.46)	<0.001*
Treatment duration for diabetes	0 - 2 years	33 (39.8%)	1			
	3 - 5 years	16 (36.4%)	1.15 (.54 - 2.4)	0.71		
	6 - 10 years	2 (12.5%)	4.6 (.99 - 21.67)	0.52		
	>10 years	2 (100%)	0	0.99		

*Statistically significant

CHAPTER 5: DISCUSSION

5.1 Introduction

This chapter will discuss the findings of the study in relation to the problem statement and the available literature. The discussion points will be as follow: The attainment of glycaemic control in quarter 4, 2019; socio-demographic factors, clinical factors and the treatment factors influencing glycaemic control.

Based on the lessons learnt from the 90/90/90 cascade of HIV & AIDS, the National Department of Health SA has outlined a similar 90/60/50 cascading approach for managing NCDs (National Department of Health [NDOH], 2022). In the management of diabetes, the cascade proposes that:

- 90% of all people over 18 will know whether or not they have raised blood glucose;
- 60% of all people with raised blood glucose will receive the intervention;
- 50% of people receiving interventions are controlled (NDOH, 2022).

5.2 The proportion of patients that attained glycaemic control

In this study, 33% of patients reached glycaemic control, defined by HbA1c less than or equal to 8% as per the local guidelines (KTU, 2020). This relaxed HbA1c target is acceptable in people with advanced complications and low life expectancy (WHO, 2020). Still, it is difficult to compare the effect of integrated care as available literature uses the HbA1c value of less than 7% as a target for glycaemic control (WHO, 2020). The virtual cohort analysis of diabetes and TB in PLHIV from the Khayelitsha Sub-district by Tamuhla and colleagues in 2021 reported 24.5% of participants with an HbA1c less than 7% at baseline, although only 85% of that population had evidence of treatment for diabetes (Tamuhla *et al.,* 2021). In contrast, a retrospective cross-sectional study of PLHIV with type 2 diabetes at an urban academic HIV clinic in the United States of America in 2008 showed poor glycaemic control in only 33% of patients with HbA1c greater than or equal to 7.5% used as a measure for inadequate glycaemic control (Satlin, Hoover & Glesby, 2011).

The use of HbA1c as a measure for glycaemic control in this patient cohort of PLHIV is influenced by haemolysis (Diop *et al*., 2006 as cited by Coelho *et al.*, 2018). The study by Kim and colleagues (2014) showed a 19% underestimation and 27% overestimation of glycaemic control with HbA1c. The same study suggests that HbA1c should be

complemented with accurate fingerpick reporting in this patient population (Kim *et al.*, 2014). The finger-prick reporting of blood glucose was not included in our study. However, empowering the patient to monitor and record these values in between facility contact sessions will encourage the patient to become an active role player in their health management and will provide additional monitoring information.

5.3 Socio-demographic characteristics associated with glycaemic control

The majority (66, 9%) of participants were female, with a median age of 49 years, while 25.6% were male, with a median age of 54 years. This is similar to the population described in other studies of diabetes in the HIV-positive population cohort in Khayelitsha (Tamuhla *et al*., 2021). In this cohort, age was not a determinant of glycaemic control. The female predominance in this study is consistent with the findings around health-seeking behaviour in the community (Ntwana, 2005). However, this does not reflect the general sex distribution [ratio of 95.7] between genders in the community (Stats SA, 2011). The association of gender with glycaemic control was statistically significant. Females were less likely to achieve glycaemic control in this study, and the association remained statistically significant when included in the multivariate analysis ($p = 0.02$). Similar associations of female gender as a socio-demographic determinant of uncontrolled Type 2 diabetes in primary health care facilities in the OR Tambo District have been reported (Adeniyi *et al*., 2016) however, the author argues that a population-based study is required to determine the true prevalence of uncontrolled diabetes in men (Adeniyi *et al*., 2016). The study by Chetty and Pillay showed that gender did not play a significant role in HbA1c levels with a positive family history of diabetes (Chetty & Pillay, 2020).

5.4 Clinical factors associated with glycaemic control

The HIV viral load monitoring showed that 83% (n=132) of the study population had a suppressed viral load in quarter 4, 2019. This is lower than the 97% viral load suppression rate reported in the study on vertical ART adherence club care (Tsondai *et al.*, 2017) and the viral load suppression rates in the Gausi *et al.* (2021), study that measured viral load suppression rates in co-morbid clubs. The study into co-morbid club care reported viral load suppression of 98% at 12 months prior to enrolment into co-morbid clubs, 99.5 % viral load suppression at the point of enrolment and 99.4% twelve months after enrolment into co-

morbid clubs. Compared to the findings of the study by Gausi and colleagues, viral load suppression is higher in an integrated group-based model (Gausi *et al*., 2021) than with individualised, integrated care. Viral load suppression was not associated with glycaemic control in our study.

BMI was poorly recorded in this study, with 61.6% (n=88) of study participants not having a valid BMI recorded by quarter 4 of 2019. In cases where BMI was recorded, 87.7% (n=50) were obese and 5.3% (n=3) were overweight. A systematic review and meta-analysis in Ethiopia showed that the magnitude of being overweight among adult HIV-positive people on ART ranged from 6.4 % to 36.1% and for obesity, this ranged from 0.2% to 9.4% (Kabthymer, *et al.,* 2021). A prospective cohort study into weight gain in PLHIV on ART in South Africa found that the largest increase in BMI occurred in the first year on ART (Brennen, *et al.,* 2019). Literature from research conducted within the Khayelitsha area showed that the same positive connotations of being overweight, which was found in the adolescent population of the African community in South Africa (Puoane, Tsolekile & Steyn, 2010), persists into adulthood (Mvo, Dick & Steyn, 1999). An ancillary study to the Prospective Urban and Rural Epidemiology (PURE) study (Teo *et al.,* 2009) looked into weight discordance among overweight and obese South Africans (Okop, Levitt & Puoane, 2019). The study by Okop and colleagues was conducted on community participants and found that 85% of the obese and 79% of the overweight participants underestimated their weight. In addition, 41% of obese and 43% of overweight participants were satisfied with their body sizes (Okop, Levitt & Puoane, 2019). This is an indication that health promotional programmes should be targeted at different stages throughout the patient's life course and should be targeted at different levels, from the individual, to the community and on the healthcare platforms at different organisational levels.

The poor recording of BMI has been reported in other studies. A study into the adherence to diabetes clinical care guidelines in Kenya (Atieno Jalang'o, Tsolekile & Puoane, 2014) showed that 6 out of 377 patients had BMI calculations on their records at baseline, with a further decline in weight measurements at follow-up visits. Similarly, the integrated management of HIV and NCDs in the Limpopo province of South Africa was analysed by Murudi-Manganye and colleagues, who found that BMI at first visit was only assessed on 3.1% (n=19) patients while 593 (96.6%) patients did not have a BMI measurement recorded at baseline. This analysis also showed a further decline to 2% (n=12) in patients who had an annual BMI assessment while on ART (Murudi-Manganye, Makhado & Sehularo, 2021).

The reasons for the omission of this data element by clinicians were not explored as part of this study. However, the poor recording of this data element by clinicians is a missed opportunity for the early detection of preventable secondary complications. In this study, BMI continued to be poorly recorded despite this being included as a screening element in the routinely used integrated patient stationery items. This illustrates the importance of the health care worker as a policy actor (Walt & Gilson, 1994) when rolling out new policies at the primary care level in order to ensure that policies are acted on and therefore experienced by the patient as intended. These stationery items are intended to prompt clinicians to the routine monitoring requirements of patients enrolled in chronic care services. This poses a challenge to interventions aimed at addressing obesity within the public health sector if both patients do not recognise obesity (Okop, Levitt & Puoane, 2019) and the healthcare provider does not monitor levels of overweight and obesity. The long-term complications of being overweight or obese impact quality of life and are often associated with tangible as well as intangible financial burdens to the patient as well as the health system. The expansion of dietician services within the primary care setting will greatly benefit this patient cohort. In the absence of this service at the facility, referral pathways need to be intact. The association of BMI and glycaemic control could not be computed due to insufficient data.

5.5 Medical treatment factors and glycaemic control

All study participants were on combination ART regimes which included 2 NRTIs. The NRTI class of ART adds to metabolic abnormalities, which include insulin resistance, lipodystrophy and mitochondrial dysfunction (Kalra *et al.*, 2011). This effect was more prominent with stavudine (which is no longer routinely used in the public health sector) but is also significant with AZT, and these effects are evident in PLHIV treated for long periods with NRTIs (Kalra *et al.*, 2011). The participants on ABC/3TC regime were less likely to achieve glycaemic control than patients on a TDF/FTC NRTI combination.

The local guidelines prescribe that patients be commenced on a TDF/FTC NRTI regime as a first option and changed to an ABC/3TC NRTI option if TDF/FTC is contra-indicated due to renal dysfunction (Knowledge Translation Unit, 2020). The reasons for the substitution of TDF/FTC were not formally included in the study. However, the inference is drawn that the patients on ABC/3TC had a contra-indication to TDF/FTC, which suggests that these patients had the additional complication of renal dysfunction.

Patients who had been on ART for 6-10 years were 3.9 times as likely to achieve glycaemic control than patients on ART for 0-2 years in the univariate model, however, when included in the multivariate analysis, neither the NRTI combination nor the duration on treatment maintained statistical significance.

Dolutegravir was introduced as the first-line option in South Africa in November 2019. (NDOH, 2020). In the Western Cape, Dolutegravir was rolled out in February 2020 as the first-line option in a fixed dose combination consisting of Tenofavir, Lamivudine and Dolutegravir (TLD) (Western Cape Department of Health, 2020b). This falls outside of the sampling timeframe for this study, and therefore only one patient on an integrase inhibitor is included in this study.

In the ADVANCE study in South Africa, patients were randomised to 1 of 3 treatment arms containing Dolutegravir (DTG) plus either TAF/Emtricitabine (EMB) or TDF/ EMB, or EFV/TDF/EMB. In this study, potential genetic associations with weight gain were identified in patients on DTG /TAF/EMB or DTG/TDF/EMB (Cindi *et al.*, 2021). As weight gain is a risk factor for the development of non-communicable diseases, including diabetes, both the patient and provider require a renewed focus on the monitoring of body weight within this population. The SAILING, SPRING2, SINGLE and VIKING trials reported severe hyperglycaemia with or without life-threatening acute complications after using integrase inhibitors (Hailu, Tesfaye & Tadesse, 2021).

All study participants had been on treatment for diabetes for a minimum of 18 months. In this study, 60.4% (n = 96) of patients had insulin included in their treatment regime. The study did not make the distinction between basal vs biphasic insulin, nor did it make the distinction between the type of oral diabetic treatment agent, e.g. biguanide or sulfonylurea or both.

Most (58.5%) of patients were on treatment for less than three years, although the duration of treatment for diabetes was not associated with glycaemic control. In a paper by Kalra *et al*., the authors argue that "Insulin is the drug of choice for the management of diabetes with HIV" (Kalra *et al*., 2011: 5). The reasons stated are because insulin reduces inflammatory markers, it does not have drug-drug interactions with ART, and it is not contra-indicated with renal or hepatic impairment. In addition, it can be used for both insulin deficiency and resistance at the appropriate doses, and it does not increase CVD risk (Kalra *et al.*, 2011).

In this study, the patients with no insulin included in their regime were three times as likely to reach glycaemic control at quarter 4, 2019, as patients with insulin included in their diabetes

treatment regime, and this association was statistically significant. This association remained statistically significant when included in the multivariate analysis. The literature reviews also showed that HIV infection and malnutrition lead to low insulin production and insulin deficiency in that inflammation, as measured by elevated CRP, was associated with reduced insulin secretion (Faurholt-Jepsen *et al.*, 2019). However, despite the majority of patients having insulin in their regime in our study, this was not associated with glycaemic control.

A study into the use of HbA1c and fasting plasma glucose results to guide treatment changes in patients with type 2 diabetes in the Tygerberg Sub-district (Monanabela, Van Huyssteen & Coetzee, 2019) found that HbA1c levels were available to guide 245 prescription changes. However, the study found that 78.4% had no change or a lateral change in their follow-up prescriptions, 6.1% had therapy adjustments opposite to what the guidelines advise, and only 15.5% had appropriate therapy adjustments (Monanabela, Van Huyssteen & Coetzee, 2019). Our study did not look into the change in prescriptions, however this discrepancy between guidelines and clinical practice is described in the literature as "clinical inertia" (Andreozzi *et al.*, 2020). Clinical inertia happens where guidelines exist, and the clinician is familiar with the guidelines; the clinician believes that the guidelines are applicable to the patient; the clinician has the resources to apply the guidelines, yet the guidelines are not applied in clinical practice (Andreozzi *et al.*, 2020). Clinical inertia in diabetes care has also been described in the 2012 SOLVE study in North America (Khunti *et al.*, 2012 as cited by Andreozzi et *al.*, 2020), the 2013 GUIDANCE study in Europe (Stone *et al*., 2013 as cited by Andreozzi *et al.*, 2020) and in Japan (Satoh *et al*., 2018 as cited by Andreozzi *et al.*, 2020). Measures to address clinical inertia are the adoption of monitoring systems to assess the quality of care, which will enable health professionals to evaluate their performances, reflect on these and adopt strategies that will improve outcomes (Andreozzi *et al*., 2020). The presence of clinical inertia was not assessed in our study.

Patient-related factors, such as adherence to the insulin-containing diabetic medication, the appropriate storage of insulin as well as the appropriate administration of insulin, was not included in this study.

The "hypothetical willingness" to start insulin was studied in the South African Tswane Insulin Project (TIP) and showed that approximately half (51.9%) of Type 2 insulin-naïve patients expressed unwillingness to initiate insulin therapy (Piotie *et al.*, 2020). The reasons for the unwillingness were related to anxiety and fear around needles and injections, lack of

knowledge on insulin and concerns about being unable to cope with insulin and the related costs (Piotie *et al.*, 2020). These factors were not explored as part of this study.

5.6 Group-based care

In this cohort, 96.2% of the participants accessed care for both HIV and diabetes outside of the group-based care setting, with only 6 participants (3.8%) enrolled in group-based care in December 2019. Apart from the 6 participants enrolled in group-based care in December 2019, an additional 22 participants had previously been in group-based care but were removed from integrated group care. In this study, insufficient numbers of study participants were identified to compare the outcomes of group-based care versus individualised care. The available literature from the study into PLHIV and NCD multi-morbidity attending integrated care clubs in Cape Town (Gausi *et al*., 2021) showed that optimal glycaemic control (defined as HbA1c less than 7.5%) was recorded in 87.5% of diabetics at the point of enrolment, but decreased to 53.3% at 12 months after enrolment into the integrated clubs (Gausi *et al.*, 2021). This may indicate that group-based care for PLHIV and diabetes co-morbidity requires a revised framework for more frequent monitoring.

CHAPTER 6: RECOMMENDATIONS, LIMITATIONS AND CONCLUSIONS

6.1 Introduction

As Integrated Clinical Service Management was identified as a key focus within the Ideal Clinic Realisation Model, this study shows areas where services at the primary level will require renewed focus to address the management of diabetes in the PLHIV to achieve the "90/60/50" targets for NCDs (NDOH, 2022). The findings from this study and the subsequent recommendations speak to improvements on the health platform; however, the value of health promotional activities within the community to reduce the onset of diabetes and obesity should not be disregarded.

6.2 Recommendations

6.2.1. Service delivery re-orientation

The integrated management of diabetes is available at all Community Day Centres and City Health clinics in the Khayelitsha Sub-district; however, this is not the case at all facilities within City Health due to the facility grading systems. Expanding community-based interventions could supplement sub-optimal management at the facility level to assist clients with glycaemic control. The utilisation of a ward-based PHC outreach team (WBPHCOT) intervention (NDOH, 2018) to assist with health literacy around optimal weight management, continuous monitoring of finger-prick glucose and monitoring the adherence to medication at the community level will be of great benefit in this population. The Differentiated Models of Care (DMOC) framework (WCDOH, 2018b) was produced to guide differentiated models of care and the management of adult patients who are stable on treatment for diabetes, hypertension and ART outside of the traditional facility-based management. DMOC models could be beneficial in providing health prevention and education to build on self-management of chronic conditions.

6.2.2. Task-shifting within the health workforce

The team-based care module within the HEARTS technical package guides task-shifting related to the care of cardiovascular diseases (CVD) (WHO, 2020). Task-shifting allows clinical care to be reassigned from one level of the healthcare worker to another for services to be rendered more efficiently (WHO, 2020). Multi-disciplinary teams may include clinical staff as well as counsellors, dieticians and community health workers (CHWs). The expansion of dietician services to provide health education and clinical guidance on the risks

associated with the nutritional transition and the high levels of obesity for not only diabetes but numerous NCDs will have far-reaching positive effects on a population health level. Setting targets for the patient on the optimal HbA1c percentage at pre-treatment counselling sessions (similar to the counselling sessions when commencing ART) should be encouraged.

The CDC's National Diabetes Prevention Program (DPP) has been noted globally as one of the most effective interventions based on lifestyle change (Knowler *et al.,* 2002, as cited in Catley *et al.,* 2019). An adaptation of the DPP for LMICs "Lifestyle Africa", with the key adaptation for the delivery of the programme by CHWs, was developed with input from community advisory boards (Catley *et al.,* 2019). The utilisation of CHW in this manner should be explored.

6.2.3. Improving health information systems

Information on 28 study participants was excluded from this study due to incorrect data capturing and information. At the same time, information on 57 study participants could not be obtained due to missing patient folders. Incorrect and missing health information results in wasted opportunities to optimise the patient's health. The quality of data capturing in electronic health records is an area which requires additional focus and training if health systems are to monitor and evaluate their performance against relevant indicators accurately. Moreover, improving health information systems will assist in implementing surveillance systems which will lead to appropriate policy decisions and allocation of resources. The use of electronic health records eliminates the problem of misplaced and duplicate folders.

6.2.4. Leadership and Governance

Current evidence on the effects of integrated care is uncertain (Rohwer *et al.,* 2021 & Adeyemi *et al.,* 2020). Clinical inertia on the part of the healthcare practitioner needs to be addressed through training and ongoing monitoring of the use of guidelines and supporting tools like integrated stationery. This can be monitored through folder audits and evaluated against key performance areas for the individual practitioner, but also included in the Ideal Clinic audit requirements and sub-district monitoring indicators.

6.3 Limitations

The retrospective study design had various limitations. In this study we were restricted to the routine data which was expected to be documented as part of the routine services rendered.

The data source included the patient's clinical paper-based records and the data from the Provincial Health Data centre. This study was dependent on the quality of recordkeeping in clinical folders and the accuracy of capturing electronic data, which is dependent on the behaviours of other parties in the primary health care service (clinicians, clerical staff and health information management). Sub-optimal recordkeeping and capturing have resulted in missing information on certain variables which were of interest and, as a result, have limited the study's ability to describe and analyse the study population. The sample size was constrained by the inclusion and exclusion criteria and has further been limited by patient records of eligible patients not being located.

6.4 Conclusions

In this study, the integrated management of diabetes in the PLHIV population in primary care services revealed that 33.3 % of HIV-positive patients on treatment for diabetes reached glycaemic control, below the target of 50% set by the National Department of Health. Females were less likely to achieve glycaemic control. The majority of patients in this study had insulin included in their treatment regime, yet people on insulin were less likely to obtain glycaemic control. BMI was poorly recorded in this study. This highlights the need for clinical services in primary care to refocus the training of staff to combat clinical inertia as well as increase efforts in the areas of the education of patients, which will enable them to become active managers in their healthcare.

The potential benefits of HIV-NCD service integration include the reduction of fragmented services with the increased efficiency in resource usage, but care must be taken to ensure that integrated services are adequately resourced to avoid the risk of reducing the quality of existing HIV services.

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Appendix 1: Data Extraction Tool

Patient no	Facility code	Demographic Characteristics		Clinical Characteristics						Current ART Regime				Current Diabetes Regime			Integrated Mode of care		
		Age	Gender	BMI Q4 2018	BMI Q4 2019	VL Q 4 2019	VL Q 4 2018	HbA1c Q 4 2019	HbA1c Q 4 2018	NRTI	PI	Integrase inhibitor	Duration on current regime	Insulin included	Insulin not included	Duration on current treatment	Individualized	Group based	Duration enrolled in mode of care at Q4 2019

Appendix 2: Ethics Clearance

UNIVERSITY of the WESTERN CAPE

60 YEARS of hope, action & knowledge

29 November 2021

Dr D Abrahams
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number:	BM21/10/18
Project Title:	Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in City of Cape Town Primary Health Care facilities
Approval Period:	**19 November 2021 – 19 November 2024**

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 and the requested amendment to the project.

Any further 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.

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via:
https://sites.google.com/uwc.ac.za/permissionresearch/home

The permission letter must then be submitted to BMREC for record keeping purposes.

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

NHREC Registration Number: BMREC-130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

Appendix 3: Approval from City Health

CITY OF CAPE TOWN
ISIXEKO SASEKAPA
STAD KAAPSTAD

CITY HEALTH

Dr Natacha Berkowitz
Epidemiologist: City Health

T: 021 400 6864 F: 021 421 4894
E: Natacha.Berkowitz@capetown.gov.za

Ref: 9499 2022-01-31

RE: Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in the City of Cape Town Primary Health Care facilities.

Dear Dr Dianne Abrahams

Your research request has been approved as per your protocol. Please refer to the subsequent pages for the approval of any facilities or focus areas requested. Approval comments on any proposed impact on City Health resources are also provided. Line management approval is also required for City Health employee initiated research.

Eastern & Khayelitsha:

Contact Person: Prof Vera Scott (Area East Manager)

Tel/Cell: 021 360 1258/082 308 8059

Email: Vera.scott@capetown.gov.za

Please note the following:

1. All individual patient information obtained must be kept confidential.
2. Access to the clinic and its patients must be arranged with the relevant Manager such that normal activities are not disrupted.
3. A copy of the final report must be uploaded to https://web1.capetown.gov.za/web1/mars/ProjectClosure/UploadReport/0/9499, within 6 months of its completion and feedback must also be given to the clinics involved.
4. Your project has been given an ID Number (9499). Please use this in any future correspondence with us.
5. No monetary incentives to be paid to clients on the City Health premises
6. If this research gives rise to a publication , please submit a draft before publication for City Health comment and include a disclaimer in the publication that "the research findings and recommendations do not represent an official view of the City of Cape Town "
7. As the research is approved as per submitted protocol, any changes to the protocol need to be submitted and approved by City Health prior to implementation.
8. We are currently not approving research for joint authority facilities (Dirkie Uys, Durbanville, Heideveld, Kasselsvlei, Nolungile, Nyanga, Parow, Ravensmead, Scottsdene) as they are in the process of being consolidated into one authority.

Thank you for your co-operation and please contact me if you require any further information or assistance.

Kind Regards
Dr Natacha Berkowitz Epidemiologist: City Health

Appendix 4: Approval from PHDC

Annexure A

APPLICATION FOR ACCESS TO HEALTH DATASETS

The following application form is to be completed by all person/persons/organisations/groups who wish to access to health-related datasets from Western Cape Department of Health and is to be completed in accordance with the Departments' *Guidelines on requests for access to patient datasets from the Department of Health*. Please note that application for use of data does not guarantee that the data request will be approved. If the intended purpose for data access is altered or extended in anyway, a new agreement must be entered into.

Applicant details: *(Refers to the detail of the person requesting the change.)*

Name:	Dianne	**Surname:**	Abrahams
Designation / Rank:	Clinical Medical Officer	**Date:**	22/12/2021
Organisation:	City of Cape Town / University of the Western Cape		
Email:	Dianne.Abrahams@capetown.gov.za	**Tel/Cell:**	082 405 4119

Please supply the contact detail of the person to whom the processed application must be returned.

Details of Data Request: (please append any additional information where necessary)

Type of Data Requested : (please tick appropriate option)	Aggregated data	Non - certified individualised data	Identified individualised data √

Please provide a short description of the data requested. Please attach a list/attach a list of the variables required.

Gender	Single Patient Viewer/Paper-based records
Age	Single Patient Viewer/Paper based records
Current ARV Regime	Single Patient Viewer / Paper-based records
Duration in years on current ARV regime	Single Patient Viewer/ Paper-based records
Viral load results	Single Patient Viewer/Paper based records
Last recorded HbA1c	Single Patient Viewer/ Paper-based records

Do you have a National Health Research Database ref no.?	Yes	No√	Number:
Time period the data should cover:	Start date: 01/07/2017		End date: 31/12/2019
Frequency of Access: (please tick appropriate option)	Once-off		Periodically √

If periodically, please specify time frames for access: Time period for data extraction is expected to occur between 1 February 2022 – 30 April 2022. I am a part- time student and therefore data extraction will occur over a period.

Is the data to be used for research purposes?	Yes√	No

Please provide a brief motivation for this request, highlighting the purpose for which the data will be used

Research project forms part of a Mini-thesis required as partial fulfilment for a Masters in Public Health degree (UWC)

Study not funded/funded by: Not Funded

Do you have a security protocol for handling the data (attach detail if necessary)?	Yes √. Following identification of patients via PREHMIS, the variable of interest will be collected from SPV. Unique identifiers will be generated consisting of a combination of facility code and partial folder number in order to de-identify participants. Extracted data will be stored on a password protected Excel spread sheet and will be stored for three years. A secondary document containing the link between the unique study identifier and the patient's folder number will be stored	No

5th Floor, 8 Riebeek Street, Cape Town, 8001, PO Box 2060, Cape Town, 8000
Tel: +27 21 483 9366 Fax: +27 21 483 6058

	separately. Only anonymous data with a unique identifier will be entered into the database	

PHDC Manager- Technical assessment and comments: A named dataset has been supplied and individualised and anonymised data will be returned	☒ Feasible *Where relevant:* ☒ Protocol cover ☒ Ethics ☐ Consent docs

Assigned PHDC analyst: Florence **Assigned Time:**	**PHDC Manager Signature:**	**Date:** 3 August 2022

Outcome of Application: (To be completed by the Designated Health Authority)

Name:	Dr M Moodley, Director: Health Intelligence	**Surname:**	
Designation / Rank:		**Signed:**	
Application Approved:	Yes X / No	**Date:**	20 August 2022

TERMS OF AGREEMENT FOR ACCESS TO HEALTH DATASETS

The Western Cape Department of Health is committed to ensuring availability of data that supports the provision of health care and other essential services to authorised Users. This agreement aims to ensure the authorisation, maintenance of confidentiality and appropriate use of datasets provided to Users.

This agreement is between:

The Western Cape Government, Department of Health, hereafter "the Department"

AND

Dianne Abrahams, hereafter "the User"

1. Application for use of data must be made through the channels identified in the "*Guidelines on requests for access to patient data and patient information systems*" document.
2. This agreement sets forth the terms and conditions to which the Department will disclose certain confidential health information in the form of a Dataset(s).
3. The User agrees that the Department is the owner of the Dataset(s).
4. Permitted Uses and Disclosures:

4.1. Except as otherwise specified herein, the User may make all uses and disclosures of the (*insert name of Data Set's*) Dataset(s) necessary to conduct the "Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in City of Cape Town Primary Health Care facilities" for the period starting (*1 February 2022*) and ending (*30 April 2022*).

4.2. The User will receive the Dataset(s) **periodically** per (*insert frequency*), from the designated Department official.

4.3. In addition to the User, the individuals, or classes of individuals, who are permitted to use or receive the Dataset(s) for purposes of the Identified Project include: (*Dianne Abrahams*).

5. User Responsibilities:

5.1. The User will not use or disclose the Dataset(s) for any purpose other than permitted by this Agreement pertaining to "Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in City of Cape Town Primary Health Care facilities" for which written approval was granted.

5.2. The User agrees that the Dataset(s) provided will not be released to any third party that is not included by the provisions of the agreement between the primary parties, without the written permission of the Department. A third party will be required to complete an agreement as well.

5.3. The User agrees that the Department will be provided with an opportunity to comment and give feedback prior to the finalisation of any report/publication derived from the Dataset(s) according to the following conditions:

5.3.1. The data will be used to compile "Factors associated with glycaemic control in people living with HIV and Diabetes Mellitus within integrated care models in City of Cape Town Primary Health Care facilities" for completion of Masters in Public Health qualification.

5.3.2. The report will be sent to the Department for perusal prior to finalisation. The latter should respond or react within 31 working days on the report being issued. If this period lapses it will be interpreted as a confirmation that the Department acknowledges the presentation and interpretation of data as correct and factual in the report.

5.4. The User will ensure that the Department is acknowledged in any output resulting from the use of the data including.

5.5. The User will communicate any data quality issues identified to the Department, to improve the dataset.

5.6. The User agrees that any use of the Dataset(s) or reliance by the User on any of the Dataset(s) is at the User's own risk and that Department shall not be held liable for any loss or damage howsoever arising as a result of such use.

5.7. The User agrees that he/she will make no statement nor permit others to make statements indicating or suggesting that interpretations/views drawn from the findings are those of the Department.

5.8. The User agrees that he/she will maintain confidentiality in accordance with item 6. Below.

6. Data Security and Confidentiality:

All Dataset(s) from the Western Cape Department of Health are to be treated as confidential and used in accordance with the following security standards:

6.1. Database storage: At a minimum the database must have user level security, may not be housed on laptops or external media unless these are encrypted. Ideally the data should be stored on a central server with restricted access and not be stored on portable computer equipment like memory sticks, external hard drives and laptops.

6.2. The Data Sets(s) must be password protected and such passwords are not to be shared with anyone other than the principle user.

6.3. Data may not be linked to personally identifiable records from any other source unless prior approval has been explicitly granted.

6.4. File storage: At a minimum files will be stored with AES encryption e.g. 7-zip, and 15 character passwords which include numbers, special characters and letters.

6.5. Passwords and files may not be provided together but using two different methods of communication e.g. data zipped and e-mailed while password is SMS'ed to User.

6.6. When the timeframe for the agreed utilisation of the data expires (see item 4.1. above) the data must be destroyed in all its forms.

7. In making information available, the Department of Health reserves the right to set conditions in which its staff (including academic staff in joint provincial posts) should be invited to participate in any research undertaken that uses the data they have generated with a view to co-authorship of the final report/s.
8. The User accepts that this data is routinely collected as part of service delivery and therefore the data quality may not be of the highest quality.
9. Failure to adhere to the written agreement can and may be sanctioned

Signatories:

Dianne Abrahams		22/12/2021
User's Name (Print)	Signature	Date
Dr M Moodley		20 August 2022
Department of Health (Designated authority)	Signature	Date