RATIONAL DRUG THERAPY MONITORING IN TYPE 2 DIABETES MELLITUS: USING GLYCATED HAEMOGLOBIN AS A GUIDE FOR CHANGE IN THERAPY

KHATHATSO MONANABELA

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DEDICATION

I dedicate this thesis to my loving husband, Joseph Monanabela, and my baby girls, Nthati and Mpho Monanabela for their support and sacrifices. Thank you for believing in me and always understanding when I had to leave to spend time in Cape Town to complete the study.

To my “late brother”, Kelebone Patrick Jane, thank you for always encouraging me to be the best.

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A thesis submitted in fulfilment of the requirement for the degree of Magister Pharmaceuticae in the School of Pharmacy University of the Western Cape

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KEY WORDS

RATIONAL MEDICINE USE

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GLYCATED HAEMOGLOBIN

SOUTH AFRICA

WESTERN CAPE

ABSTRACT

RATIONAL DRUG THERAPY MONITORING IN TYPE 2 DIABETES MELLITUS: USING GLYCATED HAEMOGLOBIN AS A GUIDE FOR CHANGE IN THERAPY

Type 2 diabetes mellitus is a progressive disease characterised by defects in insulin secretion, insulin action or both. Proper management of diabetes with appropriate drug and lifestyle interventions, guided by proper glycaemic monitoring has shown improved glycaemic control and a substantial decrease in morbidity associated with complications and mortality. Evidence-based guidelines for the appropriate management of diabetes, suggests the use of glycated haemoglobin (HbA1c) and fasting plasma glucose (FPG) as monitoring indicators and have set targets levels that indicate appropriate glucose control. In the event of suboptimal control, actions steps to adjust pharmacotherapeutic treatment has been set out. Of the two aforementioned glycaemic monitoring indicators, HbA1c is termed the 'gold standard' as it provides the most comprehensive data i.e. it reflects both fasting and postprandial glucose concentrations over a 3 months period as compared to FPG which only show glucose levels for a few hours.

The aim of this study was to describe the use of glycaemic monitoring indicators in patients with type 2 diabetes mellitus, classified as stable, treated at primary health care facilities in the Cape Town Metropolitan Region in South Africa. The study was a descriptive, retrospective and quantitative in design. Data were collected from patient medical records and included glycaemic monitoring tests and results as well as prescribing records for a maximum period of 18 months.

The study comprised of 575 participants from five primary health care facilities in the Western Cape Metropole region. All participants had FPG results, while HbA1c results were recorded for 86% of participants at least once. More than 70% of participants with either a FPG or HbA1c result showed suboptimal glucose control i.e. were outside of the target range. In 181 opportunities for intervention in participants with HbA1c results outside target, 113 (62.4%) did not have any therapy adjustments, 19 (10.5%) had the total daily dose increased, 6 (3.3%) had total daily dose decreased, 9 (5.0%) had a step-up in regimen, 5 (2.8%) had a step down in regimen and 29 (16.0%) had a lateral regimen change. In 852 opportunities for intervention in participants with FPG results outside target, 609 (71.5%) did not have any therapy adjustments, 47 (5.5%) had the total daily dose increased, 18 (2.1%) had the total

daily dose decreased, 16 (1.9%) had a step-up in regimen, 15 (1.8%) had a step down in regimen and 147 (17.3%) had a lateral change in regimen.

This study has demonstrated that in the primary healthcare facilities investigated, FPG was the most often used gycaemic monitoring indicator, glycaemic monitoring of patients mostly show suboptimal glucose control and that opportunities to optimise pharmacotherapy in diabetes management are mostly missed.

DECLARATION

I declare that the work presented in this thesis, "*Rational drug therapy monitoring in type 2 diabetes mellitus: using glycated haemoglobin as a guide for change in therapy*", is my own work, that it has not been submitted before for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged as complete references

Khathatso Monanabela

December 2015

Signed……..

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My children Nthati and Mpho for the time I had taken away from them

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LIST OF ACRONYMS

AACE	American Association of Clinical Endocrinologists
ACCORD	Action to Control Cardiovascular Risk in Diabetes
ADA	American Diabetes Association
ADVANCE	Action in Diabetes and Vascular Disease Controlled Evaluation
AIDS	Acquired Immunodeficiency Syndrome
BMI	Body Mass Index
CHC	Community Health Centre
CVD	Cardiovascular Disease
DCCT	Diabetes Control and Complications Trial
DM	Diabetes Mellitus
DoH	Department of Health
FPG	Fasting Plasma Glucose
GDP	Gross Domestic Product
HbA1c	Glycosylated Haemoglobin A1c
HIV	Human Immunodeficiency Virus
IDF	International Diabetes Federation
IDFE	International Diabetes Federation Europe
NICE	National Institute for Health and Clinical Excellence
NDP	National Drug Policy
NHI	National Health Insurance
PHC	Primary Health Care
PPP	Purchasing Power Parity
SA	South Africa
SEMDSA	Society for Endocrinology Metabolism and Diabetes of South Africa
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus

UKPDS	United Kingdom Prospective Diabetes Study
VADT	Veterans Affairs Diabetes Trial
WC	Western Cape
WHO	World Health Organisation

CHAPTER 1: INTRODUCTION

1.1 INTRODUCTION

The focus of this dissertation is on the use of HbA1c results, as the main glycaemic control indicator together with other monitoring parameters, on the therapeutic management of type 2 diabetes mellitus patients attending primary health care facilities in the Western Cape province of South Africa. The main focus is on patients classified as stable which implies good glycaemic control and /or low risk for developing complications by using retrospective patient data.

1.2 BACKGROUND TO THE STUDY

Non-communicable diseases (NCDs) are diseases that progress slowly over a long period of time and are non-infectious in nature (Puoane et al. 2013). NCDs mainly consist of cardiovascular diseases, cancers, respiratory diseases and diabetes. When combined together they are the leading causes of mortality globally (Department of Health (DoH) 2013).

Three hundred and forty seven million people were reported to have been affected by diabetes mellitus (DM) in 2008 globally (Danaei et al. 2011), with an estimate that this number will increase to 366 million people in 2030 (WHO 2010). The World Health Organization (WHO) (2010) further stated that in 2000, 814 000 people were affected by DM in South Africa (SA) and this number is expected to increase to 1-1.5 million people in 2030 (WHO 2010). Currently the prevalence of DM in SA is estimated at 9.0% in adults aged 30 years and older (Bertram et al. 2013).

There are several factors contributing to this predicted increase in NCDs, which include rapid epidemiological transition of people from rural to urban areas, ultimately resulting in physical inactivity and unhealthy eating habits which serve as the link to chronic diseases of lifestyle such as type 2 diabetes mellitus (Peer et al. 2012). Ageing populations, obesity and ethnicity are also associated with the observed increased prevalence posing a major burden on the patient's well-being and financial security. An increase in NCDs also increases the burden on health care service delivery and medical expenditure (Peer et al. 2012). Treatment of chronic diseases puts much strain on the already overburdened health system, because of the additional resources required.

1.3 PROBLEM STATEMENT

Despite the evidence that shows the benefits of attaining glycaemic goals of therapy and costs diabetes incurs, the management of diabetes is still suboptimal globally (Zhang et al 2000). Del Prato and associates (2005) stated that more than 60% of patients are not reaching glycaemic targets, and urgent steps are required in order to increase the proportions of patients achieving their glycaemic goals to reduce the risk of complications (Del Prato et al. 2005). The study conducted on microvascular complications in Durban South Africa in the Indian population, showed that patients who have long-duration diabetes mellitus, 64.5% had retinopathy, 25% had persistent proteinuria and hypertension was observed in 86% of the patients (Motala 2013). In the group that was diagnosed as patients with type 1 diabetes, retinopathy was found in 53.2% of patients, persistent proteinuria was found in 23% and hypertension in 34% indicating a high prevalence of microvascular complications (Motala 2013).

Management of DM requires a multi-disciplinary approach which involves patient participation, health personnel and other T2DM patients (Pawaskar et al. 2007). Inconsistent patient follow-ups, non-adherence to anti-diabetic medication and failure of physicians to change therapy plays a major role in patient outcomes (Wetzler & Snyder 2000). In attaining individualised glycaemic target usually requires the use of multiple anti-diabetic medications which increase adverse drug reactions affecting patient adherence. Adverse effects include weight gain and hypoglycaemia associated with the use of insulin or sulphonylureas and gastrointestinal side effects with metformin (Ismail-Beigi et al. 2011).

With regards to health care personnel, patient follow-up and therapy adjustments are important when HbA1c levels are >8%. However, considerable variations in the regularity of follow ups and therapy adjustment persist (Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) 2012; American Diabetes Association (ADA) 2014). The inconsistent use of HbA1c in monitoring and guiding treatment change by physicians in T2DM patients compromises the quality of care. HbA1c ≥8% is a proven risk factor for the development of microvascular complications and poor quality of life in individuals with diabetes (Zhang et al. 2000). Every 1% increase in HbA1c is associated with a 38% risk of macrovascular event, a 40% risk in microvascular event and a 38% risk of death (Zoungas et al. 2012).

1.4 RESEARCH QUESTIONS

The following research questions can be formulated based on the forgoing discussion:

- Is HbA1c used as the main glycaemic control indicator?
- How are the results of monitoring indicators used and responded to?
- Are the patients maintaining their glycaemic control?
- Are therapy adjustments based on the results of the monitoring indicators?

1.5 PRIMARY AIM AND OBJECTIVES

The primary aim of this study was to describe the use of glycaemic monitoring indicators in patients with type 2 diabetes mellitus, classified as stable, treated at primary health care facilities in the Cape Town Metropolitan Region in South Africa.

Specific objectives were to:

- Describe glycated haemoglobin and fasting plasma glucose results according to risk stratification as per evidence-based management guidelines.
- To assess if treatment regimens and adjustments are done in accordance with glycated haemoglobin and fasting plasma glucose results as per evidence-based management guidelines.

1.6 RESEARCH METHOD

The research method consists of two sections in conjunction with the specific research objectives, namely a literature review and an empirical investigation.

1.6.1 Literature review

The aim of the literature review is to identify methods that are implemented internationally and nationally to monitor the glycaemic control indicators in type 2 diabetes mellitus patients.

A discussion on the management of diabetes mellitus will also form part of the literature review.

1.6.2 Empirical investigation

The empirical investigation constitutes several steps, namely: the selection of the research design, the composition of the research population, the selection and application of the criteria and measuring instruments for data analysis, data application and data analysis, reliability and validity, the report and discussion of the empirical investigation, and the conclusion recommendations based on the results of the empirical investigations as well as the limitations of the investigations.

1.6.3 Report and discussion of the results of the empirical investigations

The report and discussion of the results of the investigation are illustrated graphically and in tables, in order to ensure clarity and to achieve the set aims of the investigation.

1.6.4 Conclusion, recommendations and limitations of the study

The conclusion of the study, based on the results of the literature review and investigation, as well as the recommendations derived from this study on the use of glycaemic monitoring indicators in patients with type 2 diabetes mellitus will be discussed in chapter 7. Attention will be brought to the limitations encountered during the study throughout chapters 2, 3 and 4 with further detailed discussion of these limitations in chapter 6.

1.7 DIVISION OF CHAPTERS

The division of chapters will be as follows:

Chapter 1: Introduction

Chapter 2: Health in South Africa

Chapter 3: Diabetes mellitus

Chapter 4: Methodology

Chapter 5: Results

Chapter 6: Discussion and limitations of the study

Chapter 7: Conclusions and recommendations

1.8 CHAPTER SUMMARY

In this chapter the problem statement, research questions and objectives, research method and division of chapters were discussed.

In the following chapter health in South Africa will be discussed.

CHAPTER 2: HEALTH IN SOUTH AFRICA

2.1 OVERVIEW OF THE CHAPTER

In this chapter, healthcare in general is discussed, which includes different types of healthcare as well as the way in which healthcare services are rendered and facilitated in various settings in South Africa with emphasis on the Western Cape. The distinction between private and public healthcare will be discussed with more focus on the public health sector. Burden of disease and its impact on the health sector will be discussed. Lastly the discussion will be focused on healthcare and concepts which will include; Health Framework, National Core Standards and National Drug Policy.

2.2 INTRODUCTION

In South Africa, the increasing cost of healthcare has become problematic for all health care stakeholders, including patients. This escalation in healthcare spending is due to increased life expectancy, increased patient expectations, higher standards of living and more demand for health care quality and services which is worsened by the observed quadruple burden of the disease (Dhamend 2011). The South African government also realises the importance of health care and therefore remains one of the South African Government's main concerns, particularly since the current system has been described as failing to produce a successful health care outcome pre and post-1994 (Matsoso & Fryatt 2013).

The Department of Health has therefore set out a ten-point plan to address current healthcare shortcomings and established a workable healthcare system in South Africa (Department of Health (DoH) 2011). The ten point plan are:

- Provision of strategic leadership and creation of a social compact for better health outcomes
- Implementation of National Health Insurance (NHI)
- Improving the quality of health services
- Overhauling the health care system and improving its management
- Improving human resource management, planning and development

- Revitalisation of infrastructure
- Accelerated implementation of HIV/AIDS and Sexually Transmitted Infections and increased focus on TB and other communicable diseases
- Mass mobilisation for better health for the population
- Review of the National Drug Policy
- Strengthening research and development

Although healthcare includes many aspects and elements as illustrated in the ten-point plan, the important area of healthcare to be highlighted in this chapter is that of improving the quality of health services for better health outcomes with regard to burden of disease. Implementing a successful health care system that addresses all the healthcare needs of the patient as set out in the ten-point plan is seen as a South African priority, and this chapter aims to further explore the various elements of healthcare and specifically the burden of the disease and its impact in the public health sector facilities. The focus will specifically be on quadruple burden of diseases which encompasses, HIV and AIDS epidemic, tuberculosis, maternal and child mortality, Intentional and non-intentional injuries and non-communicable diseases. This is also in-line with the government's objective of "a long and healthy life for all" (DoH 2013). To further address this, the government is in the process of establishing the national health insurance (NHI) to increase and promote access to healthcare through the establishment of the following goals (DoH 2011):

- provide improved access to quality health services for all South Africans irrespective of whether they are employed or not
- pool risks and funds so that equity and social solidarity will be achieved through the creation of a single fund
- procure services on behalf of the entire population and efficiently mobilise and control
- strengthening of the financial resources to help contain costs

- Strengthen the under-resourced and strained public sector to improve health systems performance.

2.3 HEALTHCARE DELIVERY

The World Health Organisation (WHO) (2000), in its 2000 World Health report, defines a healthcare system as follows:

"Health systems consist of all the people and actions whose primary purpose is to improve health. They may be integrated and centrally directed, but often they are not. After centuries as small-scale, largely private or charitable, mostly ineffectual entities, they have grown explosively in this century as knowledge has been gained and applied. They have contributed enormously to better health, but their contribution could be greater still, especially for the poor. Failure to achieve that potential is due more to systemic failings than to technical limitations. It is therefore urgent to assess current performance and to judge how health systems can reach their potential".

The World Health report (WHO 2000) describes a good health system, most importantly, as contributing to good health. It further explains a health system as an organisation with a series of activities with the same aim of improving; maintaining and restoring health for the population it serve, being service providers, funders, policy makers or administrators. The health system therefore has the responsibility of emphasising prevention and promotion to improve on elements that can be prevented and not neglect care and treatment to improve health outcomes (NCD strategic plan 2013-17).

2.4 SOUTH AFRICAN HEALTHCARE SYSTEM

Governments of countries have different perspectives on how to achieve good healthcare service to all patients. In response to accessible quality healthcare the government of South Africa proposed to establish national health insurance. Tanner (2008) agrees that there are different health care models followed and used across the world. Each country's health care system is a result of "its unique conditions, history, politics, and national character", and many are undergoing reform. For example Canada uses a single payer system while Germany uses employment based system insurance for its people (Tanner 2008). South Africa seems to have a combination between a single payer system, where the government pays for all medical needs (i.e. SA public health sector), and a managed competition system, where the

private sector can charge within a regulated environment and patients are free to choose which medical scheme to belong to (Erusmus 2011).

According to Schaay & Sanders (2008) there are three areas of serious concern in the SA healthcare system:

- A significant increased burden of disease related to HIV/AIDS
- Notable weakness in certain areas of health system management
- A low level of health outcomes when compared to the country's expenditure on healthcare

Peltzer (2009) found that, of all South African patients who received in-patient care, 72.2% attended a public and 24.3% a private facility. Of patients who received outpatient care at a facility, 58.7% attended a public and 35.7% a private facility. This shows that the public sector is more utilised than the private sector.

2.4.1 Public healthcare in South Africa

South Africa has a two-tiered health care system with separate public and private streams. The public health sector is however, stretched and under-resourced, generally funded by tax covering 85% of the population and the remainder of the population covered by the private health sector (Presidency 2006). It can generally be stated that the public healthcare system in South Africa is not a successful one, based on various measurements. Kleinert and Horton (2009) found that South Africa spends more on health than any other African country at 8.7% of its gross domestic product (GDP). This is similar to the healthcare spending in Sweden (8.9% of GDP).Yet South Africa is one of only 12 countries worldwide in which maternal mortality and mortality for children younger than 5 years have actually increased since 1990 (Kleinert & Horton 2009).

Econex (2013) showed that in 2013 infant mortality rate was estimated at 41.7 per 1000 live births, while maternal mortality rate was estimated to be 333 per 100 000 live births in 2009. This emphasizes the fact that South African health system performs poorly when comparing its impact on the health status of the nation to countries with a similar or poorer per capita GDP (Kleinert & Horton 2009). Life expectancy was estimated to be 70 years in 2011 globally while in 2013 life expectancy was estimated at 57.7 years for males and 61.4 years

for females in South Africa. This is largely from high prevalence of HIV, which was estimated at 10% with 5.26 million people living with HIV in 2013. Tuberculosis and non-communicable diseases are also contributing to the observed low life expectancy rates, these indicates that the South African healthcare faces overwhelming challenges (Econex 2013).

This viewpoint is further supported by Econex research which found that the poorest households, who are eligible for free public health care, pay considerable sums for private health care. They found that user dissatisfaction in the public sector were mostly due to long waiting times, unobtainable medication and rude medical staff. In the private sector, dissatisfaction was mainly due to the perceived high price of the services (Econex 2010). According to a comparative study of the quality of health systems in 48 developed and developing countries in 2008, it was found that South Africa's public sector ranked eighth from the bottom, while the private sector ranked sixth from the top (Econex 2010).

Poor health services in the public health sector are worsened by the rising prevalence of non-communicable diseases. Isaac et al (2014) showed that the ratio of chronic conditions to those of acute conditions was 82%: 18%, the study findings also indicate that most adults attending public sector facilities in the Western half of the Cape Town Metropole had chronic conditions. The cost of treating these conditions was significantly greater than that of treating acute conditions and estimated to be second to human resource (57%) and medicine cost were found to be 19% or R132 million (Isaacs et al. 2014).

The Department of Health indicated in its strategic plan for 2010-13 that it intends to establish a National Health Insurance (NHI) system as part of its health reform process. The aim of the NHI was to improve the financing and delivery of "an efficient, equitable, and sustainable health care system in pursuit of universal health care for all" (DoH 2010). The proposed NHI system focused on developing an essential health care package, the creation of an NHI fund to provide financial resources and defining the role of private funders and providers in the system (DoH 2010).

In the Green Paper on NHI released in August 2011, it was stated that the NHI will offer all South Africans and legal residents access to a defined package of comprehensive health services. It will also offer care at all levels, from primary health care to specialized secondary care, and highly specialized tertiary and quaternary levels of care (DoH 2011).

According to the NHI Policy Document (DoH 2011a), quality of service was to be ensured by:

- A radical improvement in the quality of services in the public health facilities. This means massive investment in improvement of health infrastructure, both buildings and equipment.
- Compliance to certain basic standards, and the creation of an overseeing body called the Office of Health Standards Compliance.
- A great improvement to public health care management. This was to be achieved as part of the 10-point program and speaks of a complete overhaul of the health care system.

According to a KPMG report investigating the impact of NHI in South Africa, economic benefit estimates illustrate that a one year increase in a nation's average life expectancy can increase GDP per capita by 4% in the long run. Having a healthier labour force can also result in increased productivity. Based on international studies, labour force productivity can increase between 20% and 47.5% (DoH 2011b) as illustrated in Table 2.1.

Table 2.1 Public health expenditure of various countries expressed as various ratios (KPMG 2011)

Country	**Public Expenditure on health as % of GDP**			**Public Health Expenditure as a % of total Government Expenditure**			**Public Health Expenditure per capita PPP (constant 2005 prices, US$)**		
	2007	2008	2009	2007	2008	2009	2007	2008	2009
Australia	5.56	5.56	5.56	17.10	17.10	17.10	2 190.38	2 200.64	2 211.92
Brazil	3.51	3.72	4.13	5.37	5.96	6.08	342.13	385.33	430.82
Canada	6.70	6.84	7.50	17.11	17.19	17.01	2 573.52	2 688.39	2 882.95
China	1.92	2.05	2.29	10.27	10.27	10.27	106.13	125.62	155.04
India	1.21	1.35	1.37	4.06	4.41	4.06	33.48	39.51	43.14
Russia	3.45	3.10	3.51	10.21	9.17	8.53	580.96	633.26	668.74
South Africa	3.45	3.27	3.41	11.06	10.39	9.27	336.72	334.44	345.72
United Kingdom	6.91	7.16	7.81	15.65	15.12	15.12	2 465.16	2 662.19	2 842.59
United States	6.97	7.26	7.88	19.00	18.73	18.68	3 239.53	3 425.90	3 602.45

Key: GDP-Gross Domestic Product

PPP- Purchasing Power Parity

Table 2.1 shows that in terms of public health expenditure as a percentage of GDP and public health expenditure as a percentage of total government expenditure, South Africa is comparable with countries such as Russia and Brazil. However, in terms of the public health expenditure per capita, South Africa compares poorly with countries such as Australia and the United Kingdom, where there are national health systems.

2.4.2 Private healthcare in South Africa

The private sector serves only 16% of the population yet consumes over 50% of the total healthcare spending in South Africa. It would seem that although public health care is provided mostly free of charge to users of public health services, private health care users are responsible for the bulk of their own medical expenses in the form of payments to medical schemes and this is from members predominantly from the high income groups, formally employed. The government funds private healthcare through specialised insurance funds, for example the road accident fund and workmen's compensation (Econex 2013).

The private healthcare which is also an essential tool to the right of access to health care (Francis 2013) produced the health outcomes in 2008 that were ranked alongside the healthcare sectors of countries such as Australia, Sweden, Belgium, Switzerland and Ireland (Econex 2013). The linkage of the private sector with the public sector is a health system success even though the huge load on the health system increases as HIV/AIDS and TB transits to becoming chronic diseases requiring lifelong treatment and care (Coovadia et al 2009).

2.5 HEALTH FRAMEWORK

According to WHO (2007) health systems framework consists of all organizations, people and actions whose primary interest is to promote, restore or maintain health. For example, all health systems have to provide services, develop health workers, mobilize and allocate finances, ensure health system leadership and governance. Framework is meant to measure performance, understand the factors that contribute to it, improve it, and respond better to the needs and expectations of the people within the country (Schaay et al 2011). Figure 2.1 illustrates the WHO health system framework building blocks.

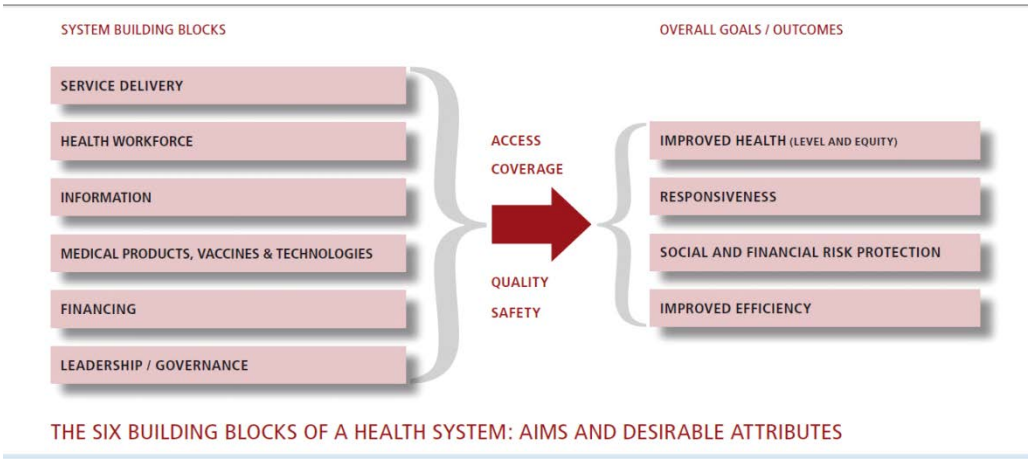

Figure 2.1 The World Health Organisation system framework building blocks (WHO 2007)

2.5.1 Service Delivery

Service delivery refers to what the system does not what it is, it also refers to the way inputs such as money, staff, equipment and drugs are combined to allow the delivery of health interventions with minimum waste of resources (WHO2000).

2.5.2 Health Workforce

Health workforce involves making use available multi skilled personnel, more especially in disadvantaged areas and strategies to retain personnel, to ensure equity and accessibility of health services for patients (WHO2007).

2.5.3 Information

Health information is used by policy-makers, planners, health care providers, development partners and the general public to track health-system performance, to support better health policies and make effective health-related decisions; it is a national asset (WHO2007).

2.5.4 Medical products, vaccines & technologies

Essential medicines should always be available at affordable costs to individuals and systems. They should be in adequate amounts, in the appropriate dosage and in good quality. They should be selected based on efficacy, safety and cost effectiveness (WHO2007)

2.5.5 Financing

The goal of health financing is to ensure adequate spending on health and effective allocation of financial resources to different types of public and personal health services. Health financing is important in analysing health policies, sources of funds and effectiveness of health services delivered to the population (WHO2007).

2.5.6 Leadership / governance

Health governance refers to the wide range of functions carried out by governments to improve population health while ensuring equity in access to services, quality of services, and patients' rights (WHO2007).

The South African health framework has been formulated in-line with the WHO framework for strengthening and assessing the performance of health systems (Schaay et al 2011). Figure 2.2 shows the national health framework of South Africa

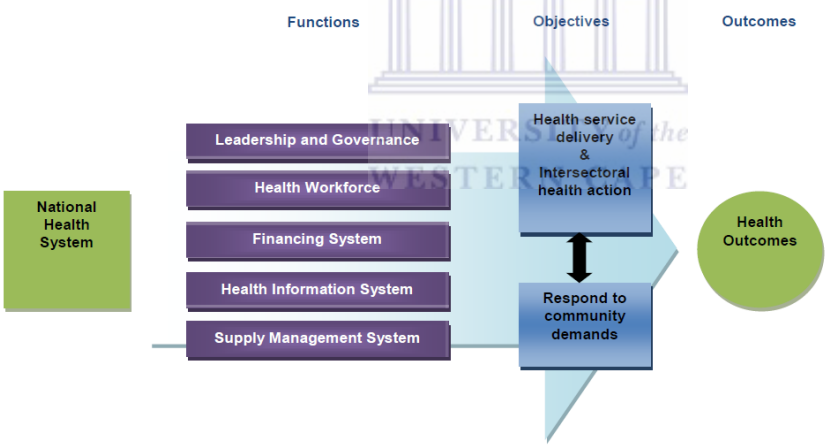

Figure 2.2 The national health framework of South Africa (Adopted from Schaay et al (2011))

Figure 2.2 shows that for a health system to be able to measure its performance and achieve its objectives which are delivery of accessible, equitable and good quality health services which addresses the demands of the citizens, the national health system has to embark on a number of activities. For example, ensuring appropriate stewardship; developing human resources for health; mobilising and allocating adequate finances; developing and maintaining a well-functioning health information system and ensuring equitable access to essential medical products, vaccines and technologies (Schaay et al 2011).

2.6 NATIONAL CORE STANDARDS

The importance of good quality care in patients and monitoring of the outcomes of healthcare was facilitated through the establishement of the National Core Standards by National Department of Health. The National Core Standards are tools used to achieve, guide and monitor the quality of health outcomes in both the patients and personnel and also the health establishments (National Department of Health (NDoH) 2011).

The following objectives were set to achieve this:

- To develop a benchmark of quality care which should be found in all health centres across the country.
- To develop a monitoring system which will assess all health establishments, identify gaps and appraise improvements.
- Certification of health establishments with set standards (NDoH 2011)

The Department of Health has also developed seven domains of national core standards which are areas of potential risk and therefore needs attention (Connell 2014), these are

- Patient rights
- Patient safety, clinical governance and care
- Clinical support services
- Public health
- Leadership and corporate governance
- Operational management
- Facilities and infrastructure

Each domain is further sub-divided into sub-domain to make the main domains easily implemented and monitored, the first three domains dealt with the main business of the health system which is delivering quality health care to patients, and health outcomes while the last

four domains deals with ensuring that the core business is easily implemented (Schaay et al 2011) Table 2.2.

Table 2.2 The domains and sub-domains of the Department of Health

Domain	Sub-domain
Domain 1: Patient Rights	Respect and dignity Information to patients Physical access Continuity of care Reducing delays in care Emergency care Access to package of services Complaints management
Domain 2: Patient Safety, Clinical Governance and Care	Patient care Clinical management for improved health outcomes Clinical leadership Clinical risk Adverse events Infection prevention and control
Domain 3: Clinical Support Services	Pharmaceutical services Diagnostic services Therapeutic and support services Health technology services Sterilisation services Mortuary services Efficiency management
Domain 4: Public Health	Population-based service planning and delivery Health promotion and disease prevention Disaster preparedness Environment control
Domain 5: Leadership and Corporate Governance	Oversight and accountability Strategic management Risk management Quality management Effective leadership Communications and public relations
Domain 6: Operational Management	Human resource management and development Employee wellness Financial resource management Supply chain management Transport and fleet management Information management Medical records
Domain 7: Facilities and Infrastructure	Buildings and grounds Machinery and utilities Safety and security Hygiene and cleanliness Linen and laundry Food services

Adopted from Whittaker et al 2011

Although healthcare with regard to national core standards includes many facets and elements as illustrated in the domains and their sub-domains the current chapter is interested in the first four domains which deals specifically with the health system concepts.

2.7 TYPES OF HEALTHCARE

The WHO (1948) defines health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”.

A health system focuses on the health of people and consists of many components (World Bank 2007). The functions of a health care system are service provision, and also regulation, policy creation and management of resources (human or medical products such as medication or equipment). It is the responsibility of, among others, ministries of health, health care providers and organisations, pharmaceutical companies and health care funders. A health care system influences the lives of patients and their families in the broader community (World Bank 2007). Marmor & Wendt (2012) define health care as “the work that patients, doctors, nurses, druggists, and hospitals do when facing real or feared illness”.

Berry & Mirabito (2010) describe the basic functions of a health care system as including primary care, doctors’ visits, inpatient treatments and tests (ambulatory care) as well as emergency treatment.

2.7.1 Primary health care

According to the WHO’s Primary Care Division (WHO 2010), the main goal of primary healthcare is better health for all. The five elements needed to achieve this goal are:

- reducing exclusion and social disparities in health
- organizing health services around people's needs and expectations
- integrating health into all sectors
- pursuing collaborative models of policy dialogue (leadership reforms)
- increasing stakeholder participation

Primary care is defined by Rothman & Wagner (2003) as “the provision of integrated, accessible health care services by clinicians who are accountable for addressing a large majority of personal health care needs, developing a sustained partnership with patients and practicing within the context of family and community”. Majority of chronic illnesses are managed in primary health care. This was evident in the United States of America where by

90% of diabetic patients were managed in the primary care indicating that efforts in improving primary care must be maintained (Rothman & Wagner 2003).

In South Africa, the concept of primary health care (PHC) emerged during the 1970s when health care concepts began to change generally and specifically in relation to the developing world (Schaay & Sanders 2008). The development of community orientated primary care in South Africa led to more focus on outreach beyond hospitals to more outlying health centres. This even reached out as far as individual households. South Africa like the developed countries more patients seen in the primary health care facilities are patients with chronic illnesses. This was evident in the Western Cape where 23 395 hypertensive and 13 338 diabetic patients attend primary health care services monthly (Parker et al 2012).

Department of Health's 10-point plan in addressing the current shortcomings established a workable healthcare system in South Africa which looked at, revitalisation of primary health care entailing completion of the audit of primary health care infrastructure and services, acceleration of infrastructure delivery of primary level facilities, and refurbishment and preventative maintenance of all hospitals. The plan was that "district teams" were to be appointed to manage the primary health care facilities in each of the 52 districts (DoH 2010).

Schaay et al. (2011) state that the primary health care system in SA has failed to reach several goals and standards over the past years and describe the envisaged primary health care re-engineering as follows (Schaay et al 2011):

- Greater focus on the delivery of community-based services, with an emphasis on disease prevention, health promotion and community participation. This will not only cure but also prevent. These outreach activities are to be performed by a primary health care outreach team consisting of nurses and community health workers, who are supported by facility-based and specialist support teams of health professionals.

- Greater attention will be given to those factors outside the health sector that impact on health (social factors influencing health).

2.7.2 Ambulatory care

Stedman's Medical Dictionary (2013) describes ambulatory care as "medical or surgical health treatment provided during an episode of care that does not require an overnight stay in

a medical facility and from which the patient goes home; outpatient rather than inpatient care". According to Eggli et al. (2006) ambulatory care is a growing avenue for health care in Switzerland, and there is a growing need for information about the cost and the quality of care to be made more widely available. There is also a need for performance measurement systems for ambulatory care in this country. In Taiwan, the total ambulatory care was a cost driver in the health care system, with expenditure amounting to 66% of the total medical expenses. In the same year, inpatient care cost the country 34% of total medical expenses (Yeh et al. 2005).

In a study in the US performed by Amal et al. (2010) increasing co-payments for ambulatory care reduced the use of outpatient care among elderly patients in managed-care plans. However, this decline was offset by an increase in hospitalisations. These expensive hospitalisations were particularly prevalent among those with chronic diseases. Increasing co-payments for ambulatory care among elderly patients may therefore be seen to have negative health consequences and may increase spending for health care (Amal et al. 2010).

Ambulatory or outpatient care is therefore an important part of the health care provision chain, as it is more advanced than primary care, but it can still screen and prevent or recommend patients being admitted to hospital for inpatient care. Cost of ambulatory care, however, seems to be high in the instances mentioned.

Harris et al. (2011) state that in South Africa, primary health care is mostly utilised by lower income and education groups, while the rich are three times more likely to use private hospitals and private ambulatory care like GPs and dentists. Peltzer (2009) agree that primary health care is the most frequently used system in SA and mention that, in many areas of South Africa, the primary health care (PHC) facilities are the only available or easily accessible health service for local communities. PHC services are therefore often overburdened.

2.7.3 Hospital care

According to Chen et al. (2010), high and growing hospital costs are a reality. When comparing hospital costs in the private and public sector using Council for Medical Schemes (CMS) data, Schussler (2009) found that the total cost per admission into private hospitals increased by 22.1% from 2001 to 2006, and the total cost per admission into public hospitals

from 2001 to 2006 increased even more, by 57.7%. Hospital costs, however, are just one of the components of health care that have increased over the past years in South Africa.

Schussler (2009) discusses changes in health care costs when compared to Consumer Price Inflation (CPI) and found that, when comparing price increases from 2000 to April 2008, medical schemes had the highest increase (158% to CPI), followed by doctors (which includes nursing fees) at 137% over the total period. Optician fees increased by 87% and private hospital inflation were 74%. Overall Consumer Price Index (CPIX) was relatively lower at 64%, whilst public hospitals inflation was only 13%.

Litvak & Bisognano (2011) found that the new Affordable Care Act in the US will likely have the net effect of a large influx of new patients who have health insurance, including many who are likely to be older and sicker than current patients. At the same time, hospitals may face greater financial pressure than ever before. They further proposed that US hospitals will need to become more efficient in order to lower costs, and the activities suggested to achieve this include (Litvak & Bisognano 2011):

- Reducing patient length of stay (LOS)
- Expanding hospital capacity
- Expanding staff
- Increasing bed occupancy

Chang et al. (2004) describe several input factors that were taken into consideration when determining the quality of hospital care in Taiwan:

a. Number of patient beds (including general beds, special treatment beds, psychiatric beds, chronic beds, tuberculosis beds and leprosy beds)

b. Number of doctors and physicians

c. Number of nurses (including registered professional nurses and registered nurses)

d. Number of medical support personnel (including pharmacists, assistant pharmacists, medical technologists, medical technicians, medical radiological technologists, midwives and dieticians)

The three outputs considered were:

a. Number of patient days which include general care, acute and intensive care, and chronic care patient days

b. Number of ambulatory and emergency clinic visits

c. Number of patients receiving surgery

2.7.4 Pharmaceutical care

Allemann et al. (2013) define pharmaceutical care as "the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes".

According to Björkman et al. (2008), pharmaceutical care is a worldwide movement among pharmacists. The term presents new ideas about how to take care of patients' medication related needs and has stimulated pharmacists to develop the pharmaceutical profession.

The philosophy of pharmaceutical care encourages pharmacists to practice beyond ensuring that patients receive the right drug in the right dose in the right form at the right time. Pharmacists should now also see to it that medication-related health outcomes are optimized (Allemann et al 2013).

According to the American Society of Hospital Pharmacists (ASHP 1993), the mission of the pharmacist is to provide pharmaceutical care. Pharmaceutical care is defined as "the direct, responsible provision of medication-related care for the purpose of achieving definite outcomes that improve a patient's quality of life".

The ASHP (1993) also lists the following outcomes to be achieved by pharmaceutical care:

- Cure of a patient's disease
- Elimination or reduction of a patient's symptomatology
- Arresting or slowing of a disease process
- Prevention of a disease or symptomatology

2.8 NATIONAL DRUG POLICY

An access to essential medicines is an essential component of a health system. In relation to provision of healthcare services the South African government established National Drug Policy to promote accessibility, availability and affordability of essential medicines that are safe and effective (DoH 1996).

The establishment of the National Drug Policy among other aspects deals with the following:

It covers a wide range of how pharmaceutical services will be managed within the country. For example it includes, monitoring of prices, licensing of premises and professionals, and who should handle and dispense medicines. Increase availability of essential medicines in the public sector as well as the private sector. Improve quality of care to patients with a consequent impact on health outcomes (DoH 1996).

National Drug Policy was established with the following objectives to deliver its mandate for the benefit of the citizens of South Africa. Table 2.3

Table 2.3 Objectives of the National Drug Policy (DoH 1996)

Objective	Expected outcome
Health objectives	To ensure the safety, efficacy and quality of drugs To ensure good dispensing and prescribing practices To promote the rational use of drugs by prescribers, dispensers and patients through provision of the necessary training, education and information To promote the concept of individual responsibility for health, preventive care and informed decision making.
Economic objectives	To lower the cost of drugs in both the private and public sectors To promote the cost-effective and rational use of drugs To establish a complementary partnership between Government bodies and private providers in the pharmaceutical sector To optimize the use of scarce resources through cooperation with international and regional agencies
National development objectives	To improve the knowledge, efficiency and management skills of pharmaceutical personnel To re-orientate medical, paramedical and pharmaceutical education towards the principles underlying the National Drug Policy To support the development of the local pharmaceutical industry and the local production of essential drugs To promote the acquisition, documentation and sharing of knowledge and experience through the establishment of advisory groups in rational drug use, pharmacoeconomics and other areas of the pharmaceutical sector

2.9 SUMMARY OF THE CHAPTER

Rational use of medicines is defined by WHO as “patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements” (WHO 1985). It is estimated that half of all medicines globally are inappropriately prescribed, dispensed or sold (Hogerzeil 1995). Failure to prescribe in accordance with clinical guidelines is one of the common causes of irrational use of medicines. Lack of access to medicines as well as inappropriate doses result in serious morbidity and mortality in chronic diseases such as diabetes (WHO 2002).

Globally as well as on a local level attempts have been made to reduce the burden of non-communicable disease on health care systems as well as improve patient outcomes. In the Western Cape province of South Africa the health department has made it a goal to improve health outcomes of chronic diseases, like diabetes. In the context of the discussed policy documents, frameworks and goals, this study aims to provide evidence on prescribing and therapy monitoring practices of diabetes mellitus patients in public primary health care facilities. These data should be useful in identifying the current use of glycated haemoglobin and fasting plasma glucose and its correlation with evidence-based guidelines.

CHAPTER 3: DIABETES MELLITUS

3.1 OVERVIEW OF THE CHAPTER

In Chapter 3, diabetes mellitus is discussed, with reference to pathogenesis and classification, pathophysiology and natural history, clinical presentation which includes treatment goals, pharmacological treatment, treatment monitoring and adjustments, and, complications are discussed.

3.2 INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent chronic diseases globally, and continues to increase in number and significance (Wetzler & Snyder 2000). Diabetes is defined as a group of metabolic disorders that are characterised by hyperglycaemia which result from defects in insulin secretion, insulin action or both. DM is categorised into four types on the basis of aetiology and clinical presentation: type l diabetes, type 2 diabetes, gestational diabetes and other types of diabetes from other causes (Sicree, Shaw & Zimmet 2012).

The World Health Organisation (WHO) stated that in 1995 DM was already estimated to have affected 135 million people globally (WHO 2010). In Africa 7.8 million people in 1997 were also reported to have been affected by DM (Molleutze & Levitt 2005). Danaei et al (2011), have reported that 347 million people were affected by DM in 2008 globally, with an estimate that the number will increase to 366 million people in 2030 (WHO 2010). WHO (2010) further stated that in 2000, 814 000 people were affected by DM in South Africa (SA) and this number is expected to increase to 1-1.5 million people in 2030 (WHO 2010). Currently the prevalence of DM in SA is estimated at 9.0% in adults aged 30 years and older (Bertram et al. 2013), with the prevalence of 4.2% in female and 2.7% in males in the Western Cape in 2005 (Molleutze & Levitt 2005).

Type 2 DM (T2DM) make up 85 to 95% of all diabetes types in high income countries and constitutes even higher percentages in low and middle income countries (Sicree et al. 2012). The prevalence of T2DM is increasing rapidly worldwide. As such, T2DM is a common serious global health problem which have evolved in many countries along with rapid cultural and social changes such as, increasing urbanization, ageing populations, dietary changes, reduced physical activity, obesity and other unhealthy lifestyle-associated behavioural patterns (Sicree et al. 2012; Igbojiaku et al. 2013).

T2DM is classified as a chronic metabolic disorder characterised by progressive worsening hyperinsulinaemia and insulin resistance which if left untreated or managed poorly leads to high morbidity and mortality from microvascular and macrovascular complications (Chan, Abrahamson 2003). Alternatively, proper management of diabetes with appropriate drug and lifestyle interventions have yielded improved glycaemic control and a substantial decrease in morbidity associated with complications and mortality (Nathan et al. 2009a). The primary therapeutic goal for T2DM thus necessitate tight glucose control set at an individualised target, based on patient age, risk factors and complications (Wetzler, Snyder 2000). A useful monitoring tool for glucose control is glycated haemoglobin, also abbreviated as HbA1c (Nathan et al. 2005).

3.3 PATHOGENESIS OF DIABETES MELLITUS AND CLASSIFICATION OF DIABETES MELLITUS

Diabetes mellitus is defined by the American Diabetes Association (2010) as "a group of metabolic diseases characterised by hyperglycaemia, resulting from defects in insulin secretion, insulin action, or both". Diabetes mellitus can be classified into four different types, (American Diabetes Association 2010) which are described in Table 3.1.

Table 3.1 Classification of diabetes mellitus

Type	**Description**
Type 1: Insulin-dependent diabetes	It occurs when there is an insulin deficiency (complete or severe), associated with the autoimmune destruction of beta β-cells of the pancreas (Triplitt 2011).
Type 2: Non-insulin dependent diabetes	This type is described as a combination of "absent or inadequate pancreatic insulin secretion", together with "tissue resistance to the action of insulin''(Triplitt et al. 2014)
Type 3: Other specific types of diabetes	This type of diabetes may occur as a result of genetic syndromes, pancreatic disorders and drugs (Mbanya & Ramiaya 2006).
Type 4: Gestational diabetes	This condition is described as either the initial development or the detection of glucose intolerance during pregnancy (Mbanya & Ramiaya 2006). Glucose intolerance may develop during pregnancy

Type	Description
	because of the high levels of anti-insulin hormones that are released from the placenta, especially during the third trimester. Most often, glucose tolerance normalises after six weeks, but in some patients, it may continue and manifest as type 2 DM (Mbanya & Ramiaya 2006).

Type 1 and Type 2 DM are the major classifications of diabetes conditions that are encountered in Sub-Saharan Africa (Mbanya & Ramiaya 2006). There are specific characteristics which differentiate these two types of DM. For the purpose of this thesis the focus will be on Type 2 DM.

3.4 AETIOLOGY AND NATURAL HISTORY OF TYPE 2 DIABETES MELLITUS

Insulin resistance and an insufficient insulin secretion response are considered to be the causes of type 2 DM. However, the specific aetiologies of insulin resistance and secretion in type 2 DM are relatively unknown (Mbanya & Ramiaya 2006). The cells in the liver, skeletal muscles and adipose/fat tissue become less sensitive to insulin and ultimately become insulin resistant (Hawkins et al. 2002: Alberti, Zimmet & Shaw 2006). When insulin resistance occurs, glucose can no longer be absorbed in the cells, since insulin is the hormone that enables glucose absorption (Hawkins et al. 2002, Alberti et al 2006). The glucose molecules remain in the blood stream, which prompts the pancreas to produce more insulin in order to compensate for insulin resistance and absorb the glucose molecules (Alberti et al. 2006). The constant demand for more insulin production eventually puts a lot of pressure on the β cells of the pancreas and ultimately leading to their decreased functioning (Alberti et al. 2006). When the β cells are no longer able to produce insulin, the person becomes hyperglycaemic characterised by an increased plasma glucose levels. At this stage, the patient is diagnosed with type 2 DM (Hawkins et al. 2002, Alberti et al 2006).

Urbanisation and changes in lifestyle associated with economic developments that have been observed in Africa are similar to international trends (Dalal et al. 2011). In Sub-Saharan Africa people migrated from rural environments to urban areas, this was inevitably associated with a shift in lifestyle from a relatively healthy traditional pattern, to the urban scenario of a western diet high in saturated fat and low in fresh fruit and vegetables (Gill et al. 2009). Low levels of exercise, smoking, increased alcohol intake and urbanisation are the major factors

leading to the development of type 2 DM. This rapid epidemiological transition is driving the emergence of high and increasing prevalence rates of type 2 DM in South Africa (Bertram et al. 2013).

3.5 COMPLICATIONS

The ADA (2014) reports that there is "long-term damage, dysfunction and failure of different organs; especially the eyes, kidneys, nerves, heart and blood vessels", linked to the chronically increased blood glucose levels evident in diabetics. These complications form part of the major factors accounting for the increased morbidity and mortality rates on a global level; and they may be broadly classified into the following two categories: macrovascular and microvascular (ADA 2014). As the names describe, macrovascular complications involve the large arteries, whereas microvascular complications include those affecting the smaller blood vessels and capillaries (Triplitt et al.2014). Table 3.2 contrasts examples of the two different types of complications of DM.

Table 3.2 Macrovascular and microvascular complications of diabetes mellitus.

MACROVASCULAR COMPLICATIONS	**MICROVASCULAR COMPLICATIONS**
Stroke	Amputation
Angina	Autonomic Neuropathy
Myocardial Infarction	Diabetic Retinopathy
Peripheral Vascular Disease	End-stage renal disease
Cardiac Failure	Erectile Dysfunction
Transient Ischaemic Heart Attack	Micro-/Macro-albuminuria
	Osteomyelitis
	Peripheral Neuropathy

Adopted from SEMDSA 2012 & ADA 2014

In 2006, Mbanya and Ramiaya reported on studies performed on the South African prevalence of diabetes complications. In a study performed by Gill, Huddle and Rolfe in 1995 in a secondary care clinic, 42% of 64 patients were found to suffer from neuropathy. In another study performed by Bawa, Bradshaw, Levitt, Maphumolo and Zwarenstein in 1997, 37% of 300 patients in a primary care clinic, were reported to have suffered from

nephropathy. In 1997, in a study conducted by Becker, Joannou, Kalk, Mahanlal, Mahomed and Ntsepo, retinopathy was found to be prevalent amongst 37% of the 507 patients who were attending a secondary care clinic.

3.6 TREATMENT

3.6.1 Treatment goals

Goals of therapy in diabetes mellitus are to control blood sugar level, achieve and maintain HbA1c values below the patient's individualised target levels prevent acute complications of glycaemia and manage chronic conditions associated with diabetes, e.g hypertension and dyslipidaemia. Also prevention and treatment of microvascular and macrovascular complications of diabetes (Department of Health (DoH) 2008; SEMDSA 2012)

3.6.2 Drugs

The pharmacological management of T2DM entails the use of oral hypoglycaemic agents and insulin, either as monotherapy, or in combination. The hypoglycaemic agents that are available in the public sector are; metformin, sulfonylurea derivatives e.g gliclazide, glimepiride and glibenclamide and insulin (DoH 2008; DoH 2012). The oral hypoglycaemic agents are categorised according to their different mechanisms of action. Table 3.3 summarises all the different types of oral hypoglycaemic agents in terms of their mechanisms of action, mean lowering of HbA1c, therapeutic considerations and disadvantages.

Table 3.3 Anti-diabetic medications used in the management of T2DM adopted from SEMDSA (2012)

Class	Drug	Mean lowering of HbA1c	Therapeutic considerations	Disadvantages
Alpha-glucosidase inhibitors	Acarbose	<1%	Weight neutral as monotherapy, targets postprandial hyperglycaemia	Gastrointestinal effects, needs frequent doses
Biguanides	Metformin	1-2%	First line drug in obesity, reduces cardiovascular events and mortality	Gastrointestinal side-effects.
Incretins	Dipeptidyl peptidase-4 inhibitors: linagliptin, saxagliptin, sitaqliptin, and vildagliptin	<1%	Weight neutral, improves postprandial hyperglycaemia	

Class	Drug	Mean lowering of HbA1c	Therapeutic considerations	Disadvantages
	Glucagon-like peptide agonists: Exenatide and Luraglutide	1-2%	Causes weight loss, possible potential for improved beta cell function	
Insulin secretagogues	Sulphonylureas: Glibenclamide, Gliclazide, Glimepiride and Glipizide Meglitinides: Nateglinide Repaglinide	1-2% 1% 1-2%	Well tolerated, relatively rapid glucose-lowering response. Associated with less hypoglycaemia than sulphonylureas	Hypoglycaemia relatively common but variable, glibenclamide can cause severe hypoglycaemia and weight gain. Causes hypoglycaemia and weight gain.
Insulin	Rapid-acting analogues Short-acting regular Intermediate-acting Long-acting basal analogues Pre-mixed human Pre-mixed analogue	>2%	Potentially greatest HbA1c reduction and no maximal doses, numerous formulations and delivery systems allow for regimen flexibility.	Significant risk of hypoglycaemia. Increased risk of weight gain.

3.6.3 Treatment monitoring

Glycaemic control and frequent monitoring are essential in the management of diabetes (Del Prato et al 2005). Diabetic Control and Complications Trial (DCCT), United Kingdom Prospective Diabetes study (UKPDS) and Action in Diabetes and Vascular Disease: Preterex and Diamicron Modified-Release Controlled Evaluation (ADVANCE) have shown in their studies that there is a correlation between glycated haemoglobin, glucose level and the risk of the development of both macrovascular and microvascular complications (Patel et al. 2008; Igbojiaku et al 2013). Glycated haemoglobin (HbA1c) is a measure that reflects both fasting

and postprandial glucose concentrations over a 3 month period (Sherifali et al. 2010) and is therefore an immportant indicator for assessing the quality of diabetes care in patients (Zhang et al. 2000). Nathan et al. 2008, further highlighted that HbA1c is thus used as a gold standard in assessing chronic glycemia.

In a nine-year follow-up study involving 4662 men and 5570 women, Khaw (2003) demonstrated that a 1% rise in the level of HbA1c was associated with an increased risk of death of up to 28% and 24% in women and men respectively. Alternatively, Tkac (2009) and Del Prato et al. 2005 have highlighted that findings from the UKPDS study, have revealed that a decrease in HbA1c resulted with a decreased chances of myocardial infarction by 14%. While Zhang et al 2000, have found that HbA1c of >9.5% was a risk factor for the progression and poor life in individuals with diabetes.

The American Association of Clinical Endocrinologists (AACE) (2007) issued guidelines that placed emphasis on the importance of achieving and maintaining glycaemic levels as close as possible to the normal non-diabetic level (American Association of Clinical Endocrinologists 2007). These recommendations are based on the findings from epidemiological studies mentioned earlier. Many countries have developed management guidelines with specified glycaemic targets in order to manage and monitor these chronic conditions as illustrated in Table 3.4.

Table 3.4 General glycaemic targets for the care of patients with diabetes as recommended by various organizations and Department of Health (2008) primary health care guidelines.

Organization	**HbA1c (%)**	**Fasting Plasma Glucose (mmol/L)**	**Postprandial glucose (mmol/L)**
DoH (2008) (Primary health care)	<7	4-6	4-8
SEMDSA (2012)	<7	4-6	4-8
American Diabetes Association (2014)	<7	3.9-7.1	<10
American Association of Clinical Endocrinology (2007)	≤6.5	<6.0	<7.8
International Diabetes Federation-Europe (IDFE) (2007)	≤6.5	≤6.0	≤7.5
National Institute for health and Clinical Excellence (NICE) 2014	≤6.5	<6	<7.0

However, HbA1c differs from other monitoring parameters in that it must be individualised, because it is influenced by age, race/ethnicity, type and duration of diabetes, comorbidities and patient adherence (Zhang et al. 2000).As illustrated in Table 3.5.

Table 3.5 Individualised targets for glycated haemoglobin, fasting plasma glucose and postprandial glucose (SEMDSA 2012)

Patient type	Target HbA1c	Target FPG	Target PPG
Young, stable patient at individualised targets, this patient is at low risk of developing complications. Newly diagnosed No cardiovascular disease	<6.5%	4.0-7.0mmol/L	4.4-7.8mmol/L
Majority of patients	<7%	4.0-7.0mmol/L	5.0-10.0mmol/L
Elderly patient unstable at individualised targets and the body fails to recognise episodes of hypoglycaemia due to lack of symptoms. This patient is at high risk of developing cardiovascular complications due to hypoglycaemia.	<7.5%	4.0-7.0mmol/L	<12.0mmol/L

The Society for Endocrinology, Metabolism and Diabetes of South Africa have indicated a strong epidemiological evidence that HbA1c levels >7.5% in T2DM have a 2.5-5 fold greater relative risk of developing microvascular complications, and a 5 fold greater risk of developing peripheral artery disease (SEMDSA 2012).

Regular monitoring and appropriate response to abnormal results have been shown to reduce complications such as myocardial infarction, cerebrovascular accidents and retinopathy in diabetic patients (Igbojiaku et al. 2013). Current South African guidelines for primary health care indicate that all people with diabetes should have their HbA1c repeated either every 3-6 monthly for those with therapy adjustments or HbA1c levels above target, or annually for those with HbA1c levels at target and no therapy adjustments Table 3.6 (DoH 2012).

Table 3.6 Diabetes monitoring tests and frequencies (DoH 2008)

Test	Frequency
HbA1c	Every 3-6 monthly if treatment changes or goals not met. Annually monthly if stable.
Fasting plasma glucose test	Every routine diabetes visit
Postprandial glucose test	Every routine diabetes visit
Random glucose test	Every routine diabetes visit
Blood pressure	Every routine diabetes visit
Serum potassium	Annually
Serum creatinine	Annually
Waist circumference	Every routine diabetes visit
Comprehensive foot examination	Every routine diabetes visit,
Fundoscopy	Annually
Proteinurea	Every routine diabetes visit
BMI	Every routine diabetes visit
Lipids profile	Annually

3.7 ADJUSTING TREATMENT

Diabetes treatment is adjusted based on HbA1c results (Nathan et al. 2008). Results from the UKPDS 33 shows that from the newly diagnosed type 2 diabetes patients treated with the intensive glycemic control with sulphonylureas or insulin obtained a median HbA1c of 7.0% during a 10-year follow-up while patients in the conventional group (managed with lifestyle modification) obtained a median HbA1c of 7.4% (Tkác 2009). A significant risk reduction of 12% in the incidence of any diabetes related endpoint in the intensive group was observed. The diabetes-related death and all-cause mortality were both not significantly reduced by 10% and 16% respectively (Tkac 2009).

Tkac (2009), and MacIsaac & Jerums (2011) have highlighted that in UKPDS 34 of 1704 overweight patients with type 2 diabetes were randomised to intensive treatment by metformin, sulphonylurea/insulin or to conventional treatment. Patients treated by intensive metformin treatment had median HbA1c level of 7.4% during the follow-up, while patients in the conventional group had median HbA1c level of 8.0%. Patients allocated to metformin when compared to the conventional group had significantly reduced risk for diabetes related

end point by 32%, for diabetes death by 42%, for all-cause mortality by 36% and for fatal/non-fatal myocardial infarction by 39% (MacIsaac & Jerums 2011). Holman et al.(2008) further indicated that in the same study, patients allocated to metformin when compared to patients allocated to insulin/sulphonylurea had lower risk for any diabetes related endpoint, for all-cause mortality and for stroke. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial 10251 patients with mean age 62years and median duration of 10 in diabetes were randomly selected and assigned to intensive glucose-lowering treatment with a target of HbA1c <6% or to a standard diabetes treatment targeting HbA1c level in the 7.0-7.9% (Tkac 2009). There was no specific treatment in either group (Holman et al 2008). The intensive group obtained a median HbA1c of 6.4% while the standard group obtained a median 7.5% (Holman et al 2008).

The study was terminated after 3.5 years of follow-up in 2008 because of observed 22% significant increase in all-cause mortality and 35% increase in cardiovascular mortality in patients with intensive glycemic control (Tkac 2009). The primary end point of the study was non-significantly reduced in the intensive treatment group by 10%. While significant reduction in the incidence of nonfatal myocardial infarction by 24% was observed in the intensive therapy group. The analysis from this group revealed a significantly more beneficial effect on primary endpoint reduction in the intensive treatment group in patients without previous cardiovascular disease with diabetes control of HbA1c of 8.4% (Tkac 2009).

In the ADVANCE study, 11140 patients with mean age 66years and mean diabetes duration of 8 years were randomly assigned to intensive treatment with the use of gliclazide modified release and other drugs with a target of HbA1c <6.5% or standard treatment(Holman et al 2008). The median follow-up of patients was 5years. The primary endpoint of combined major macrovascular and microvascular events was reduced significantly by 10% in the intensive treatment group. 6% reduction in the incidence of macrovascular events was observed. In comparison to ACCORD trial no significant increase in all-cause mortality was observed. The most pronounced effect in this study was a 21% reduction of the development of new or worsening nephropathy (Tkac 2009).

In the Veterans Affairs Diabetes Trial (VADT) , 1791 patients with mean age of 60 years and mean diabetes duration of 11.5 years were randomly assigned to intensive diabetes treatment aiming for HbA1c <6% and standard treatment group aiming for HbA1c<9% (Duckworth et

al. 2011). The goal for HbA1c between group differences was 1.5%. The intensive group had median on-treatment HbA1c was 6.9% and 8.4% for the standard group. The primary endpoint was any major cardiovascular event. After the median follow-up of 5.6 years, there was observed a non-significant reduction of primary endpoint in the intensive treatment group by 12%. Patients treated with intensive regimen had reductions in worsening albuminuria by 38% with borderline significance (Tkac 2009).

The Prospective Pioglitazone Clinical Trial in Macrovacular Events (PROactive) study consisted of 5238 patient with developed macrovascular diseases. The interventional study group patients were given pioglitazone in addition to the previous treatment (Tkac 2009; Aguilar 2011). The treatment resulted in on-study difference of HbA1c level by 0.6% between the treatment groups. The patients on pioglitazone had non-significantly reduced the incidence of widely defined primary endpoint by 10%. The incidence of secondary endpoint (total mortality, non-fatal myocardial infarction and stroke) which was not predefined in the study design significantly reduced by 16% in the pioglitazone treatment patients (Tkac 2009; Aguilar 2011). In patients with previous stroke, pioglitazone treatment reduced fatal and non-fatal stroke by 47% and in patient with previous myocardial infarction pioglitazone reduced fatal and non-fatal myocardial infarction by 28% (Tkac 2009). The results of these epidemiological studies leads to an individualisation of diabetes control goals (table 3.5). According to SEMDSA the general goal of HbA1c<7% should be maintained, but for certain groups of patients more stringent goal must be recommended based on the subgroup analysis of the mentioned studies (SEMDSA 2012).

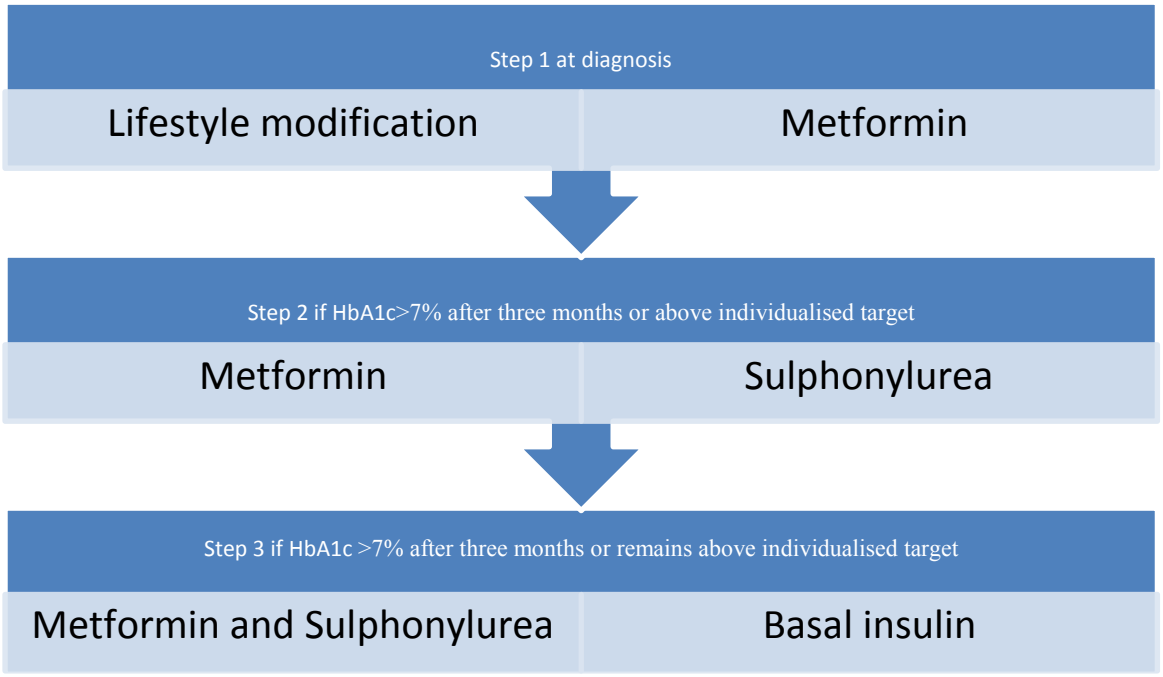

Figure 3.1 Step wise approach in the management of T2DM to reach individualised glycaemic targets (SEMDSA 2012)

Following lifestyle modification, a stratified selection of therapy is suggested based on the level of HbA1c (HbA1c 6.5%– 7% monotherapy, HbA1c >7% after three months on treatment dual therapy, and HbA1c >7.0% after another three months or above individualized target combination dual/triple and/or insulin therapy) (SEMDSA 2012). Choice of therapy is also made based on the risks of weight gain and hypoglycemia, the potential benefits with regard to CV risk and lipid profile, and correction of hyperglycemia (Aguilar 2011). Use of insulin and sulphonylureas, as reported in the UKPDS, were associated with weight gain, and these agents provided no benefit with regard to blood pressure, lipids, or cardiovascular risk (Aguilar 2011). Evidence from epidemiological studies supports the idea that complete care for patients with T2DM requires treatment of all cardiovascular risk factors. However, long-term follow-up of large clinical trials, including the UKPDS, indicated that treatment to HbA1c of 7.0% in the years close to diabetes diagnosis may be associated with improvement of long-term cardiovascula risk (Nathan et al. 2009b). Ten-year follow-up of obese patients with T2DM treated in UKPDS with metformin revealed sustained benefit of intensive therapy with regard to risk reduction for any diabetes-related end point, myocardial infarction, and death from any cause despite integration of HbA1c after the first year(Aguilar 2011). Thus, a lower HbA1c may be a good target for younger patients with a shorter duration of T2DM and those with no history of cardiovascular disease where one hopes to prevent coronary heart

disease/cardiovascular disease events, whereas a less intensive goal may be appropriate for older patients with a longer history of T2DM and evidence of coronary heart disease (Aguilar 2011).

3.8 SUMMARY OF THE CHAPTER

This chapter discussed Pathogenesis and classification of DM. A brief overview of the aetiology and natural history of T2DM were discussed. Epidemiology, mortality and cost implications of diabetes were also highlighted. The clinical presentation treatment goals, anti-diabetics and their mean lowering of glycated haemoglobin were highlighted. Treatment monitoring and adjustments in therapy were thoroughly discussed. The chapter was then concluded by a discussion of diabetes complications and their impact in South Africa.

CHAPTER 4: METHODOLOGY

4.1 INTRODUCTION

In this chapter the research methodology is discussed. Followed by research design, selection and composition of the study population, study variables, and statistical analysis of the data are discussed. The reliability and validity of the research instruments are also discussed, and finally a chapter summary is given.

4.2 RESEARCH METHODOLOGY

4.2.1 The literature review

The literature search was conducted as follow:

Electronic databases: Google Scholar, PubMed, Medline, Science Direct, Cochrane library and Archives. Electronic Journals: European Heart Journal, Journal of American Diabetes Association, Journal of Endocrinology, Metabolism and Diabetes of South Africa, etc. Text books, Acts and Regulations. Government publications and chronic disease management guidelines from Department of Health Western Cape were also used.

Search terms: Type 2 diabetes mellitus (T2DM), glycaemic monitoring indicators, Diabetes management guidelines

4.2.2 Research Design

This study is descriptive, retrospective and quantitative in nature. Descriptive studies can be used for the purposes of observing, documenting and describing situations of naturally occurring aspects of a certain theory to serve as a starting point for hypothesis generation. For example, the natural history of disease is essential to judging the effect of therapeutic interventions (Polit & Beck 2004). Polit & Beck (2004) defines retrospective designs as designs in which a phenomenon existing in the present is linked to a phenomenon that occurred in the past, before the study was initiated. This means the researcher is interested in a present outcome and tries to determine factors that caused it. This study can be considered quantitative, as data were statistically analysed and compared in order to make certain assumptions and conclusions.

4.3 SELECTION AND COMPOSITION OF STUDY POPULATION

4.3.1 Study setting

The population of the Western Cape is estimated to be 5.3 million people and represents approximately 10,45% of the total national population (Western Cape Destination Fact Sheet:2013). The coloured demographic group represents 50% of the total population of the Western Cape, followed by the Black 30.1%, White 18.4% and Indian/Asian 1.3% (Western Cape Destination Fact Sheet:2013). The Cape Metropole constitutes 64.2% of the total population of the Western Cape (Regional Development Profile City of Cape Town: 2012). It is further divided into 8 health sub-districts. The study was conducted in the Tygerberg region of the Cape Town Metropole. The Tygerberg health district is situated central in the Metropolitan as shown in Figure 1. Tygerberg covers approximately 11985 hectare (City of Cape Town: Tygerberg Health District 2013). The population size was estimated at 597732 in 2011, with the coloured ethnic group being the most predominant (66%) in the area. Black Africans constitute 19.3%, whites 10.8% and Indians/Asians 1.4% (City of Cape Town: Tygerberg Health District 2011).

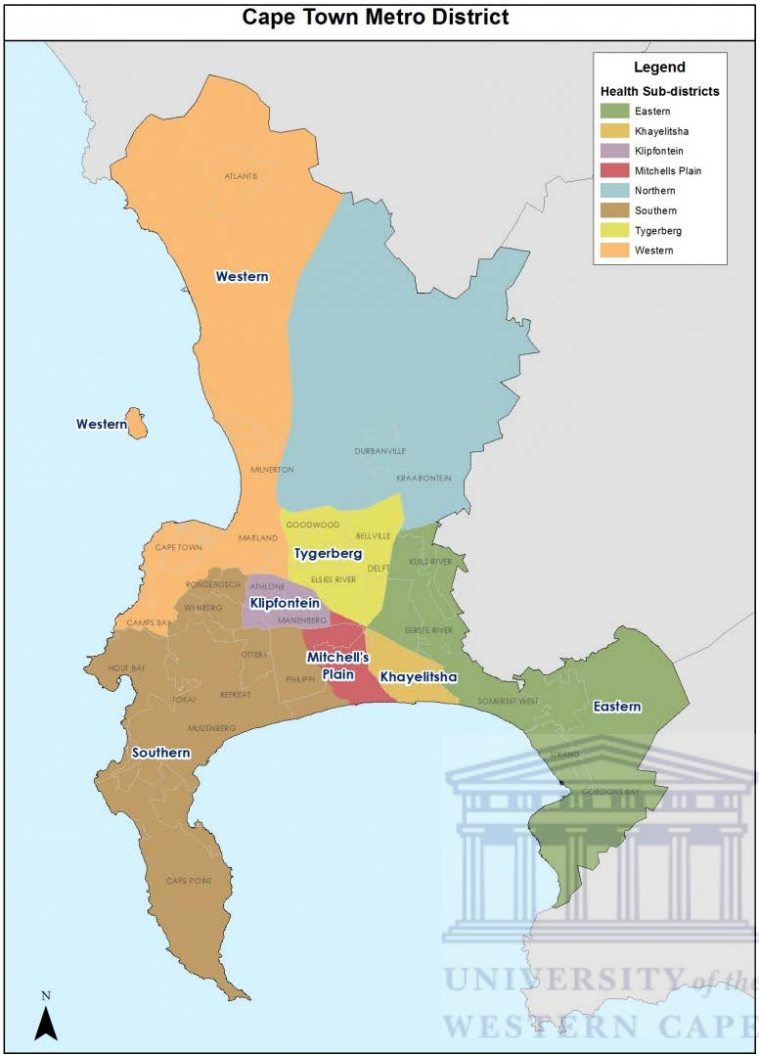

Figure 4.1 Map of the Cape Town Metropole indicating 8 sub-districts, this study was done in the Tygerberg sub- district.

Community health centres (CHC) at the primary health care level of the public sector healthcare system are involved with the chronic management of diabetic patients. After initial diagnosis and stabilisation at primary health care level patients are referred to an appropriate level of care. The levels of care include community-based, primary health care or hospital level, which correlates to the stratification categories of chronic patients which include stable, 'at risk' and decompensated, respectively (Table 4.1).

These levels have been assigned to streamline clinical management. According to protocol, the stable group is those patients who are controlled at their individualized HbA1c and blood pressure levels. These patients are decanted to the community level of care which means that they receive a 6 month repeat prescription from the clinical nurse practitioner or medical officer at their CHC, which is sent to the chronic distribution unit (CDU). Every two months

patients come to collect their medication either at a pick up point which may be at the CHC or at community diabetes club. A register for all the club members is kept at the diabetes club for scheduling of appointments and also sent to the CDU. Once the six-monthly prescription runs out, patients are reviewed by the clinical nurse practitioner or medical officer at the PHC facility for re-categorisation. The 'at risk' group are those who require more frequent review at the out-patient department of a CHC by the medical officer or family physician on a monthly basis in order to optimise management interventions and patient support structures to prevent progression of the disease into complications. The decompensated group are those who require same day referral to the hospital due to diabetic ketoacidosis, pregnancy or patients less than 30 years of age. They are either acutely decompensated or those who need specialist care.

Table 4.1 Chronic disease stratification table for diabetes mellitus used at community health centres in the Western Cape Province (Western Cape Government: Health 2012)

Criteria for stratification	**Gold standard**	**Community Based Service: Stable**	**Primary Health Care: At risk**	**Hospital: Decompensated**	
				Acute	**Specialist**
Glycemic control and complexity	Individualised HbA1c target Low risk: ≤6.5% Majority: ≤7% High risk: ≤7.5-8.5%	Controlled at individualised HbA1c target of ≤6.5% ≤7% ≤7.5-8.5% with hypo-unawareness or poor short term prognosis	HbA1c above individualised target HbA1c >11% On anti-diabetic medications And with significant co-morbidities	Diabetic ketoacidosis	Poor glycemic control despite optimal PHC management. Pregnancy Age <30 years
Blood pressure control and complexity	Low risk diabetic patient BP<140/80mm Hg For a high risk BP<150/90	Controlled at target 140/80mmHg and 150/90mmHg	BP>180/110mmHg and patient is on several blood pressure medications	BP>180/110mmHg With one of this symptoms: Headache, difficulty in breathing, visual symptoms, chest	Intolerance to multiple antihypertensives. Suspect secondary course Poor BP control despite optimal

Criteria for stratification	Gold standard	Community Based Service: Stable	Primary Health Care: At risk	Hospital: Decompensated	
				Acute	Specialist
				pain, leg swelling and confusion	management
Total cholesterol	<4.5mmol/L	<4.5mmol/L	>6.5mmol/L on statins		>7.5mmol/L or triglycerides >15mmol/L despite statins

4.3.2 Sampling strategy

The first level of sampling was done using purposive sampling to select the facilities, and this was based primarily on the staff complement that manages chronic patients at the facility. It included the availability of a family physician, permanent / part-time medical officer and clinical nurse practitioner at the facility. This was done in consultation with the pharmacy managers and family physicians in the facilities.

The second level of sampling was done randomly from diabetes club registers so that each individual had the probability of being selected and the generalizability of the study results can be possible. Patients with T2DM were selected as those treated with oral anti-diabetics and insulin.

4.4 SELECTION CRITERIA

4.4.1 Inclusion criteria

The study population comprised of all T2DM patients, older than 18 years of age, who have been on anti-diabetics for a minimum of 6 months and categorised as “stable”. Also, they were with or without the following co-morbidities: cardiovascular diseases, renal diseases, peripheral vascular diseases and ophthalmic complications.

4.4.2 Exclusion criteria

All patients younger than 18 years of age, those who have been on treatment for less than 6 months and categorised as at risk or decompensated, and patients with type 1 diabetes mellitus were excluded.

4.5 DATA SOURCES

Patient medical records in the facilities were used as data sources. The folders were selected randomly on the diabetes club register as there is no electronic system available. The folder contains patient demographics, medical history, laboratory and clinical monitoring information, such as anti-diabetic medication regimens, glycaemic monitoring indicators and other clinical information such as co-morbidities/complications.

4.6 DATA COLLECTION

The principal investigator was responsible to inform facility managers at each facility included in the study about the research project. Confirmation of ethical approval as well as proposal documents were given to each facility as soft copies via email and hard copies before commencement of the actual data collection. The data collection tool was designed to collect an 18 month's period information for all variables relevant to chronic diabetes monitoring as set out by the Department of Health (Appendix 1). Twelve final year pharmacy students were trained to assist with data collection and data capturing. The registry personnel in the hospital assisted with folder drawing. Data collection was carried out from 11th February 2015 to 9th June 2015.

4.6.1 Validity of measurement tools

The data collection tool was designed in such a way that it contained all the variables relevant to the chronic diabetes monitoring set out by the Department of Health (Western Cape Government: Health 2012).

4.6.2 Pilot study

The principal investigator piloted the study in one facility to pre-test the data collection tool and the data collection process. Findings from the pilot study revealed possible limitations to the study, and based on these findings, the tool was modified accordingly. It was found that the date of first diagnosis with T2DM was not available in the patient medical records and also the social history (diet, exercise, smoking and alcohol) was not included in the routine chronic medical check list, hence they were excluded for data collection.

4.7 DATA MANAGEMENT AND MEASUREMENT

Data was captured into an electronic spreadsheet using Microsoft Excel®. After data capturing, the data collectors were paired into groups of two and checked for accuracy of capturing. One reading from the data collection form while the other reading from the Excel® spreadsheet. This was done twice by 2 different pairs and the process was supervised by primary researcher. The final spreadsheet was exported into SPSS version 23 for statistical analysis.

Data from the data collection tool was categorised into four sections, as described below. Appendix 1 gives detailed information of all variables included.

Demographics – examined factors as, gender, age, date of birth, race/ethnicity, smoking, alcohol use and allergy.

Diagnoses – it included all the medical history of the patient e.g Type 2 DM and Co-morbidities.

Laboratory and clinical monitoring information- it included, HbA1c, fasting plasma glucose and blood pressure.

Medication – it included anti-diabetic medication regimens and medication for co-morbidities.

4.7.1 Description of variables used in the analysis

This section describes how data was organised to meet the objectives of the study. Table 4.2 describes the type of variable, unit of measurement and generation of variable. The variables generated to meet objectives are then described.

Table 4.2 Description of variables used in the analysis

Variable	Type	Description
Gender	Numeric	Male or female
Age (years)	Categorical	Calculated from South African ID and presented as categories.
Glycated haemoglobin (HbA1c) (%)	Scale	Three level variable: low risk (<6.5), majority (7) and high risk (7.5-8.5). It was analysed to establish percentages of participants with results within target values.
Fasting plasma glucose (FPG) (mmol/L)	Numeric	FPG, measurement of glucose level for just few hours. It was analysed to establish percentages of participants with results within target. The set target for all age groups is <7mmol/L.
Systolic blood pressure (SBP) (mmHg)	Numeric	SBP, recorded systolic blood pressure. It was analysed to establish percentages of participants who are hypertensive and monitor the level of control. With the target of <140mmHg for the majority and <150mmHg.
Diastolic blood pressure (DBP) (mmHg)	Numeric	DBP, recorded diastolic blood pressure. It was analysed to establish percentages of participants who are hypertensive and monitor the level of control. With the target of <80mmHg and <90mmHg.
Body mass index (BMI) (kg/m^2)	Numeric	BMI, calculated from weight in kg/ (height in m)². It was analysed to establish nutritional status of participants and find percentages of overweight or obese. With the target value of $\leq 25 kg/m^2$.
Total cholesterol (mmol/L)	Numeric	Recorded cholesterol. It was analysed to establish the percentages of participants who have dyslipidaemia. With the target value of <4.5mmol/L.
Prescription	Numeric	Two level variable: given or not given. Data relating to the anti-diabetic medication were collected from the last 3 prescriptions written for the patient. They were analysed according to anti-diabetic drugs prescribed as well as therapy adjustments when compared to the previous prescription. Depending on the number of repeats on the prescription patient medication were available for a maximum of 18 months and possible treatment adjustment could have taken place.

4.8 DATA ANALYSIS

With the use of both Microsoft Excel® and SPSS version 23, various data analyses were performed for the study sample. The prevalence of HbA1c testing, fasting plasma glucose

testing, blood pressure testing, and body mass index measurements were analysed. The analysis of comorbid disease states, anti-diabetic use and therapy adjustments analysis were selected and utilized as measuring instruments for data analysis in order to achieve the objectives of the investigation. The results are presented in chapter 5.

4.8.1 Analysis of the therapeutic management of T2DM

The number of anti-diabetics prescribed for each patient was evaluated. Anti-diabetics referred to all oral anti-diabetics used and insulin. Insulin included all of the insulin preparations that were dispensed to patients. Biphasic insulin analogues, biphasic insulins, intermediate-to-long acting insulins and long-acting insulins were all categorised as insulin. The product name field was used to determine the category distribution of all anti-diabetics prescribed in the study. The terms used in the study were: monotherapy, dual therapy and triple therapies. Monotherapy referred to metformin or sulfonylurea monotherapy, dual therapy referred to metformin and sulfonylurea, metformin and insulin or sulfonylurea and insulin, while triple therapy referred to metformin, sulfonylurea and insulin.

4.8.2 Comorbid disease analyses

The nature of the comorbid disease states and their management were considered in the analysis.

4.9 STATISTICAL ANALYSIS OF THE DATA

Microsoft Excel® and SPSS version 23 were used for statistical analysis. Descriptive and inferential statistical methods were employed for the analysis. All data set were analysed for normality using Shapiro–Wilk test. Normally distributed data were analysed using parametric tests. Parametric tests used were one-sample t-test, paired t-test and repeated measures ANOVA.

4.9.1 Descriptive statistics

To obtain descriptive statistics, frequencies were used for categorical variables where by the response was classified into how many males or female were actually in the study or gave the response (Pallant 2011). Pallant (2011) describes frequency as the number of occurrences of a determinable entity per unit of time or population (Pallant 2011). Later cross tabulation was

done to compare the variables in the two groups. These helped to determine the relationship between and among the two groups in the same and different variables.

4.9.2 Inferential statistics

Inferential statistics were used to test whether the results of the data analysis were due to relationships or random factors. They helped to confirm or reject the predictions being tested (Field 2009). Effect size which is the magnitude of the differences between two groups was analysed using P value from correlation bivariate analysis with an option of Spearman Correlation Coefficient because of the nature of the variables which were mostly ordinal. The p-value of an analysis was calculated in order to determine whether a result was statistically significant. In essence, statistical significance indicated the degree to which the result being analysed were accurate and represented the population.

When the p-value of an analysis was 0.05 or less it indicated that there was a 95% probability that the relation between the variables being assessed in the sample happened by chance (Field 2009).

4.10 RELIABILITY AND VALIDITY OF THE DATA

The data was verified with respect to age, diagnosis, duration on treatment and clinical category. Data collection tools used in this study included all variables relevant to chronic diabetes monitoring as set out in the study conducted by the Western Cape Department of Health 2012.

4.11 ETHICAL APPROVAL FOR THE STUDY

A research proposal was submitted to the University of the Western Cape Ethics Committee and approval granted (registration no 14/9/50) for the conduction of the research. An approval was obtained from the Western Cape Provincial Health Research Committee (reference no 2014RP137, Appendix 2) to gain access to the health facilities and patients medical records to be used in the study.

For confidentiality reasons, before data collection from the patient medical record ensued, a unique identifier was assigned to each participant via the patient identification tool (Appendix 3). The data collection tool only contained the unique identifier. Furthermore, due to the retrospective nature of the study, there were no face to face interactions with participants thus

no informed consent was taken. At facilities where the study was done information forms were provided for the facility managers after the presentation of the study objectives and methodology (Appendix 4).

The study was conducted with the ethical principles of the Declaration of Helsinki (World Medical Association. 2013).

4.12 SUMMERY OF THE CHAPTER

In this chapter, empirical investigation of the study which included, research design, selection and composition of study population, data collection, data management and measurement, data and statistical analysis, reliability and validity of the data were discussed.

In the following chapter analysis on the available data and results of the empirical investigation will be discussed.

CHAPTER 5: RESULTS

5.1 INTRODUCTION

This chapter outlines the results of the empirical investigation. Firstly demographic characteristics of the study population are presented, then participant's glycaemic monitoring results are categorised into stable and unstable according to evidence-based management guideline targets for glycated haemoglobin (HbA1c) and fasting plasma glucose (FPG) levels. Finally treatment and treatment adjustments among patients whose glycaemic monitoring parameters are within and outside target will be presented.

5.2 DEMOGRAPHICS OF THE STUDY POPULATION

Data were collected from 596 patient medical records treated at 5 community health centres in the Cape Town Metropolitan region South Africa. Twenty-one participants were excluded from data analysis because of the following reasons;

- Six participants had no oral anti-diabetics only insulin was prescribed therefore it was not possible to be certain of a type 2 diabetes mellitus diagnosis.
- Four participants had only one glycaemic test result
- Three had only one prescription with no follow-up information
- Five participants had abnormally low HbA1c results
- Three participants had no medication information. The demographic characteristics of the study population (575) are summarised in Table 5.1.

Table 5.1 Demographic information of the study population (n: 575)

Variable	Number	Mean ± Standard deviation	Minimum - Maximum	Target range
Age in years	575	57±11.38	29-92	N/A
Gender				N/A
Male	206 (36%)			N/A
Female	369 (64%)			N/A
HbA1C (%)	493	8.78 ± 1.63	5.1-17.1	N/A
Low risk category	13	8.15 ± 1.63	5.9-12	<6.5%
Majority category	219	8.80 ± 2.12	5.2-15.2	<7%
High risk category	261	8.75 ± 2.37	5.1-17.1	<7.5%
Fasting plasma glucose (mmol/L)	570	10.03 ± 3.62	4.0-21.1	<7 mmol/L
Systolic blood pressure (mmHg)	562	139.68 ± 21.82	101-217	<140mmHg
Diastolic blood pressure (mmHg)	562	79.91 ± 11.13	50-116	<80mmHg
Total cholesterol (mmol/L)	433	5.19 ±1.25	1.1-9.4	<4.5mmol/L
Body mass index (kg/m2)	400	31.61 ± 6.16	17.93-56.36	<25kg/m2
Male	140	30.72 ± 5.71	19.14-50.27	<25kg/m2
Female	260	32.09 ± 6.35	17.93-56.36	<25kg/m2

Key: N/A not applicable

The study comprised both males (36%) and females (64%) with the mean age 57±11.38 years. The average HbA1c for all participants was 8.78%. Mean fasting plasma glucose concentration for the study population was 10.03mmol/l. The mean systolic and diastolic blood pressure of the study participants were within the target ranges of less than 140/80mmHg. The average BMI of both males and females were 31 and 32 respectively indicating that most participants were obese. Total cholesterol of the study participants (n=433) was 5.13mmol/L which is above the target of less than 4.5mmol/L. The participants were further analysed into respective target levels to establish the proportion of participants with results within and outside target as illustrated in Table 5.2.

Table 5.2 Demographic information of the study participants (n=575) stratified according to target and risk categories.

Variable	**Stratification categories (range)**			
HbA1c (%)	Stable	At risk	Decompensated	
Low risk category (29-35 years) < 6.5%	2	11	0	
Majority category (35-55 years) <7%	42	177	0	
High risk category (>55 years) <7.5%	94	167	0	
Fasting plasma glucose (mmol/L)	Stable <7	At risk	Decompensated	
	130	444	0	
Systolic blood pressure (mmHg)	Stable < 140mmHg	Mild 140-159	Moderate 160-179	Severe 180 or more
	283	181	67	31
Diastolic blood pressure (mmHg)	Stable <80	Mild 80-99	Moderate 100-109	Severe 110 or more
	238	292	27	5
Body mass index (kg/m2)	Normal <25	Overweight 25.0-29.9	Mildly obese 30.0-34.9	Moderately obese
Male	19	51	40	30
Female	25	82	85	68

Table 5.2 shows that a total of 138 participants had HbA1c results within target at baseline while a total of 355 participants had HbA1c results outside target. One hundred and thirty (23%) participants had FPG results within target and 444 (77%) outside target. These numbers shows that the majority of participants' glycaemic levels either HbA1c or FPG were outside target ranges. A total of 98 participants had the decompensated systolic blood pressure and 32 had decompensated diastolic blood pressure. The table also shows that the total of 44 (11%) which is 19 males and 25 females had BMI levels less than 25kg/m2 which

is within target, while 356 (89%) participants, 121 male and 235 females had BMI levels above the recommended levels, indicating that majority of the study population was obese.

5.2.1 Co-morbidities and complications

The majority of T2DM patients in the study (93%) had been diagnosed with and were being treated for at least one other disease state. Only 7% (42) of the participants did not have other co-morbidities. Table 5.3 gives detailed information of participant's co-morbidities and complications.

Table 5.3 Co-morbidities and complications of participants (n=575)

	Specific disease	**N=575**	**Prevalence (%)**
Cardiovascular diseases	Hypertension, Ischaemic heart disease and coronary heart disease	1	0.2
	Hypertension and coronary heart disease	3	0.5
	Hypertension, ischaemic heart disease and dyslipidaemia	3	0.5
	Hypertension and ischaemic heart disease	6	1
	Hypertension, dyslipidaemia and cardiac congestive failure	1	0.2
	Hypertension and cardiac congestive failure	3	0.5
	Hypertension and dyslipidaemia	116	20
Ophthalmic diseases	Hypertension and glaucoma	1	0.2
	Hypertension and mild retinopathy	1	0.2
Renal diseases	Hypertension and chronic renal diseases	1	0.2
Peripheral vascular diseases	Hypertension and peripheral neuropathy	2	0.4
Complications	Blindness and hypertension	1	0.2
None		42	7
Dyslipidaemia only		17	3
Hypertension only		377	66
Total		575	100%

Table 5.3 shows that hypertension either alone (n=377) or in combination with other conditions was the most prevalent co-morbidity, followed by dyslipidaemia in combination with hypertension (n=116) and dyslipidaemia only (n=17).

5.3 GLYCAEMIC MONITORING INDICATORS USED IN THE STUDY

Glycaemic monitoring indicators that were used throughout the 18 months for which data was collected for the study participants included HbA1c and FPG. Figure 5.1 shows the number of HbA1c and FPG results of 575 participants taken during the 18 month period. HbA1c use declined throughout the eighteen month period from 86% of participants having one result, 2 results for 52% and only 10% of participants having three results. FPG use was almost constant throughout the 18 month period.

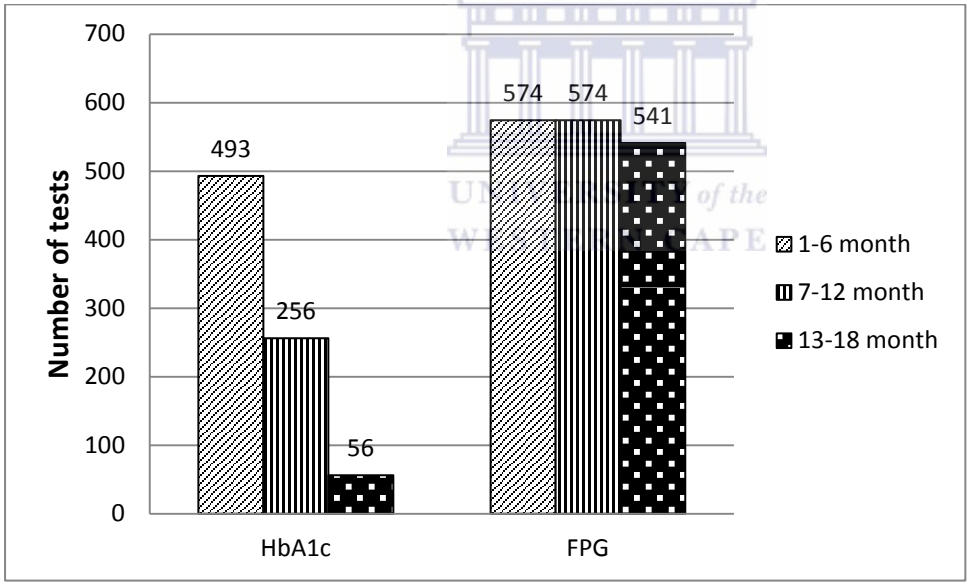

Figure 5.1 The number of HbA1c and FPG results recorded throughout the 18 months follow-up period (n=575)

5.3.1 Assessment of glycated haemoglobin results of participants

The last three HbA1c test results were recorded covering the 18 month period. Table 5.4 summarises the average HbA1c readings of the three sets of results, stratified according to risk category.

Table 5.4 Summary of HbA1c results from initial reading (HbA1c 1) to most recent reading (HbA1c 3) according to risk category.

	N=493	Mean ± standard deviation	N=256	Mean ± standard deviation	N=56	Mean ± standard deviation
Low risk	13	8.154±1.62	7	8.043±1.33	1	
Majority	219	8.799±2.12	108	8.658±2.00	23	9.409±2.09
High risk	261	8.749±2.37	141	8.853±2.39	32	8.672±1.90
Total	493		256		56	

Figure 5.2 shows the average HbA1c results as a percentage of participants who did not meet target at the different readings during the 18 month period. According to the figures >60% of participants had HbA1c consistently above recommended targets.

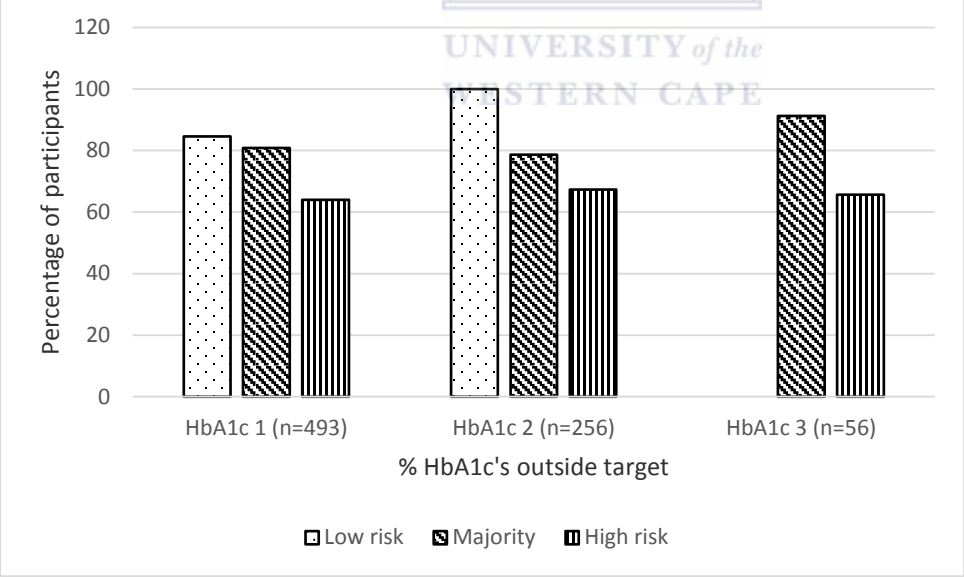

Figure 5.2 Percentage of participants with glycated haemoglobin results outside target

The initial HbA1c results were further used to determine if the difference between the actual results and the set target was significant i.e. not due to chance. Using a one-sample t-test (two tailed). Table 5.5 shows that HbA1c 1 results are significantly higher than target over all three risk categories.

Table 5.5 Initial HbA1c results for participants (n=493)

Risk category	Number of results	Within target (%)	Outside target (%)	Target value	P-value
Low risk	13	2 (15.4)	11 (85)	6.5	0.003
Majority	219	42 (19)	177 (81)	7	0.000
High risk	261	94 (36)	167 (64)	7.5	0.000
Total	493	138 (28)	355 (72)		

Glycated haemoglobin results of participants who had more than one HbA1c result during the 18 month follow-up period were further analysed to detect any sequential differences that could indicate an improvement or deterioration in diabetes management. For participants who had two HbA1c results (n=256) (HbA1c 1: 8.59±2.17; HbA1c 2: 8.75±2.23), no significant difference (p = 0.236) were observed between the initial and second results with a paired t-test.

5.3.2 Assessment of fasting plasma glucose results in participants

Table 5.6 summarises the fasting plasma glucose results over the 18 month follow-up period. The total percentage of participants who had FPG result was 99% in first and subsequent test, with 94% of participants having a third result. Figure 5.3 distinguish FPG results into the percentages of participants who did not meet target at the different readings during the 18 month follow-up period.

Table 5.6 Summary of fasting plasma glucose results from the initial reading (FPG 1) to most recent reading (FPG 3).

	Number of participants tested	Mean ± standard deviation	Minimum -maximum
FPG 1	574	10.03±3.61	4.0-21.1
FPG 2	574	10.24± 3.75	4.0-21.9
FPG 3	541	10.09± 3.58	3.9-23.6

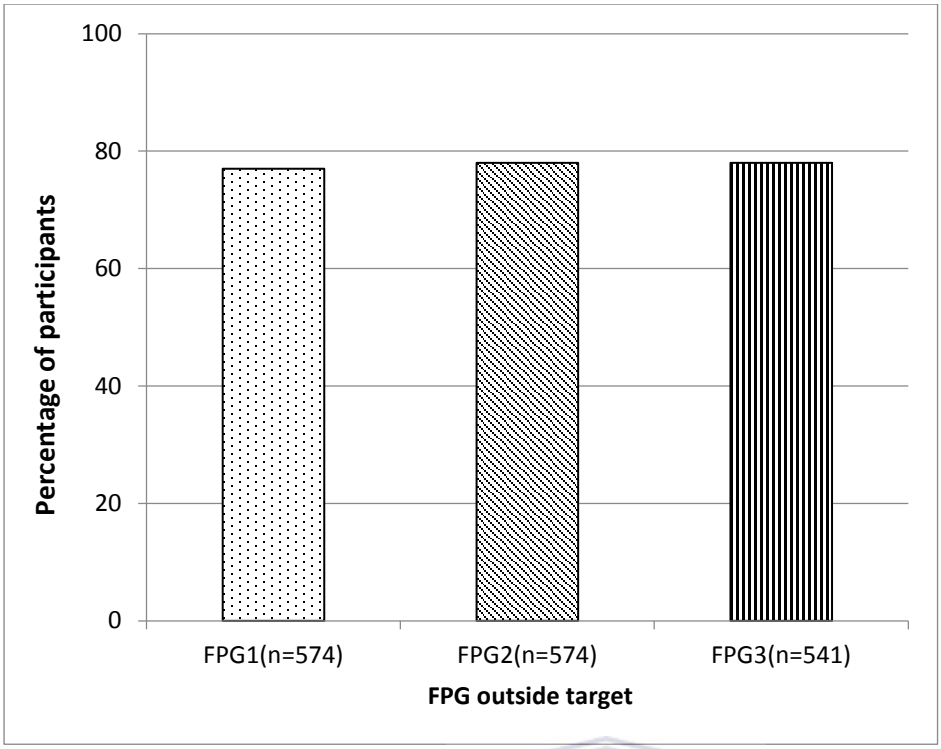

Figure 5.3 Percentage of participants with fasting plasma glucose results outside target

Initial FPG results (FPG 1) indicate, 130 (23%) participants had the results within the target range while, 444 (77%) participants had the results outside the target range. The FPG results were further used to determine if the difference between the actual results and the set target was significant i.e. not due to chance. The target value for FPG is not individualized, that means there are no categories and <7mmol/L applies to all participants. The target value (7mmol/L) and the group mean (FPG 1 mean =10.03, standard deviation= 3.62) revealed a statistically significant difference (using one sample t-test, two-tailed) p=0.000. The second and the third FPG results when compared with the target value, also revealed the statically significant difference (using one paired t-test, two tailed) p=0.000.

Fasting plasma glucose results of participants who had more than one FPG result during the 18 month follow-up period were further analysed to detect any sequential differences that could indicate an improvement or deterioration in diabetes management. The means for FPG were compared at three different intervals to establish any differences; there was no statistical difference (using repeated measures ANOVA) in between the means as shown in Table 5.7.

Table 5.7 Association between FPG results for participants who had three consecutive tests (n=541)

Time levels	Mean	p-value
FPG 1 (n=541)	10.01 ± 3.60	0.283
FPG 2 (n=541)	10.25 ± 3.74	0.283
FPG 3 (n=541)	10.09 ± 3.58	0.283

5.3.3 Analysis of study participants' gender, age and body mass index with respect to glycaemic results

A multivariate analysis was done on the following variables; gender, age and body mass index to analyse for the correlation with glycaemic level. In participants with glycated haemoglobin, there was no correlation between age and HbA1c in low risk (p=0.275), majority (p=0.126) and the high risk (p=0.139) using Pearson correlation (for scale variables). This shows that attaining glycaemic control by HbA1c was not influenced by age or risk category. The relationship between gender and HbA1c was statistically significant with a negative correlation (r=-0.647, p=0.031, two tailed) in participants in low risk with HbA1c outside target, this shows that the female in 29-34 years had the advantage of having good or low HbA1c results compared to their male counterparts using Spearman correlation (for nominal variables).

There was no correlation between HbA1c and gender in participants with HbA1c results outside target in the majority category (34-55years) p= 0.387. In the high risk category gender did not have any correlation with HbA1c results outside target (p=0.860). Being male or female did not play any role in influencing HbA1c results in the majority and high risk, in participants with results within target in these age groups there was no correlation observed, with p=0.327 and 0.237 in majority and high risk respectively.

The study population comprised of more obese participants, the BMI did not have any correlation with HbA1c results either within or outside target in all age groups. In the low risk category there was no correlation between BMI and HbA1c outside target (p=0.465), in the majority category with HbA1c outside target there no correlation with BMI being normal or obese (p=0.326 and p=0.695 respectively). In HbA1c within target in the same category, still there was no correlation with BMI and HbA1c (p=0.100).

In the high risk category, there was no correlation between BMI and HbA1c outside target among obese and healthy weight participants (p=0,979 and 0.547 in obese and healthy respectively). The same pattern was observed in participants with HbA1c results within target, there was no correlation observed in obese and healthy weight participants (p=0.866 in obese and 0.219 in healthy participants).

In general the low risk female participants were shown to have a better chance of having good glycaemic control with HbA1c, than male of the same age or females in other age or risk categories. BMI did not have any significance across all age groups and gender in influencing the outcome of HbA1c.

5.3.4 Analysis of the participants who had fasting plasma glucose results

In participants with FPG results within target, there was no correlation between age and FPG in low risk (p=0.935, two tailed). In the majority category there was a correlation between age and FPG (r=0.181, p=0.005, two tailed) using Pearson correlation (scale variable) (n=238). In the high risk category there was no correlation between age and FPG results within target. This shows that only the majority category has the advantage of attaining better glycaemic control as compared to other age groups.

Gender and FPG results within target has shown no correlation (p=0.298, two tailed) using Spearman correlation. This means that being a male or female does not have any impact on glycaemic control with respect to FPG. There was no correlation with BMI and gender (p=0.500, two tailed). Even though the results have shown that female were more likely to be obese. There was no correlation between BMI and gender in participants with FPG results within target.

In participants with FPG results within target but obese, there was still no correlation between gender and BMI (p=0.784) and gender and FPG results (p=0.706, two tailed), using Spearman correlation. The results of participants within target have only shown a correlation between the 35-55 years age group and glycaemic control.

In participants with FPG results outside target, there was no correlation between the low risk (29-34 years) and FPG (p=0.102). In the majority category there was a correlation between FPG and age (r=141, p=0.049, two tailed). This shows that the 34-55 age groups had an advantage of having good FPG results. In the high risk (>55 years) there was no correlation

(p=0.0201). FPG results and gender had no correlation (p=0.176), gender did not have any impact on attaining or not attaining glycaemic control. Obesity or normal weight did not have any effect on FPG levels as results have shown a no correlation in both obese and healthy participants p= 0.148 and 0=371 in obese and healthy respectively.

5.4 ASSESSMENT OF THE PHARMACOTHERAPEUTIC MANAGEMENT OF PARTICIPANTS

A total of 3 prescriptions per participant were recorded, which amounted to 1 725 prescriptions for 575 participants. The last 3 prescriptions written culminated in a minimum of 12 months and a maximum follow-up duration of 18 months (6 repeats / prescription).

The anti-diabetics were grouped according to the following regimens: mono therapy, dual therapy, mono and insulin and dual and insulin. Mono therapy encompassed metformin or sulfonylurea monotherapy. Dual therapy were defined as a combination of metformin and a sulfonylurea. Then 'mono and insulin' included either metformin and insulin or a sulfonylurea and insulin. While 'dual and insulin' entailed; metformin, sulfonylurea and insulin.

Anti-diabetic dosages and regimens of all participants were evaluated and analysed for any changes or adjustments made in follow-up prescriptions i.e. differences between prescription 1 and prescription 2; and between prescription 2 and prescription 3. Adjustments were classified according to dosage changes and regimen changes. Dose changes were classified as an increase or decrease in daily dose. Regimen changes were classified into step-up, step down or a lateral change. Step up regimen changes can be classified if the change was upwards i.e. from mono to dual therapy, from dual to triple therapy, and, from dual to mono and insulin. Step down regimen changes would be defined as the opposite of step up. Lateral changes were a switch in drug within the same regimen for example if sulphonylureas was changed to metformin or vice versa. Table 5.8 provides a summary of treatment regimens and regimens changes recorded in all participants over the course of the three prescriptions.

Table 5.8 Summary of treatment regimens and adjustments for 3 consecutive prescriptions in the 575 participants

Treatment regimen	Anti-diabetic agent	Prescription 1	Prescription 2	no change between P1 & P2	Daily dose increased	Daily dose decreased	Step-up regimen	Step down regimen	Lateral regimen change	Prescription2	Prescription3	no change between P2 & P3	Daily dose increased	Daily dose decreased	Step-up regimen	Step down regimen	Lateral regimen change
Mono therapy	Metformin	198	189	175	6	1	14	0	2	189	196	174	8	0	5	0	2
	Gliclazide	23	20	17	1	0	3	0	2	20	13	11	0	0	1	0	8
	Glimepiride	0	7	0	0	0	0	0	0	7	15	7	0	0	0	0	0
	Glibenclamide	5	0	0	0	0	1	0	4	0	0	0	0	0	0	0	0
Dual therapy	Metformin + Gliclazide	181	188	149	13	7	4	3	5	188	106	94	5	2	1	11	75
	Metformin + glimepiride	11	30	8	0	0	0	2	1	30	115	26	1	0	0	1	2
	Metformin + glibenclamide	44	29	22	1	0	0	1	20	29	14	13	0	0	0	3	13
Mono + insulin	Metformin + insulin	51	50	32	7	2	0	0	10	50	56	39	2	1	0	2	6
	Gliclazide + insulin	7	7	4	2	0	0	0	1	7	6	6	0	0	0	0	1
	Glimepiride + insulin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Glibenclamide + insulin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + Insulin	43	42	22	6	3	0	3	9	42	26	13	6	1	0	4	18
	Metformin + Glimepiride + insulin	4	8	3	1	0	0	0	0	8	26	7	0	0	0	0	1
	Metformin + glibenclamide + insulin	8	5	4	1	0	0	1	2	5	2	2	0	0	0	0	3
Total		575	575	436	38	13	22	10	56	575	575	392	22	4	7	21	129

Table 5.9 summarises the overall treatment regimens and adjustments for all participants (n=575) from prescription 1 to prescription 2 and prescription 2 to prescription 3. The results revealed that between prescription 1 and prescription 2, out of 575 participants, 75.8% did not have any therapy adjustments, 6.6% had the total daily dose increased, 2.3% had the total daily dose decreased, 3.8% had a step–up in regimen and 1.7% had a step-down and 9.7% had a lateral change in regimen. The changes between prescription 2 and prescription 3 revealed that, 68.1% did not have any therapy adjustments, 3.8% had the total daily dose increased, 0.7% had the total daily dose decreased, 1.2% a step-up in regimen and 3.7% had a step down and 22.4% had lateral changes made to their regimen.

5.4.1 Analysis of treatment regimens and therapy adjustments in participants who had glycated haemoglobin results

For this section, only participants who had HbA1c results available at the time of the issuing of the prescription were included in the analysis. A total of 133 participants had HbA1c results recorded that fell between the dates between prescription 1 and prescription 2. The treatment regimen adjustments of these 133 participants were separated according to those with results that fell within target (n=38) and outside target range (n=95). It was found that in 38 participants who had initial HbA1c results within target, 78.9% participants did not have any therapy adjustment, 7.9% had the total daily dose increased, no one had the daily dose decreased and no one had a step-up regimen, while 10.5% had the step down regimen and 2.6% had a lateral change in regimen (Appendix 7).

Appendix 8 summarises the treatment regimen and adjustments from prescription 1 to prescription 2 of participants with HbA1c results outside target (n=95). The results revealed that out of 95 participants, 60% did not have any therapy adjustments, 17.9% had the total daily dose increased, 3.1% had total daily dose decreased, 8.4% had a step-up in regimen, 3.1% had a step down in regimen and 7.4% had the lateral regimen.

A total of 112 participants had HbA1c results recorded that fell between the dates of prescription 2 and prescription 3. The treatment regimen adjustments of the 112 participants were separated according to those results that fell within target (n=26) and outside target range (n=86). It was found that in 26 participants who had HbA1c results within target, 73% participants did not have any therapy adjustments, and no one had dose changes or a step-up in regimen, while 3.8% had a step-down in regimen and 23.1% had a lateral change in regimen (Appendix 9).

Appendix 10 summarises the treatment regimens and adjustments from prescription 2 to prescription 3 of participants with HbA1c 2 results outside target range (n=86). The results revealed that out of 86 participants, 65.1% did not have any therapy adjustments, 2.3% had the total daily dose increased, 3.4% had the total daily dose decreased, 1.2% had a step-up in regimen, 2.3% had a step down in regimen, and 25.6% had a lateral change in regimen.

Figure 5.4 shows the summary of therapy adjustments for the participants with HbA1c results within target and outside target ranges for the 18 month follow-up period. Most participants had no change in their prescriptions, 76.6% of participants within target did not have any therapy adjustments and 62.4% of participants outside target did not have any therapy adjustments.

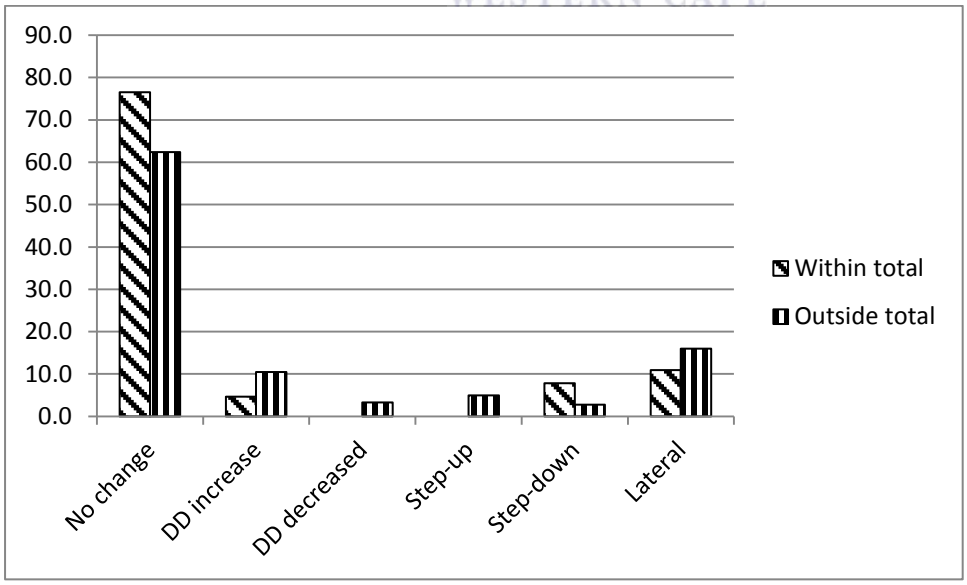

Figure 5.4 Summary of therapy adjustments in participants with glycated haemoglobin results within and outside target

5.4.2 Analysis and determination of treatment regimens in participants who had fasting plasma glucose results

For this section, only participants who had FPG results available at the time of the issuing of the next prescription were included in the analysis. A total of 553 participants had FPG results recorded at a date between prescription 1 and 2. The treatment regimens of participants with FPG results within target (n=120) and results outside target (n=433) ranges were analysed separately to determine rational therapy adjustments. Appendix 11 shows that of the 120 participants who had FPG results within target available at the time of writing prescription 2, 82.5% did not have any therapy adjustments, 3.3% had the total daily dose increased, 1.7% had the total daily dose decreased, 4.2% had a step-up in regimen, 0.8% had a step down in regimen and 7.5% had a lateral regimen change.

Appendix 12 summarises the treatment regimens and adjustment from prescription 1 to prescription 2 of the participants with FPG results outside target (n=433). The results revealed that out of 433 participants, 76% did not have any therapy adjustments, 6.7% had the total daily dose increased, 3.2% had the total daily dose decreased, 2.5% had a step-up in regimen, 2.3% had a step down in regimen and 9.2% had a lateral regimen change.

A total of 537 participants had FPG results recorded that fell between the dates between prescription 2 and prescription 3. The treatment regimen adjustments of the 537 participants for those that results fell within and outside target ranges were analysed separately to determine rational therapy adjustments. It was found that in 118 participants who had FPG results within target, 77.1% participants did not have any therapy adjustments, 3.4% had total daily dose increased, no one had a daily dose decrease or step-up in regimen, 5.9% had a step-down in regimen and 13.6% had a lateral regimen change (Appendix 13).

Appendix 14 summarises the treatment regimens and adjustments from prescription 2 to prescription 3 of participants with FPG results outside the target range (n=419). The results revealed that out of 419 participants, 66.8% did not have any therapy adjustments, 4.3% had the total daily dose increased, 1% had the total daily dose decreased, 1.2% had a step-up in regimen, 1.2% had a step down in regimen and 25.5% had a lateral regimen change.

Figure 5.5 shows the summary of therapy adjustments for the participants with FPG results within target and outside target for the 18 months follow-up period. Most participants had no in their prescriptions, 79.8 % of participants within target had no therapy adjustments and 71.5% of participants outside target had no therapy adjustments.

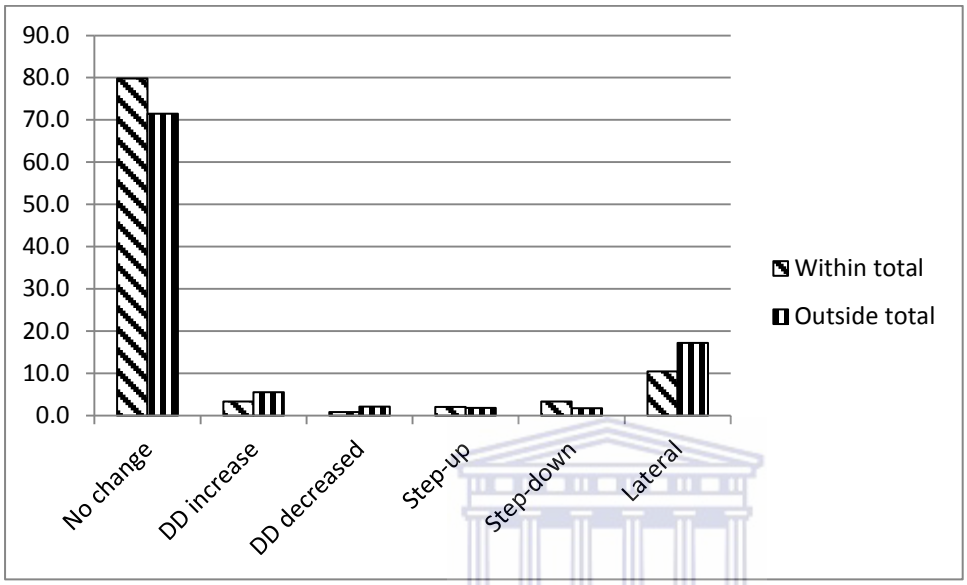

Figure 5.5 Summary of therapy adjustments in participants with fasting plasma glucose results within and outside target

5.5 SUMMARY OF THE CHAPTER

In this chapter demographics of the study population, glycaemic monitoring indicators used in the study and assessment of the pharmacotherapeutic management of participants were presented.

Discussion of the results follows in the next chapter.

CHAPTER 6: DISCUSSION

6.1 INTRODUCTION

The findings of the study will be discussed in this chapter. Assessment of management of type 2 diabetes mellitus using glycated haemoglobin and fasting plasma glucose as monitoring parameters will be discussed first followed by prescribing patterns in patients whose monitoring parameters are not at target using evidence-based guidelines. Lastly therapy adjustments will be discussed.

6.2 DESCRIBING GLYCATED HAEMOGLOBIN AND FASTING PLASMA GLUCOSE ACCORDING TO RISK STRATIFICATION AS PER EVIDENCE-BASED MANAGEMENT GUIDELINES

6.2.1 Demographics of the study population

The study consisted of 575 patient treated at 5 community health centres in the Cape Town Metropolitan region South Africa with a mean age 57±11.38. Patients were categorized according to various age groups. The 29 to 34 years age category consisted of 14 participants, the 35 to 55 years age category consisted of 238 while participants of >55 years of age consisted of 323 participants highlighting the fact that T2DM is more prevalent in the older population. The age distribution of this study corresponds with the global trends of T2DM where by it was found that diabetes prevalence seems to be increasing more in older people (Wild et al. 2004). Similar results were reported in a South African study in Cape Town (n=200), whereby 28.7% of participants from mixed origin aged 65 years and older were found to have T2DM (Erasmus et al. 2012). The majority of study participants were female with 64% and male 36%. The predominance of the female participants in the study population is similar with previous South African studies, whereby Motala et al (2003) reported a study population of 60% females and 40% males that assessed the prevalence and knowledge of DM in the public clinics and the community (Moodley & Rambiritch 2007).

The mean HbA1c for the study was 8.78%. While the fasting plasma glucose mean was 10mmol/L which is also above the recommended target of less than 7mmol/L. The findings from this study concur with the findings of the study performed in the public sector in three major academic hospitals served by the University of the Witwatersrand namely: Johannesburg, Helen Joseph and Baragwanath, where the mean HbA1c for the study

participants (n=150) was 8.7% (Klisiewicz & Raal 2009). Amod et al (2012) in a study done in the private sector of South Africa has also reported the mean HbA1c of 8.2%. The mean FPG of greater than 7mmol/L was found in a study done in the rural black community in Limpopo with the prevalence rate of 8% and 9% in male and female respectively (Alberts et al. 2006). This indicates that despite the available evidence from clinical trials, that supports the need for achieving recommended targets, the management of diabetes patients in South Africa is still largely sub optimal (Klisiewicz & Raal 2009).

The mean systolic blood pressure of the participants was 139.6mmHg and mean diastolic blood pressure was 79.9mmHg which concurs with the latest targets of less than 140/80mmHg in T2DM patients set out by the guidelines (Society for endocrinology metabolism and diabetes South Africa (SEMDSA) 2012). This findings of blood pressure concurs with the findings of the study performed in the private sector in Durban, it was found that in contrast to other studies done elsewhere in the world, the South African patients' blood pressure is relatively well controlled whereby participants (n=899) had mean systolic blood pressure of 131.4mmHg and mean diastolic pressure of 79.4mmHg (Amod et al. 2012)

The mean BMI of 32 and 30.72 in females and males was reported which was higher than the BMI that was reported in a study done in Bellville Cape Town, where by the study found the BMI of 30.8 in females and 25.8 in males (Erasmus et al. 2012). Change in diet to more saturated fats and sugars is largely responsible for high rates of obesity characterising the emergence of non-communicable diseases in South Africa, this was observed in a study conducted among urban dwelling black South Africans which showed a strong association between increased body weight and diabetes mellitus (Peer et al. 2012). Wang et al (2005) had found that high BMI alone strongly and independently predict risk of T2DM.

Total cholesterol levels of the study participants were higher (5.13mmol/L) than the recommended target levels (< 4.5mmol/L), which explains why there was an observed high prevalence of study participants with dyslipidaemia. Three hundred (69%) participants had total cholesterol above 4.5mmol/L, which is also alarming and positive determiner in cardiovascular diseases. Norman et al (2007) had indicated that 59% of ischaemic heart disease and 29% of ischaemic stroke in South Africa are attributable to raised cholesterol levels, which compares with the world wide estimates of 32%.

Studies have revealed that the prevalence and incidence of cardiovascular diseases is increased in patients with T2DM, this concurs with the findings of this study which have revealed that 93% of the study participants with co-morbidities had cardiovascular diseases. Of these diseases the most prevalent were hypertension either diagnosed alone or with other diseases 516 (80%) and dyslipidaemia either alone or with other diseases 133 (20%). Girach & Vignati (2006), in a systematic review study have found that the presence of one microvascular complication predicts the development of another. The results of the study concurs with the results of the study that was done in the peri-urban black South Africans in Cape Town where by an optimal control of 33% and 44% was found in men and women respectively (Dennison et al. 2007).

6.2.2 Glycated haemoglobin

As described earlier in the discussion and in the literature the glycaemic results were analysed with a specific target value for every risk category. Four hundred and ninety three participants (86%) had at least one HbA1c result. The average mean HbA1c results in all risk categories throughout the 18-months follow-up period were above the targeted percentages of 6.5% for the low risk, 7% for the majority and 7.5% for the high risk. The percentage of participants who did not meet target at the different readings was higher than the percentages of participants who were within target. The initial HbA1c results have shown that only 138 (28%) of participants were within target, hence the poor glycaemic control of the 335 (72%) participants is of concern. The findings of this study concurs with the findings of the study done in the public sector in three academic teaching hospitals in Johannesburg that had found the mean HbA1c of 8.7% for all study participants (Klisiewicz & Raal 2009). Motala et al (2012) in a study done in a private sector had reported similar results of 8.7% which also concurs with the results of this study of mean HbA1c of 8.78%.

6.2.3 Fasting plasma glucose results of participants

Fasting plasma glucose was the predominantly used glycaemic monitoring test almost everyone had the test done throughout the study period. In the three consecutive test results the mean FPG was above 7mmol/L. From the initial FPG results 130 (23%) participants had the results within target range, while 444 (77%) participants had the results outside target. The percentage of participants outside target was maintained at above 77%, indicating that the glycaemic levels of participants were never satisfactorily controlled. Nthangeni et al.

(2002) had found poor glycaemic control in more than half of the study participants having FPG above 8mmol/L, which is the case in the present study done more than ten years later indicating an urgent need in glycaemic control.

6.2.4 Analysis of study participants' gender, age and body mass index with respect to glycaemic results

A significant negative association was found between a female gender and HbA1c outside target in low risk participants. Meaning that the younger the patient the higher the chances of having improved HbA1c levels. A significant positive association was found between majority age group and FPG. Participants in this age group had the advantage of having better FPG control than the other participants.

Surprisingly enough there was no correlation between gender, BMI, FPG and HbA1c. None of these were found to influence either HbA1c or FPG control of the study participants. Given the high prevalence of obesity and the number of high number of female participants in high risk group, it would have been expected that there a significant association with HbA1c and FPG results outside target.

6.3 PRESCRIBING PATTERNS IN PATIENTS WHOSE MONITORING PARAMETERS ARE NOT AT TARGET USING EVIDENCE-BASED MANAGEMENT GUIDELINES

Glycaemic control is achieved by pharmacotherapy that targets fasting and postprandial glucose levels, as well as HbA1c (Sherifali et al.2010). The therapeutic management involves the use of oral hypoglycaemic agents and insulin, either as monotherapy, or in combination (Nathan et al. 2009). The four treatment regimens namely; mono therapy, dual therapy, mono and insulin and dual and insulin, in the management of T2DM patients were prescribed. The Department of Health (2008) guidelines encourage the use of a stepwise treatment approach to adjusting therapy in the management of T2DM to reach glycaemic targets, while SEMDSA (2012) has further endorsed this by establishing individualized targets to reach glycaemic target levels. Most participants were on dual therapy (41%), followed by mono therapy (39.3%) and few were on mono and dual with insulin (10.1 % and 9.6% respectively). The study results concurs with the findings of the study done in the private sector in Durban, it was found that using triple therapy is not a common practise in South Africa insulin initiation is only done after a failure of dual therapy (Amod et al 2012). Therapy adjustments, daily

dose increases and step-up in regimen would be expected in participants with glycaemic results outside target range. Daily dose decreases, step down in regimen or lateral change in regimen would be expected in participants within target range, or due to side effects and changes in essential medicines list.

6.3.1 Therapy adjustments in participants monitored by glycated haemoglobin

The total amount of opportunities to happen for intervention in participants with HbA1c results outside target were 181, 113 (62.4%) did not have any therapy adjustments, 19 (10.5%) had the total daily dose increased, 6 (3.3%) had total daily dose decreased, 9 (5.0%) had a step-up in regimen, 5 (2.8%) had a step down in regimen and 29 (16.0%) had a lateral regimen in prescription 1 and prescription 2. Taking into consideration that the study cohort is composed of participants with cardiovascular diseases, obese and high HbA1c levels above recommended targets more therapy adjustments specifically dose increases and step up in regimen would be expected in participants with results outside target. There were 64 opportunities for intervention to happen in participants with HbA1c results within target, 49 (76.6%) did not have therapy adjustments, 3 (4.7%) had the total daily dose increased, no one had the daily dose decreased and had a step-up in regimen, 5 (7.8%) had a step down in regimen and 7 (10.9%) had a lateral change in regimen. From the participants with results within target, dose decrease, step-down in regimen and lateral regimen would be expected because of side effects or changes in essential medicines list. Intensive glycaemic control was shown to reduce microvascular complications in Japanese T2DM patients in the Kumamoto study, this shows that therapy adjustments can improve glycaemic control and delay the progression of the disease (Ohkubo et al. 1995). Diabetes treatment is adjusted based on HbA1c results (Nathan et al. 2008). Large controlled clinical trials have found that in patients with T2DM improved glycaemic control is associated with reductions in macrovascular complications (UK Prospective Diabetes Study (UKPDS) Group 1998; Stettler et al. 2006).

6.3.2 Therapy adjustments in participants monitored with fasting plasma glucose

The total amount of opportunities to happen for intervention in participants with FPG results outside target were 852, 609 (71.5%) did not have any therapy adjustments, 47 (5.5%) had the total daily dose increased, 18 (2.1%) had the total daily dose decreased, 16 (1.9%) had a

step-up in regimen, 15 (1.8%) had a step down in regimen and 147 (17.3%) had a lateral change in regimen in prescription 1 and 2. Fasting plasma glucose shows glucose levels for only eight hours (DoH 2008). Understanding the relationship between HbA1c and average glucose by prescribers can be useful in adjusting therapy (SEMDSA 2012). There were 238 opportunities for intervention to happen in participants with FPG results within target, 190 (79.8%) did not have any therapy adjustments, 8 (3.4%) had the total daily dose increased, 2 (0.8%) had the total daily dose decreased, 5 (2.1%) had a step-up in regimen, 8 (3.4%) had a step down in regimen and 25 (10.5%) had a lateral change in regimen.

6.3.3 Rational use of medicines

The prescribing patterns and therapy adjustments of participants with glycaemic results outside target and glycaemic results within target ranges are similar. The regimens were not adjusted as per the results and the change of drug within the same regimen with the same mean lowering of HbA1c is not sufficient to respond to the glycaemic levels. Inappropriate doses do not respond effectively in the management of the disease, hence resulting in serious morbidity and mortality (WHO 2002). The guidelines have endorsed a benchmark for which comparison can be made to promote rational use of medicines in the management of diseases if used appropriately (WHO 2002).

6.4 STUDY LIMITATIONS

Limitations relating to information not available in patient medical record:

- Date of first diagnosis was not available in the patient medical records, therefore duration of the participant with T2DM could not be established, so co-morbidities or complications could not be linked to the duration which is important.

- Information on lifestyle interventions e.g. smoking alcohol use, diet and physical activity was not routinely collected.

- Information on complete lipid profile was not available, only total cholesterol was there, making it difficult to comment on the management of dyslipidaemia.

- Information on ethnicity was not included, (it was derived from the name hence not reliable) therefore could not be analysed, which is important in analysing the prevalence of T2DM per ethnic group.

The study was conducted in 5 primary health centres in the public sector, which is used by public patients only, furthermore the general population of the database was used as the study population, thus the results of this study may not be representative of the trends and patterns in the population of South Africa as it reflects patterns in public practise only without considering private sector. Caution needs to be exercised when generalising the results.

6.5 SUMMARY OF THE CHAPTER

The management of T2DM using HbA1c and fasting plasma glucose as monitoring tools were discussed. The discussion further focused on medicine adjustments in patients outside glycemic target ranges, with an emphasis on the various categories for risk stratification. Appropriate use of evidence-based guidelines contributes to rational use of anti-diabetic medicines in patients with T2DM. The chapter is concluded describing the limitation of the study.

Conclusions to the above findings are discussed in the following chapter.

CHAPTER 7: CONCLUSION AND RECOMMENDATIONS

7.1 INTRODUCTION

The study aimed to describe the use of glycaemic monitoring indicators in patients with T2DM, classified as stable, treated at primary health care facilities in the Cape Town Metropolitan Region in South Africa. The study will hopefully contribute to reducing the burden of the disease through early interventions and identification of cases that needs special attention, by being able to identify the at-risk population, improving long term management and minimising the development of complications associated with diabetes. It is assumed that there will be a contribution to reduction on health care expenditure with appropriate and rational use of medicines.

7.2 SUMMARY OF FINDINGS

This study has demonstrated that from the medical records of 575 patients with T2DM managed at 5 different primary healthcare facilities; FPG was the most often used glycaemic monitoring indicator, glycaemic monitoring of patients mostly show suboptimal glucose control and that opportunities to optimise pharmacotherapy in diabetes management are mostly missed. In terms of the gold standard of glycaemic monitoring indicators, HbA1c was used less (86% of participants had at least one result) and in decreasing frequency (52% had two results and only 10% had three results) as compared to FPG.

Most patients showed suboptimal glucose control, despite the fact that the target population of the study were patients classified as stable by the primary health care clinic. In addition, longitudinal glycaemic monitoring results of both FPG and HbA1c showed no improvement over the 18 month follow-up period. This corresponds to the third main finding that showed no correlation between pharmacotherapy adjustments and the glycaemic monitoring results. This indicates that HbA1c results were not used to direct treatment changes where necessary, resulting in sub-optimal management of type 2 diabetes mellitus. Similar prescribing patterns were observed in patients with glycaemic results within target ranges as well as glycaemic results outside target ranges. It would be expected that there will not be therapy adjustments made in participants with glycaemic results within target ranges except in patients with adverse effects of drugs or change in essential medicines list which were not documented in patient medical folders, however, management of this population group were similar to patients with glycaemic results outside target.

In conclusion, chapter 2 and 3 described the health care system in South Africa and the importance of appropriate management of T2DM. The national department of health has made non-communicable disease a health priority as the burden on the health care system as well as burden on the patient's well-being. Evidence-based management guidelines are available for the appropriate and effective management of T2DM. This study is contributing to the available evidence in the literature regarding the current management challenges of T2DM, especially in the public health care sector of SA. Even though guidelines for effective treatment are available, a large number of patients accessing health care services for T2DM are not receiving adequate treatment, which potentially strains the health care system as well as decreases the quality of the life of those patients.

7.3 RECOMMENDATIONS

Health care workers should be educated on the appropriate use and interpretation of HbA1c at clinic level. Laboratory investigations recommended by guidelines for effective management of diabetic patients, specifically TDM2, should be done accordingly. Adherence to treatment guidelines should be promoted to improve rational use of medicines. Guideline implementation should be a priority for policy-makers and facility managers. There are currently poor implementation practices seen at health facilities.

A standardised patient medical folder should be used in every facility where stable TDM2 patients are treated. From the recent study conducted in health care facilities it was observed that there were inconsistencies with regards to documentation of TDM2 patient care. It is recommended that complete documentation be done in terms of social history, past medication history, laboratory investigations and patient education. This will allow for seamless patient care.

Future research should investigate the determinants of poor glycaemic control both for the prescriber and patient. Future research should also investigate whether prescribers are aware of the target ranges for various monitoring parameters used in TDM2. This again highlights the importance of guideline implementation.

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APPENDIX 1: DATA COLLECTION SHEET

Unigue ID of the patient
Date of collection
Captured by:

Sex :
M/F **Stratification category:** **Stable**
Date of birth **Smoking: Y/N** **At risk**
Race/ethinicity: Black African, 2. Coloured **Alcohol use: Y/N** **Decompensated**
3. Indian **4. White** **Allergies: Y/N** **Date stratified:**

Medical history

Monitoring Tests

TESTS	**not done**	**date**	**results**	**date**	**results**	**date**	**results**	**date**	**results**	**date**	**results**	**date**	**results**
HbA1c													
FPG													
PPG													
BP													
K													
Na													
Urea													

Waist Cir													
Foot exam													
Fundoscopy													
Creatinine													
Proteinurea													
GFR													
BMI													
Height													
Weight													
Lipids profile													
LDL													
HDL													
Triglycerides													
Cholesterol													
Urine Dipstik													
Glucose													
Protein													
Ketones													
Nitrite													
Haemoglobin													
Bilirubin													
Urobilinogen													
Acetone													
Leucocytes													
PH													
Specific gravity													

Date of first prescription			Date	Date	Date	Date
drugs	dose	frequency	Repeat	Repeat	Repeat	Repeat

Date of first prescription			Date	Date	Date	Date
drugs	dose	frequency	Repeat	Repeat	Repeat	Repeat

Date of first prescription			Date	Date	Date	Date
drugs	dose	frequency	Repeat	Repeat	Repeat	Repeat

APPENDIX II: UWC ETHICS APPROVAL

UNIVERSITY of the
WESTERN CAPE

OFFICE OF THE DEAN
DEPARTMENT OF RESEARCH DEVELOPMENT

3 November 2014

To Whom It May Concern

I hereby certify that the Senate Research Committee of the University of the Western Cape approved the methodology and ethics of the following research project by:
Dr R. Coetzee (School of Pharmacy)

Research Project:	Rational drug therapy monitoring in type 2 diabetes mellitus: using glycated haemoglobin as a guide for change in therapy.
Registration no:	14/9/50

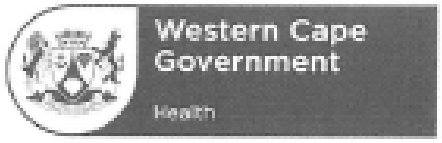
Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

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

Private Bag X17, Bellville 7535, South Africa
T: +27 21 959 2988/2948 . F: +27 21 959 3170
E: pjosias@uwc.ac.za
www.uwc.ac.za

APPENDIX III: WESTERN CAPE APPROVAL



STRATEGY & HEALTH SUPPORT
Health.Research@westerncape.gov.za
tel: +27 21 483 6857; fax: +27 21 483 9869
5th Floor, Norton Rose House, 8 Riebeek Street, Cape Town, 8001
www.capegateway.gov.za

REFERENCE: 2014RP137
ENQUIRIES: Ms Charlene Roderick

School of Pharmacy
University of the Western Cape
Private Bag X17
Bellville 7535
South Africa

For attention: **Dr Renier Coetzee, Dr Mea Van Huyssteen and Khathatso Mananabela**

Re: RATIONAL DRUG THERAPY MONITORING IN TYPE 2 DIABETES MELLITUS: USING GLYCATED HAEMOGLOBIN AS A GUIDE FOR CHANGE IN THERAPY

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research.

Please contact the following people to assist you with any further enquiries in accessing the following sites:

Bellville South CHC	**M Ferreira**	**Contact No. 021 951 2326**
Bishop Lavis CHC	**W Allies**	**Contact No. 021 934 6050**
Delft CHC	**J van Heerden**	**Contact No. 021 954 2237**
Elsies River CHC	**R Kasker**	**Contact No. 021 931 6023**
Ruyterwacht CHC	**L Baron**	**Contact No. 021 936 8769**
Reed Str. CHC	**N Lewin**	**Contact No. 021 946 3790**

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.

2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final report within six months of completion of research. This can be submitted to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).
3. The reference number above should be quoted in all future correspondence.

Yours sincerely

DR J EVANS

ACTING DIRECTOR: HEALTH IMPACT ASSESSMENT

DATE: 14/01/15

CC **L BITALO** **DIRECTOR: NORTHERN / TYGERBERG**

APPENDIX IV: UNIQUE IDENTIFIER

Unique ID	Name	surname	Date of birth	ID number	Clinic name	Number Folder	Date captured
001							
002							
003							
004							
005							
006							
007							
008							
009							
010							
011							
012							
013							
014							
015							

APPENDIX V: INFORMATION SHEET

Project Title: Rational drug therapy monitoring in type 2 diabetes mellitus: using glycated haemoglobin as a guide for change in therapy

What is this study about?

This is a research project being conducted by Khathatso Monanabela a student at the University of the Western Cape. The purpose of this study is to describe the use of glycaemic monitoring indicators in patients with type 2 diabetes mellitus, classified as stable, treated at primary health care facilities in the Cape Town Metropolitan Region in South Africa. Your facility has been purposefully selected for our data collection.

What will I be doing at the facility?

I will be capturing data into my data collection sheet from your patient medical records. We will be identifying patients from your facility through the electronic chronic dispensing unit's (CDU) database. This database provides all the names of stable chronic patients managed at your facility. Patients with Type 2 Diabetes Mellitus should appear on this database and will be identified as those treated with oral anti-diabetics and insulin. The final selection of patients will only occur once their medical records concur with the following inclusion and exclusion criteria. The inclusion criteria in the study include patients older than 18 years of age, who have been diagnosed with Type 2 Diabetes Mellitus, on treatment for a minimum of 6 months and who have been categorised as stable. Exclusion criteria include all patients younger than 18 years of age, patients with Type 1 diabetes mellitus, those who have been on treatment for less than 6 months and categorised as 'at risk' or decompensated.

How will I keep the identity of your patients confidential?

The anonymity of your patients will be ensured by the assignment of a unique identifier for each patient enrolled in the study. Before data collection from the patient medical record ensues, a unique identifier will be assigned to each new participant via a master copy form. The data collection tool will only contain the unique identifier assigned to the patient. The master copy form with the identifying information will be kept separate from the data collection sheets and will be available only for senior researchers involved in the study to verify and link patient identities across the databases. In the two electronic databases using in the study, that is, CDU will be password protected. This information, together with the data collection tool, will be kept at the School of Pharmacy of the University of the Western Cape. Once the study is completed i.e. research reports and publications written, the electronic databases and paper data collection tools will be deleted and destroyed by the principle researcher.

What are the risks of this research?

The risks for study participants are minimal as the anonymity protection will ensure confidentiality.

What are the benefits of this research?

No direct benefits for the study participants are anticipated. However, indirect benefits might include a better understanding of the use of glycated haemoglobin in the management of Type 2 Diabetes Mellitus at primary health care facilities which might be followed by recommendations and training to improve Type 2 Diabetes Mellitus management overall.

How did I get permission to access to your facility?

The researcher had to submit and obtain approval from two committees namely, the University of the Western Cape Ethics Committee and the Western Cape Provincial Health Research Committee before the study was to be conducted.

What if you have questions?

This research is being conducted by Khathatso Monanabela, a student pursuing a Masters in Pharmacy at the University of the Western Cape. If you have any questions about the research study itself, please contact; Khathatso Monanabela, Tel 0794456664, kmonanabela@gmail.com.

Should you have any questions regarding this study or if you wish to report any problems you have experienced related to the study, please contact:

Research supervisor: Dr Renier Coetzee

School of Pharmacy

University of the Western Cape

Tel; 0219593665

Private Bag X17

Bellville 7535

South Africa

This research has been approved by the University of the Western Cape's Senate Research Committee as well as the Western Cape Provincial Health Research Committee

APPENDIX VI: CONSENT FORM

Title of Research Project: Rational drug therapy monitoring in type 2 diabetes mellitus: using glycated haemoglobin as a guide for change in therapy

The study has been described to me and my questions about the study have been answered. I understand that the researcher had obtained permission to conduct the study from University of the Western Cape's Senate Research Committee as well as the Western Cape Provincial Health Research Committee. I understand that the researcher will need access to patient medical records at this facility.

Participant's name……..

Participant's signature…….

Date……..

Should you have any questions regarding this study or wish to report any problems you have experienced related to the study, please contact the study supervisor:

Research supervisor: Dr Renier Coetzee

School of Pharmacy

University of the Western Cape

Tel; 0219593665

Email: recoetzee@uwc.ac.za

Private Bag X17

Bellville 7535

South Africa

APPENDIX VII: Treatment regimens and changes in glycated haemoglobin results within target at the time of writing prescription 2 (n=38)

Treatment regimen	Anti-diabetic agent	Prescription 1	Prescription2	no change between P1 & P2	Daily Dose increased	Daily Dose decreased	Step-up regimen	Step down regimen	Lateral regimen change
Mono therapy	Metformin	21	21	18	2	0	0	0	1
	Gliclazide	0	1	0	0	0	0	0	0
	Glimepiride	0	0	0	0	0	0	0	0
	Glibenclamide	0	0	0	0	0	0	0	0
Dual therapy	Metformin + Gliclazide	10	10	9	0	0	0	1	0
	Metformin + glimepiride	0	2	0	0	0	0	0	0
	Metformin + glibenclamide	4	1	1	0	0	0	3	0
Mono + insulin	Metformin + insulin	2	2	1	1	0	0	0	0
	Gliclazide + insulin	0	0	0	0	0	0	0	0
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	1	1	1	0	0	0	0	0
	Metformin + glimepiride + insulin	0	0	0	0	0	0	0	0
	Metformin + glibenclamide + insulin	0	0	0	0	0	0	0	0
Total		38	38	30	3	0	0	4	1

APPENDIX VIII: Treatment regimens and changes in glycated haemoglobin results outside target at the time of writing prescription 2 (n=95)

Treatment regimen	Anti-diabetic agent	Prescription 1	Prescription2	no change between P1 & P2	Dose increased	Dose decreased	Step-up regimen	Step down regimen	Lateral regimen change
Mono therapy	Metformin	30	23	20	2	1	7	0	0
	Gliclazide	4	2	2	0	0	1	0	1
	Glimepiride	0	2	0	0	0	0	0	0
	Glibenclamide	1	0	0	0	0	0	0	1
Dual therapy	Metformin + Gliclazide	27	34	22	3	1	0	0	1
	Metformin + glimepiride	2	3	1	0	0	0	0	1
	Metformin + glibenclamide	3	4	2	0	0	0	0	1
Mono + insulin	Metformin + insulin	11	12	5	6	0	0	0	0
	Gliclazide + insulin	2	2	1	1	0	0	0	0
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	9	7	3	2	1	0	3	0
	Metformin + glimepiride + insulin	2	4	1	1	0	0	0	0
	Metformin + glibenclamide + insulin	4	2	0	2	0	0	0	2
Total		95	95	57	17	3	8	3	7

APPENDIX IX: Treatment regimens and changes in glycated haemoglobin results within target at the time of writing prescription 3 (n=26)

Treatment regimen	Anti-diabetic agent	Prescription2	Prescription3	no change between P2&P3	Daily dose increased	Daily dose decreased	Step-up regimen	Step-down regimen	Lateral regimen change
mono therapy	Metformin	13	14	13	0	0	0	0	0
	Gliclazide	0	0	0	0	0	0	0	0
	Glimepiride	1	1	1	0	0	0	0	0
	Glibenclamide	0	0	0	0	0	0	0	0
Dual therapy	Metformin + Gliclazide	5	1	1	0	0	0	1	3
	Metformin + glimepiride	1	7	1	0	0	0	0	0
	Metformin + glibenclamide	4	1	1	0	0	0	0	3
mono + insulin	Metformin + insulin	0	0	0	0	0	0	0	0
	Gliclazide + insulin	0	0	0	0	0	0	0	0
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	2	2	2	0	0	0	0	0
	Metformin + glimepiride + insulin	0	0	0	0	0	0	0	0
	Metformin + glibenclamide + insulin	0	0	0	0	0	0	0	0
Total		26	26	19	0	0	0	1	6

APPENDIX X: Treatment regimens and changes in glycated haemoglobin results outside target at the time of writing prescription 3 (n=86)

Treatment regimen	Anti-diabetic agent	Prescription2	Prescription3	no change between P2&P3	Daily dose increased	Daily dose decreased	Step-up regimen	Step-down regimen	Lateral regimen change
mono therapy	Metformin	18	20	16	2	0	0	0	0
	Gliclazide	2	2	1	0	0	0	0	1
	Glimepiride	1	1	1	0	0	0	0	0
	Glibenclamide	0	0	0	0	0	0	0	0
Dual therapy	Metformin + Gliclazide	30	14	13	0	1	0	1	15
	Metformin + glimepiride	5	21	5	0	0	0	0	0
	Metformin + glibenclamide	7	4	4	0	0	0	1	2
mono + insulin	Metformin + insulin	11	12	9	0	2	0	0	0
	Gliclazide + insulin	1	1	1	0	0	0	0	0
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	4	2	0	0	0	1	0	3
	Metformin + glimepiride + insulin	5	7	4	0	0	0	0	1
	Metformin + glibenclamide + insulin	2	2	2	0	0	0	0	0
Total		86	86	56	2	3	1	2	22

APPENDIX XI: Treatment regimens and changes in fasting plasma glucose results within target at the time of writing prescription 2 (n=120)

Treatment regimen	Anti-diabetic agent	Prescription 1	Prescription 2	no change between P1 & P2	Dose increased	Dose decreased	Step-up regimen	Step down regimen	lateral regimen change
Mono therapy	Metformin	63	59	55	4	0	4	0	0
	Gliclazide	7	5	5	0	0	1	0	1
	Glimepiride	0	3	0	0	0	0	0	0
	Glibenclamide	2	0	0	0	0	0	0	2
Dual therapy	Metformin + Gliclazide	27	28	24	0	1	0	0	2
	Metformin + glimepiride	0	4	0	0	0	0	0	0
	Metformin + glibenclamide	9	7	5	0	0	0	0	4
Mono + insulin	Metformin + insulin	8	8	8	0	0	0	0	0
	Gliclazide + insulin	0	1	0	0	0	0	0	0
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	4	4	2	0	1	0	1	0
	Metformin + glimepiride + insulin	0	1	0	0	0	0	0	0
	Metformin + glibenclamide + insulin	0	0	0	0	0	0	0	0
Total		120	120	99	4	2	5	1	9

APPENDIX XII: Treatment regimens and changes in fasting plasma glucose results outside target at the time of writing prescription 2 (n=433)

Treatment regimen	Anti-diabetic agent	Prescription 1	Prescription2	no change between P1 & P2	Dose increased	Dose decreased	Step-up regimen	Step down regimen	lateral regimen change
Mono therapy	Metformin	129	124	112	4	2	8	0	3
	Gliclazide	14	13	11	1	0	1	0	1
	Glimepiride	0	4	0	0	0	0	0	0
	Glibenclamide	2	0	0	0	0	0	0	2
Dual therapy	Metformin + Gliclazide	144	149	118	11	5	1	4	5
	Metformin + glimepiride	11	24	8	0	0	0	2	1
	Metformin + glibenclamide	35	20	17	1	0	0	1	16
Mono + insulin	Metformin + insulin	43	46	32	5	3	0	0	3
	Gliclazide + insulin	6	5	4	0	1	0	0	1
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	39	37	21	5	3	1	3	6
	Metformin + glimepiride + insulin	3	6	2	1	0	0	0	0
	Metformin + glibenclamide + insulin	7	5	4	1	0	0	0	2
Total		433	433	329	29	14	11	10	40

APPENDIX XIII: Treatment regimens and changes in fasting plasma glucose results within target at the time of writing prescription 3 (n=118)

Treatment regimen	Anti-diabetic agent	prescription 2	prescription 3	no change between P2 & P3	Daily dose increased	Daily dose decreased	Step-up regimen	Step down regimen	Lateral regimen change
mono therapy	Metformin	57	59	55	2	0	0	0	0
	Gliclazide	4	4	1	1	0	0	0	2
	Glimepiride	1	5	1	0	0	0	0	0
	Glibenclamide	0	0	0	0	0	0	0	0
Dual therapy	Metformin + Gliclazide	34	17	17	0	0	0	6	11
	Metformin + glimepiride	1	13	1	0	0	0	0	0
	Metformin + glibenclamide	3	3	1	0	0	0	1	1
mono + insulin	Metformin + insulin	8	7	7	0	0	0	0	1
	Gliclazide + insulin	2	2	1	1	0	0	0	0
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	7	6	6	0	0	0	0	1
	Metformin + glimepiride + insulin	0	1	0	0	0	0	0	0
	Metformin + glibenclamide + insulin	1	1	1	0	0	0	0	0
		118	118	91	4	0	0	7	16

APPENDIX XIV: Treatment regimens and changes in fasting plasma glucose results outside target at the time of writing prescription 3 (n=419)

Treatment regimen	Anti-diabetic agent	prescription 2	prescription 3	no change between P2 & P3	Daily dose increased	Daily dose decreased	Step-up regimen	Step down regimen	Lateral regimen change
mono therapy	Metformin	121	127	113	3	0	5	0	0
	Gliclazide	14	8	7	0	0	0	0	7
	Glimepiride	6	10	5	0	1	0	0	0
	Glibenclamide	0	0	0	0	0	0	0	0
Dual therapy	Metformin + Gliclazide	136	79	65	8	1	0	0	62
	Metformin + glimepiride	26	90	21	1	0	0	1	3
	Metformin + glibenclamide	21	11	11	0	0	0	3	7
mono + insulin	Metformin + insulin	44	45	37	3	1	0	0	3
	Gliclazide + insulin	4	3	3	0	0	0	0	1
	Glimepiride + insulin	0	0	0	0	0	0	0	0

	Glibenclamide + insulin	0	0	0	0	0	0	0	0
Dual + insulin	Metformin + Gliclazide + insulin	35	19	10	3	1	0	0	21
	Metformin + glimepiride + insulin	8	25	7	0	0	0	1	0
	Metformin + glibenclamide + insulin	4	2	1	0	0	0	0	3
		419	419	280	18	4	5	5	107