# COMPLIANCE WITH THE GUIDELINES FOR THE MANAGEMENT OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH HYPERTENSION AND/OR DIABETES MELLITUS

By

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I, **Dr Khayakazi Nqiwa** declare that:

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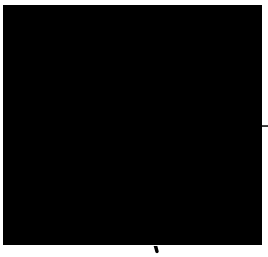
Signed: _  ____ Date: 29/03/2022_____

## Dedication

I dedicate this work to my daughter, Mbali Nqiwa, for her continuous encouragement, love, and support.

To my mother and my late father, your love, support, and confidence in me throughout my life.

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**List of abbreviation and nomenclature**

| | | |
|---|---|---|
| ACEI | : | Angiotensin-converting enzyme inhibitor |
| AF | : | Atrial fibrillation |
| ART | : | Antiretroviral treatment |
| ASA | : | Aspirin |
| BMI | : | Body mass index |
| BP | : | Blood pressure |
| CAD | : | Coronary heart disease |
| CARDIA | : | Coronary Artery Risk Development in Young Adult |
| CCB | : | Calcium channel blocker |
| CVA | : | Cerebrovascular accident |
| CVDs | : | Cardiovascular diseases |
| DBP | : | Diastolic blood pressure |
| DM | : | Diabetes Mellitus |
| DPP-4 | : | Dipeptidyl peptidase-4 |
| eGFR | : | Estimated glomerular filtration rate |
| GIT | : | Gastrointestinal tract |
| GPL-1 | : | Glucagon-like peptide-1 |
| GR | : | Glucometer reading |
| HbA1c | : | Hemoglobin A1c |
| HDL | : | High-density lipoprotein |
| HFrEF | : | Heart failure with reduced ejection fraction |
| HIV | : | Human immunodeficiency virus |
| HTN | : | Hypertension |
| IHD | : | Ischaemic heart disease |
| LMICs | : | Low and middle-income countries |
| LVH | : | Left ventricular hypertrophy |
| MHC | : | Major histocompatibility complex |
| MI | : | Myocardial infarction |
| NDOH | : | National Department of Health |

| | | |
|---|---|---|
| PC101 | : | Primary Care 101 |
| PHC | : | Primary health care |
| PI | : | Protease inhibitor |
| PTPN | : | Protein tyrosine phosphatase non-receptor type 22 |
| PVD | : | Peripheral vascular disease |
| RAAS | : | Renin-angiotensin-aldosterone system |
| SA | : | South Africa |
| SBP | : | Systolic blood pressure |
| SD | : | Standard deviation |
| SGLT2 | : | Sodium-glucose co-transporter 2 |
| SSA | : | Sub-Saharan Africa |
| TC | : | Total cholesterol |
| TG | : | Triglyceride |
| TIA | : | Transient ischaemic attack |
| WHO | : | World Health Organization |

## Abstract

**Background**: Globally, the burden of cardiovascular diseases (CVDs) is increasing. In South Africa (SA), evidence-based management guidelines and clinical tools containing symptom-based algorithms and checklists have been implemented as interventions for use by clinicians at the primary health care (PHC) level. Clinicians are expected to fully comply with these guidelines to improve the quality of care and clinical outcomes.

**Objective**: To determine clinician compliance with Primary Care (PC) 101 guidelines for the management of cardiovascular risk factors in patients with hypertension (HTN) and diabetes mellitus (DM).

**Method**: In this retrospective study, we reviewed medical records of patients aged 18 years and older who were receiving chronic care for HTN, DM, or both, at a PHC clinic, in KwaZulu Natal, SA, between June 2015 and August 2016, excluding newly diagnosed patients.

**Results**: Of the 99 patients included, 82 (83%) were females, and 88 (89%) were black; 70 (71%) patients had HTN, 27 (27%) had both HTN and DM, and 2 (2%) had DM only. The mean (SD) age was 60 (12) years. Of those with HTN (n = 70), blood pressure (BP) was measured in 57 (81%) at baseline, 56 (80%) at 6 months, and 62 (87%) at 12 months; body mass index (BMI) was documented in 10 (14%) and an estimated glomerular filtration rate (eGFR) done in 59 (84%). In those diagnosed with both HTN and DM (n = 27)**,** BP was measured in 25 (93%) at baseline, 26 (96%) at 6 months, and 24 (89%) at 12 months; glucometer reading (GR) was checked in 22 (82%) at baseline and 6 months, and 20 (74%) at 12 months; feet examination and urine dipsticks analysis were documented in 1 (4%), and eye examination and BMI in 2 (7%); eGFR was performed in 21 (78%) and hemoglobin A1c (HbA1c) in 16 (59%). Of the patients with DM only (n =2), BMI, eye and feet examination were recorded in 0% and urine dipsticks analysis done in 1 (50%).

**Conclusion**: This study showed low rate of clinician compliance with PC101 guidelines at a PHC clinic. However, reasons for clinicians' non-compliance were not explored. This emphasizes the need for future investigations to identify barriers to following guidelines.

**Keywords**: Compliance, guidelines, cardiovascular risks, hypertension, diabetes mellitus

## Chapter 1: Background and literature review

### 1.1 Introduction

Non-communicable diseases (NCDs), also known as chronic diseases, are a rising concern worldwide (1). According to the World Health Organization (WHO), approximately 41 million people die annually due to NCDs (1). Over 15 million NCD deaths are in those between 30 and 69 years, 85 % of which are from low and middle-income countries (LMICs) (1). In Sub-Saharan Africa (SSA), the proportion of NCDs increased from 18.6% to 29.8% between 1990 and 2017 (2).

Globally, CVDs consisting of coronary heart disease (CAD), stroke, peripheral vascular disease (PVD), and other cardiac and vascular conditions are the major NCDs and a leading cause of death (3). In 2019, an estimated 17.9 million people died of CVDs, and over three-quarters of those deaths took place in LMICs (3). In SSA, CVDs are responsible for over 37% of all NCD deaths (4), and a sustained increase in disability-adjusted life years (DALYs) is also observed (2).

Most CVDs are preventable, and addressing behavioral risk factors such as tobacco use, unhealthy diet, obesity, sedentary lifestyle, and excess alcohol consumption can reduce the CVD burden. In addition, screening for those at risk of developing CVDs for early detection, health education, and optimal treatment of hypertension (HTN), diabetes mellitus (DM), and dyslipidemia are necessary to reduce CVD risk (3). The WHO supports the Global Action Plan for Prevention and Control of NCDs 2013-2020. This plan aimed to reduce the number of premature deaths from NCDs through several targets. One of the targets is to reduce the overall death rate from NCDs by 25% by 2025 and at least one-third by 2030 (1).

### 1.2 Hypertension

#### *Definition and grading of hypertension*

Hypertension refers to a persistent elevation of office systolic blood pressure (SBP) of ≥140 mmHg and diastolic blood pressure (DBP) of ≥ 90 mmHg (5), and it has long been termed a “silent killer” because of its asymptomatic nature (6). Hypertension is categorized into 3 grades depending on elevated SBP and DBP; this is useful in defining the management approach. If SBP and DBP fall into different grades, hypertension is defined based on higher grades (7) (**Table 1**).

**Table 1: Definition and grading of hypertension (7)**

| Category | SBP (mmHg) | | DBP (mmHg) |
|---|---|---|---|
| Grade 1 | 140–159 | and/or | 90–99 |
| Grade 2 | 160–179 | and/or | 100–109 |

| | | | |
|---|---|---|---|
| Grade 3 | ≥180 | and/or | ≥110 |
| Isolated systolic hypertension | ≥140 | And | <90 |

Abbreviations: SBP = Systolic blood pressure, DBP = Diastolic blood pressure

***Etiology and pathophysiology of hypertension***

Hypertension can be classified into primary (essential), which accounts for 90-95%, and secondary (due to renal, vascular, and endocrine causes), responsible for 5 - 10% of all HTN cases (8). The exact etiology of primary HTN is unknown. However, various physiological mechanisms implicated in its development include cardiac output and peripheral resistance; sympathetic nervous system overactivity; renin-angiotensin-aldosterone system (RAAS); vascular cell dysfunction, and nitric oxide (NO) pathway (9, 10).

***Risk factors of hypertension***

Hypertension is a highly heterogeneous disorder with multiple risk factors; non-modifiable (age ≥ 65yrs, African descent, and genetics), and modifiable risk factors (obesity and sedentary lifestyle, high sodium intake, tobacco use, excess alcohol consumption, DM, chronic kidney disease (CKD), and dyslipidemia) (7, 11).

***Prevalence and an impact of hypertension***

Elevated blood pressure is an independent significant risk factor for most CVDs acquired in life, such as coronary heart disease (CHD), left ventricular hypertrophy (LVH), heart failure (HF), arrhythmias, stroke, CKD, retinopathy, and a major cause of premature death worldwide (12, 13). Globally, an estimated 1.13 billion people have HTN, and 27% are in Africa (13). In South Africa (SA), 30.4% of adults have HTN (5). However, despite this high prevalence, both awareness and optimal control are low amongst patients with HTN, with proportions ranging between 19-56% and 4-33%, respectively (14). In addition, black adults with HTN have a 1.3-fold higher rate of non-fatal stroke, 1.8-fold higher rate of fatal stroke, 1.5-fold mortality risk due to heart disease, and a 4.2-fold higher rate of end-stage renal disease (ESRD) than white adults (15).

***Clinical evaluation***

From the diagnosis, clinical evaluation is essential to identify modifiable risk factors, concomitant atherosclerotic risk factors such as DM and dyslipidemia, complications, and also establish an immediate and chronic care plan with the patient (7). There are tools to assess cardiovascular risk, and the European Guidelines recommend using the Systemic COronary System Evaluation (SCORE) (7). This model estimates the 10-year risk of a first atherosclerotic event concerning age, sex, smoking habits, total cholesterol (TC) level, and SBP (7).

***Goals of therapy***

Clinical trials have shown that optimally treating HTN reduces the risk of cardiovascular outcomes; stroke by 30-40%, heart failure by up to 64%, and myocardial infarction (MI) by 15-25% (16). In treating patients with HPT, the primary goal of therapy is to reduce blood pressure (BP) and prevent complications and death (9). The treatment targets for HPT are SBP to <140 mmHg and DBP to < 90 mmHg in those younger than 60 yrs of age; SBP of ≤ 130 mmHg in those with HPT and DM (130-140 mmHg in adults aged 60 years and older); and SBP of 130 – 139 mmHg in those with HPT and CKD (5, 7, 9).

***Therapeutic options for hypertension***

*Non-pharmacological treatment*

Non-pharmacological treatment involves lifestyle changes, including salt restriction, alcohol restriction, weight reduction, regular physical activity, and smoking cessation (7). However, most patients require drug therapy in addition to lifestyle modifications to achieve adequate BP control (7).

*Pharmacological treatment*

Five major classes of drugs recommended to form the basis of antihypertensive therapy since they have demonstrated effective reduction of BP and cardiovascular events in randomized control trials (RCTs) are; angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta-blockers, calcium channel blockers (CCB), diuretics (thiazide and thiazide-like diuretics) (7). They can be combined (except for ACEIs and ARBs) or used as monotherapy (7).

Pharmacological treatment of choice is influenced by comorbidities, ethnicity, pregnancy, and other patient-specific factors (9). For example, ACEI or ARBs are indicated in heart failure with reduced ejection fraction (HFrEF), post-MI, and in patients with HPT and DM to reduce albuminuria, delay onset, and progression of diabetic nephropathy; beta-blockers are recommended in clinical situations such as angina, post-MI, HF, atrial fibrillation, and young women planning pregnancy; and CCB and thiazide diuretics have been proven more efficient in black patients in reducing BP compared to other agents (7, 9).

Other classes of drugs that can be added in patients whose BP cannot be controlled by proven combination therapy include alpha-blockers, centrally acting agents, and mineralocorticoid receptor antagonists (MRAs) (7). These agents are not preferred as the first choice for treatment of HPT since they have been less widely studied in RCT and are associated with an increased risk of adverse effects (7).

**1.3 Diabetes mellitus**

***Definition, etiology, and classification***

DM is a metabolic disorder characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism, resulting in reduced insulin secretion and/or action (17). It can be classified into 4

major categories: (i) Type 1 DM (β cell destruction, usually leading to absolute insulin deficiency); (ii) Type 2 DM (insulin resistance with progressive relative insulin deficiency, or predominantly secretory defect with insulin resistance); (iii) Other types (genetic defect of β cell function, genetic defects in insulin action, diseases of the exocrine pancreas such as pancreatitis, endocrinopathies such as acromegaly, drug-induced, infection, other genetic syndromes such as down syndrome) and; (iv) hyperglycemia first detected in pregnancy (17). The classification of DM may not be determined at diagnosis; however, this should not delay therapy (17).

***Risk factors and pathophysiology***

Glucose metabolism is typically regulated by a feedback loop including islet β cells and insulin-sensitive tissues in which tissue sensitivity to insulin affects the magnitude of β-cell response (18). In insulin resistance, β cells maintain normal tolerance by increasing insulin output. However, when β cells cannot release sufficient insulin in the presence of insulin resistance, glucose concentrations rise (19). Thus, many different paths that manifest with persistent hyperglycemia are driven by various genetic and environmental factors, which result in the progressive loss of β cell mass and or function (18).

*Diabetes mellitus and genetics*

Diabetes mellitus is a polygenic disease where many common variants contribute to the occurrence of the disease. Disease heritability, defined as sibling relative risk of developing a disease, is 3 for type 2 DM and 15 for type 1 DM (20). However, maturity-onset DM of young (MODY) has a higher disease heritability of 50. In addition, mutations in any one of thirteen different individual genes have been identified to cause MODY (21). Therefore, a genetic diagnosis in this group can be critical in choosing appropriate therapy; for example, a child with KCJN11 mutation MODY should be treated with sulfonylureas rather than insulin (18).

A series of genes and loci influencing the genetic risk of immune-mediated DM have been well characterized. These include genes of the major histocompatibility complex (MHC), polymorphism of the insulin gene, and protein tyrosine phosphatase non-receptor type 22 (PTPN 22) (22, 23). The major determinants of risk for immune-mediated DM are genes within or linked to the MHC, particularly alleles of class II genes (HLA DR, DQ, and DP). In addition, MHC class I alleles have been shown to contribute to MHC influence such that for a major subset of relatives of patients, the risk is as high as 80% for siblings and 20% for the general population (18, 22, 23). Approximately 50 additional genes individually contribute more minor effects, contributing to gene variants that modulate immune regulation and tolerance. It also contributes to variants that influence responses to environmental signals and endocrine function, and some that are expressed in pancreatic β cells (18).

***Prevalence and an impact of diabetes mellitus***

The prevalence of DM has been increasing more rapidly in LMIC than in high-income countries. According to the International Diabetes Federation (IDF) recent report, 19 million adults (20-79yrs) are living with DM in Africa, and 4.6 million in SA (24). However, an estimated 60% of all adults living with DM are undiagnosed (24). Diabetes mellitus is a significant cause of blindness (retinopathy), CKD (nephropathy), CHD, and lower limb amputation (PVD and peripheral neuropathy), globally (25, 26).

***Goals of therapy in diabetes mellitus***

The goal of treatment is to prevent mortality and morbidity related to microvascular and microvascular complications. The target hemoglobin A1c (HbA1c) is ≤7% for most patients; however, in those with microvascular complications, elderly and frail, and those with frequent hypoglycemic episodes, HBA1c of 7.1 – 8.5% is acceptable (17).

***Therapeutic options in diabetes mellitus***

Patient education on self-management and lifestyle modification (diet, exercise, and smoking cessation) are essential in managing DM (17, 27). Drug therapies in DM include biguanides (metformin), sulphonylurea (gliclazide), Thiazolidinediones (pioglitazone), dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, sodium-glucose co-transporter 2 (SGLT2) inhibitors, α-glucosidase inhibitors (acarbose), and insulin (17).

Metformin monotherapy can be used, with a mean HbA1c reduction of 1.1%, 0.9% reduction if added to non-insulin agents, and a 0.6% reduction if added to insulin. In addition, metformin has been shown to improve cardiovascular outcomes and reduce all-cause mortality, diabetes-related mortality, and MI in obese patients compared to dietary changes alone (17). However, metformin is contraindicated if the estimated glomerular filtration rate (eGFR) is <30mm/min/1.73 $m^2$ (17). Gliclazide modified-release may be used as monotherapy or add-on therapy to other non-insulin agents to achieve an HbA1c reduction of 1% (17).

Pioglitazone has a similar efficacy profile with metformin and is commonly used when metformin is not tolerated, either as monotherapy, dual or triple therapy and can result in HbA1c reduction of ± 1% (17). DPP-4 inhibitors can be used in dual or triple therapy, added to metformin, sulphonylurea, SGLT 2 inhibitor, or insulin (17). It may achieve an HbA1c reduction of 0.5-1.1% when used as monotherapy (17). GLP-1 receptor agonists can be used as monotherapy, dual and triple therapy; however, they cannot be combined with DPP-4 or SGLT2 inhibitors (17). They may reduce HbA1c by 0.9-1.2% (17). The α-glucosidase inhibitors reduce HbA1c by 0.8%. (17). Insulin can be used as monotherapy or in combination with oral medication. In type 2 DM, insulin should be considered as one of the therapeutic options in patients not achieving adequate glycemic control on 2 or 3 oral glucose-lowering drugs (17)

### 1.4 Obesity

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health (28). Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters ($kg/m^2$) (28). The WHO defines overweight as BMI $\geq$ 25 $kg/m^2$ ( $\geq$ 23 kg/m2 for an Asian), and obesity as BMI $\geq$ 30 $kg/m^2$ ($\geq$ 25 for an Asian), which is then stratified into 3 classes (28, 29) (**Table 2**).

**Table 2: Classification of overweight and obesity in adults (29)**

| Classification | International BMI Category ($kg/m^2$) | BMI category for Asians |
|---|---|---|
| Overweight | 25-29.9 | 23-24.9 |
| Obese | $\geq$ 30 | $\geq$ 25 |
| Class I | 30.0-34.9 | 25-29.9 |
| Class II | 35.0-39.9 | $\geq$ 30 |
| Class III | $\geq$ 40 | |

Abbreviation: BMI = Body Mass Index

Obesity is considered the central pathophysiology for metabolic syndrome and insulin resistance and may also be associated with HTN (7, 28). Evidence suggests that weight reduction can reduce BP and cardiovascular risk (7); this makes obesity a critical modifiable condition to manage in reducing the morbidity and mortality associated with CVDs. Obesity and DM often occur concurrently (19). Expansion of adipose tissue may locally impair insulin signaling through its associated accumulation of activated macrophages that express several pro-inflammatory genes, including cytokines such as the tumor necrosis factor α (19). In addition, inflammation of the hypothalamus may also contribute to central leptin resistance and weight gain (19).

### 1.5 Relationship between hypertension and diabetes mellitus

Hypertension and DM often co-exist, and several mechanisms have been proposed to explain the association (30). These include the upregulation of the renin-angiotensin-aldosterone system (RAAS), oxidative stress, systemic inflammation, and immune system activation (30). In addition, HPT and DM are closely linked because they share risk factors, such as atherosclerosis, dyslipidemia, overweight, and obesity, with a sustained overlap in cardiovascular complications. (30-32).

### 1.6 Routine care in patients with hypertension and diabetes mellitus

Once the diagnosis of HTN or DM has been established, management interventions begin. These include inquiring about symptoms (e.g., the presence of angina, dyspnea, oedema, claudication) and risk factors (diet, smoking, alcohol use, and exercise), assessment of BMI and BP, at diagnosis and every visit; waist

circumference is also assessed at diagnosis, and further evaluation depends on the initial assessment and treatment goals (5, 33).

In those with HPT, glucometer reading (GR) monitoring is performed at diagnosis, and then yearly (or if glucosuria is present), urine dipsticks and eGFR are assessed yearly, if normal at diagnosis (5, 33). Following the diagnosis of DM, GR is monitored at every visit; urine dipsticks are analyzed yearly (or if blood glucose ≥ 15 mmol/L; HBA1c performed 3 – 6 months and then yearly; feet and eyes are examined yearly (more often if initially abnormal). In addition, urine dipsticks and eGFR are performed yearly, if normal at diagnosis (5, 33). **Table 3** shows routine care and targets in patients with HTN and DM (33).

**Table 3: Routine care in patients with hypertension and diabetes mellitus (33)**

| Assessment | Hypertension | Diabetes mellitus | Notes |
|---|---|---|---|
| **CVD symptoms and other risks inquiry** | Every visit | Every visit | Ask about chest pain, difficulty in breathing, claudication, symptoms of stroke/TIA; smoking, diet, alcohol/drug misuse, stress, exercise |
| **BP (mmHg)** | Every visit | Every visit | Target BP: < 140/90 (or SBP 120-140, DBP 70-80 if diabetic or < 130/80 if CVD, heart failure or kidney disease) |
| **Glucose (mmol/L)** | Diagnosis, then yearly (or if glucosuria) | Every visit | If glucose < 8, review in 6 months, > 8, review in 1 month |
| **BMI ($kg/m^2$)** | Every visit | Every visit | Aim for body mass index of < 25 |
| **Waist circumference (cm)** | At diagnosis, then yearly; 3-monthly if trying to lose weight | At diagnosis, then yearly; 3-monthly if trying to lose weight | Aim for < 80cm (woman) and < 94cm (man) |
| **Eyes exam** | If visual problems develop | At diagnosis, then yearly | Refer if visual problems, cataracts, or retinopathy |
| **Feet exam** | N/A | At diagnosis, 3 months, then yearly. More often, if high risk | Foot screen and foot care education |
| **Urine dipstick** | At diagnosis, then yearly | At diagnosis, then yearly | Diabetes: If there is no protein on the dipstick, check for microalbuminuria. If albuminuria or protein, start ACEI/ARB. |
| **eGFR ($mL/min/1.73 m^2$)** | Diagnosis, then yearly | At diagnosis, then yearly | If eGFR < 60 refer to the doctor. |

| | | | |
|---|---|---|---|
| **HBA1c (%)** | N/A | 6 monthly if HBA1c < 7%; 3 months after treatment change | Aim for HBA1c <7% |
| **Fasting lipids** | At diagnosis | At diagnosis | If cholesterol > 7.5, refer to specialist |

Abbreviations: CVD = Cardiovascular disease, BP = Blood pressure, BMI = Body mass index, Glucose = glucometer reading, eGFR = Estimated glomerular filtration rate, HBA1c = Hemoglobin A1c, ACEI = Angiotensin converting enzyme inhibitor, ARB = Angiotensin receptor blocker, N/A = Not applicable

### 1.7 The burden of CVD at Ugu District Municipality in KwaZulu Natal, South Africa

Southport clinic is a primary health care facility situated on the South coast of KwaZulu -Natal province, in Ugu District, SA. Southport clinic falls under the Hibiscus sub-district, on the coastal belt, and serves a varied peri-urban and rural population. The clinic operates seven days a week and provides all primary healthcare services, including human immunodeficiency virus/advanced immunodeficiency syndrome (HIV/AIDS), HTN, DM, and other chronic disease care.

In Ugu District, Year of Life Lost (YLLs ) between 2008 and 2014: stroke increased from 4.7% to 6.1%, hypertensive heart disease remained static at 2.6%, and DM slightly increased from 2.6% to 2.8% (34). The incidence of HTN in adults aged 40 years and older was 13.9 per 1000 in 2015 (34). Hypertension prevalence among 15 years and older was 11.8% in 2015 and rose to 12.8% in 2017 (34). The diabetes mellitus treatment coverage rate for those aged 15 years and older in 2017 was 30% (34).

### 1.8 Compliance with treatment guidelines

Compliance refers to the degree of conformity to the recommendations (35). In clinical practice, compliance is often used to measure the quality of care (36). Multiple factors influence compliance with recommended treatment guidelines. These include health system-related factors such as unavailability of resources, patient-related factors such as infrequent clinic visits, refusal of treatment, contraindications or adverse effects to the treatment and financial constraints, and clinician-related factors such as unawareness/knowledge, time pressure, and difficulty in changing personal routine (36-38). Evidence shows that clinicians' non - compliance to clinical practice guidelines is up to 70% and occurs across most disciplines and countries (36). For example, in SA, a study of 475 clinical encounters conducted in Potchefstroom sub-district PHC in North West Province showed that only 56% of the nurses and 75% of doctors diagnosed HTN based on the guidelines and that doctors were less compliance (56.6%) than nurses (63.6%) with drug management (38). Furthermore, a study of 500 records for patients with type 2 DM which investigated compliance with local diabetes guidelines at a district-level hospital reported clinician's poor compliance in annual HbA1c

measurements (29%), serum lipid (40%), eGFR (32%), eye examination (14%), foot examination (7.8%), urinalysis, and anthropometric measurements (4.2%) (39).

### 1.9 Problem statement

Primary health care is vital in the health care system, servicing most of the country's population (40, 41). However, to ensure the successful contribution of the primary health care system to health care, the development of standardized, evidence-based guidelines to guide primary health care workers with clinical approach and management of common conditions encountered in the primary health care (PHC) setting is essential. In South Africa, Primary Care 101(33) is such a guide. Unfortunately, many clinicians may not know this guide, and some may choose not to follow it (38, 42), and failure to optimally manage risk factors for CVD at a primary health level can result in the development of complications that may require referral to the already burdened secondary and tertiary level services and accumulation of health care expenditure. This study is relevant to Internal Medicine in that Internal medicine receives patients with medical complications that should be prevented and addressed at a PHC level.

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## Chapter 2 A Submission ready Manuscript


### Abstract

**Background**: Globally, the burden of cardiovascular diseases (CVDs) is increasing, mainly due to the rising prevalence and poor management of associated risk factors such as hypertension (HTN) and diabetes mellitus (DM). In South Africa (SA), standardized, evidence-based management guidelines and clinical tools containing symptom-based algorithms and checklists have been implemented as interventions for use by clinicians at the primary health care (PHC) level. Clinicians are expected to fully comply with these guidelines to improve the quality of care and clinical outcomes.

**Objective**: To determine clinician compliance with primary care (PC) 101 guidelines for the management of cardiovascular risk factors in patients with HTN and DM.

**Method**: In this retrospective study, we reviewed medical records of patients aged 18 years and older who were receiving chronic care for HTN, DM, or both, at a PHC clinic, in KwaZulu Natal, SA, between June 2015 and August 2016, excluding newly diagnosed.

**Results**: Of the 99 patients included, 82 (83%) were females, and 88 (89%) were black; 70 (71%) patients had HTN, 27 (27%) had both HTN and DM, and 2 (2%) had DM only. The mean (SD) age was 60 (12) years. Of those with HTN (n = 70), blood pressure (BP) was measured in 57 (81%) at baseline, 56 (80%) at 6 months, and 62 (87%) at 12 months; body mass index (BMI) was documented in 10 (14%) and an estimated glomerular filtration rate (eGFR) done in 59 (84%). In those diagnosed with both HTN and DM (n = 27)**,** BP was measured in 25 (93%) at baseline, 26 (96%) at 6 months, and 24 (89%) at 12 months; glucometer reading (GR) was checked in 22 (82%) at baseline and 6 months, and 20 (74%) at 12 months; feet examination and urine dipsticks analysis were documented in 1 (4%), and eye examination and BMI in 2 (7%); eGFR was performed in 21 (78%) and hemoglobin A1c (HbA1c) in 16 (59%). Of the patients with DM only (n =2), BMI, eye and feet examination were recorded in 0% and urine dipsticks analysis done in 1 (50%). Of the patients documented to have cerebrovascular accident/transient ischaemic attacks (CVA/TIA) (n = 4) , 1 (25%) was on a statin, and 2 (50%) were on aspirin. Two had ischaemic heart disease/coronary heart disease (IHD/CAD) and were both on statins and aspirin.

**Conclusion**: This study showed low rate of clinician compliance with PC101 guidelines at a PHC clinic. However, reasons for clinicians' non-compliance were not explored in this cohort. This emphasizes the need for future investigations to identify barriers to following guidelines.



**Keywords:** Compliance, guidelines, cardiovascular risks, hypertension, diabetes mellitus

## Introduction

Cardiovascular diseases (CVDs), consisting of ischemic heart disease (IHD), heart failure, stroke, peripheral vascular disease (PVD), nephropathy, other cardiac and vascular conditions, constitute the leading causes of global mortality (1). According to the World Health Organization (WHO), an estimated 17.9 million people died of CVDs in 2019, representing 32% of global deaths (2, 3). The majority of deaths related to CVDs are preventable by addressing behavioral risk factors such as tobacco use, unhealthy diet, and harmful alcohol use, which are associated with the development of hypertension (HTN), overweight/obesity, diabetes mellitus (DM), and hyperlipidemia (4). Hypertension and DM remain the main cardiovascular risks worldwide (5, 6). It is estimated that 1.13 billion people have HPT globally (5), and 463 million have (7). However, despite this high prevalence, awareness and control of both diseases remain poor, especially in low-and-middle-income countries (LMICs) (8-10).

In South Africa (SA), primary health care (PHC) promises to play a vital role in the health care system, servicing most of the country's population (11). However, collaborative efforts of relevant stakeholders and policymakers are required to support and strengthen the primary health care system to ensure its successful contribution to the health system (11, 12). To standardize management care and support clinicians working at the PHC level, the National Department of Health (NDOH) of South Africa developed a primary care guide that encompassed patient management as per approved policies and guidelines (13). The guide contains symptom-based algorithms and checklists that are easy to read and tailor for those clinicians who may be too busy to confirm the information on major existing trials. This guide gets updated as new evidence emerges (14, 15).

Routine screening and non-pharmacological management for those with HTN and DM often overlap because of shared underlying atherosclerotic risks, pathophysiologic mechanisms, and complications (16-18). Once the diagnosis of HTN or DM has been established, management interventions begin. These include inquiring about symptoms, such as the presence of angina, dyspnea, edema, claudication, and risk factors, such as diet, smoking, alcohol use, and exercise), assessment of BMI and BP, at diagnosis and every visit; waist circumference is also assessed at diagnosis, and further evaluation depends on the initial assessment and treatment goals (13, 19).

In those with HPT, glucometer reading (GR) monitoring is performed at diagnosis, and then yearly or if glucosuria is present, urine dipsticks and eGFR are assessed yearly, if normal at diagnosis (13, 19). Following the diagnosis of DM, GR is monitored at every visit; urine dipsticks are analyzed yearly or if blood glucose is$\geq$ 15 mmol/L; HBA1c is performed 3 – 6 months and then yearly; feet and eyes are examined yearly, or more often if initially abnormal. In addition, urine dipsticks and eGFR are performed yearly, if normal at diagnosis (13, 19).

Clinical trials have shown that optimal treatment of HTN reduces the risk of cardiovascular outcomes; stroke by 30 - 40%, heart failure by up to 64%, and myocardial infarction by 15-25% (20). The primary care (PC) 101 guide (13) recommends target systolic blood pressure (SBP) of < 140 mmHg and diastolic blood pressure (DBP) of < 90 mmHg, even tighter control (SBP 120 – 140) in those with high cardiovascular risks such as those with comorbid chronic kidney disease (CKD) or DM if tolerated. These recommendations are similar to those recommended in other guidelines, both locally and internationally (19, 21, 22). In patients with DM, the aim is to reach and maintain blood glucose < 8 mmol/L and HbA1c $\leq$ 7% in most patients (13, 23). However, in patients with microvascular complications, elderly and frail, and those with frequent hypoglycemic episodes, HBA1c of 7.1 – 8.5% is acceptable (24).

Globally, over 37 million people were living with the human immunodeficiency virus (HIV) in 2020, 67% of whom lived in Sub-Saharan Africa (SSA) (25). Access to antiretroviral treatment (ART) has changed the disease profile, people now live longer, making HIV a chronic disease (26). However, because of persistent immune activation and inflammation in treating HIV and exposure to ART such as protease inhibitors (PIs), people living with HIV are at increased risk of developing metabolic diseases such as hypertension, diabetes mellitus, dyslipidaemia, and obesity (27), hence an increased risk of cardiovascular events (28-30). Lack of management of cardiovascular risk factors at the PHC level results in increased complication and cost, morbidity, and mortality.

**Objective**

To determine clinician compliance with PC 101 guidelines for the management of cardiovascular risk factors in patients with HPT and DM.

**Methods**

This retrospective study included all patients over 18 years of age who were receiving chronic care for HPT, DM, or both, at a primary health care clinic in Port Shepstone, KwaZulu Natal province, between June 2015 and August 2016. All patients with hypertension and Diabetes mellitus during the study period were included in the study. Newly diagnosed and undiagnosed patients were excluded. The diagnoses of HTN and DM are guide by the PC101 guidelines at PHC level (13). Data retrieved included diagnoses, date of diagnosis, and initial clinic visit; demographic details (age, gender, race); BP, blood glucose according to the glucometer, BMI, urinalysis; feet and eyes exam (where necessary); laboratory investigations such as estimated glomerular filtration rate (eGFR), hemoglobin A1c (HBA1c), and lipogram. Ethics approval was obtained from the University of Kwa-Zulu Natal (UKZN) Biomedical Research Ethics committee (reference number: BE020/17). The necessary permission to conduct the study was attained from the Department of Health KwaZulu Natal and Ugu Health District.

**Statistical analysis**

Data were analysed using SPSS® 23.0 software (IBM Corp, Armonk, NY, USA). All data were assessed for normality. Frequency tables were used to assess categorical variables. Pearson's chi-square test or Fisher's exact test were used in assessing the association between categorical variables. Comparing proportions between three groups was done using analysis of variance. A p-value of $< 0.05$ was considered statistically significant.

**Results**

There were 230 patients registered to have HPT, DM, or both during the period under review. However, medical records were retrievable for 174 patients, 99 of whom were included (**Figure 1**).

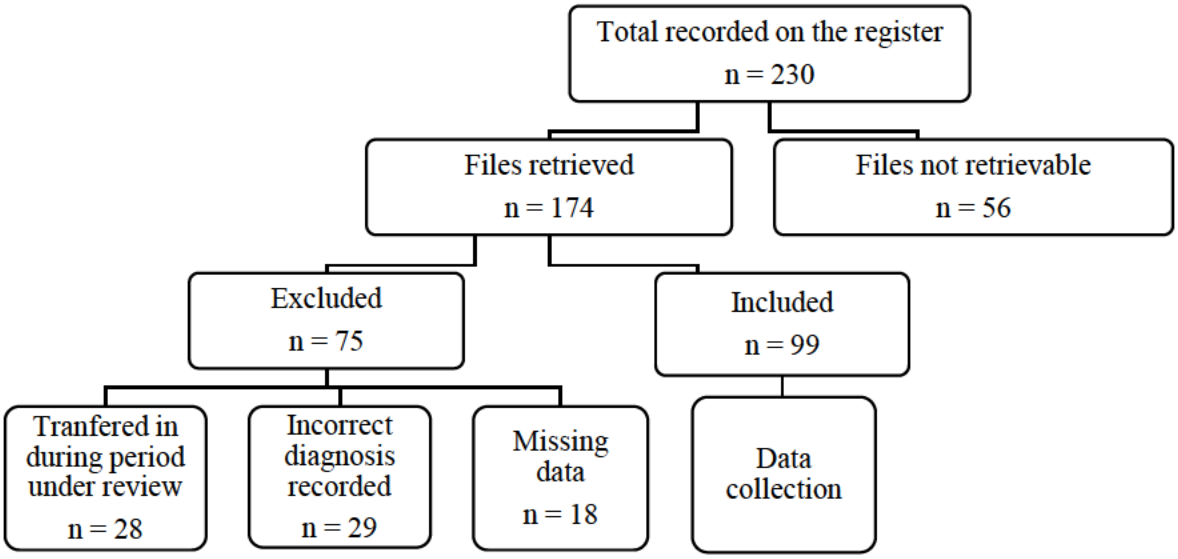


**Figure 1: A flowchart of included medical records**

Of the 99 patients included in this study, the mean (SD) age was 60 (12) years. Sixty-five (66%) were aged 55 or older. Eighty-two (83%) were female, and 89% were black ($p < 0.001$). Seventy (71%) had HPT, 2 (2%) had DM, and 27 (27%) had HPT and DM ($p < 0.001$). Seventy-two (73%) were HIV negative, 22 (22%) were infected, and 5 (5%) had an unknown status ($p < 0.001$) (**Table 1**).

**Table 1: Baseline characteristics of the study population (n = 99)**

| Variables | Categories | N (%) | p-value |
|---|---|---|---|
| Age (years) | 35-44 | 10 (10) | < 0.001 |
| | 45-54 | 24 (24) | |
| | ≥55 | 65 (66) | |
| Sex | Male | 17 (17) | <0.001 |

| | | | |
|---|---|---|---|
| | Female | 82 (83) | |
| Race | Black | 88 (89) | < 0.001 |
| | White | 10 (10) | |
| | Asian | 1 (1) | |
| Diagnosis | HPT | 70 (71) | < 0.001 |
| | DM | 2 (2) | |
| | HPT& DM | 27 (27) | |
| HIV | Negative | 72 (73) | < 0.001 |
| | Infected | 22 (22) | |
| | Unknown | 5 (5) | |

Abbreviations: DM = Diabetes mellitus, HTN = Hypertension, HIV = Human immunodeficiency virus.

Data expressed as n (%). P-values arising from the One-Sample T-Test are presented.

Significant level is $p < 0.05$.

In patients with HTN only (n = 70), BP was measured in 57 (81%) at first month, 56 (80%) at 6 months and 62 (87%) at 12 months. GR monitoring was done in 22 (31%) at first month, 16 (23%) at 6 months, and 11 (16%) at 12 months. Eye exam was assessed in 1 (1%), urine dipstick in 0 (0%) and BMI in 10 (14%) patients. eGFR was assessed in 59 (84%), TC in 40 (57%), and triglycerides in 32 (46%) patients.

In those with HTN and DM (n = 27), BP was measured in 25 (93%) at first month, 26 (96%) at 6 months, and 24 (89%) at 12 months. GR was checked in 22 (82%) at first month and 6 months and in 20 (74%) at 12 months. Feet exam and urine dipstick were assessed in 1 (4%), and eye exam and BMI were evaluated in 2 (7%). eGFR was performed in 21 (78%), HBA1c in 16 (59%), total cholesterol in 21 (78%), and triglycerides in 23 (85%).

In patients with DM only (n = 2): BP and GR monitoring were evaluated in both (100%) at all 3 visits. Urine dipstick was performed in 1 (50%), and eye and feet were examined in 0 (0%). None (0%) of the patients had BMI evaluated. Laboratory investigations (eGFR, HBA1c, total cholesterol, and triglycerides) were assessed in both (100%).

Of the two (2%) patients who had urine dipsticks evaluated in this study (n =99), 0 (0%) had documented proteinuria. None was tested for microalbuminuria.

Statistically significant differences in mean for GR at baseline (5.8 vs. 8.9 mmol/L, p < 0.001) and at 6 months (5.6 vs.10.3 mmol/L, p 0.010) were observed between those who had HTN and those who had DM. At 12 months, the mean for GR was 5.6 mmol/L in those with HTN, 13.8 mmol/L in those with DM, and 9.0 mmol/L for those with both HPT and DM, with statistically significant differences in mean in all three groups (p 0.003). Mean (SD) HBA1c was 8.9% (0.6) in those with DM and 8.7 (2.4) in those with HTN, but no significant differences in mean between these 2 groups (p 0.771). There were no statistically significant differences between all groups for mean SBP and DBP, total cholesterol (TC), triglycerides (TG), and BMI. **Table 2** show routine examination and investigations in this cohort.

**Table 2: Examination and investigation findings of the study cohort (n = 99)**

| **Variables** | **All (n = 99)** | **Hypertension (n = 70)** | | **Diabetes mellitus (n = 2)** | | **Hypertension and diabetes mellitus (n = 27)** | | **p-value** |
|---|---|---|---|---|---|---|---|---|
| | N (%) | N (%) | Mean (SD) | N (%) | Mean (SD) | N (%) | Mean (SD) | |
| SBP (mmHg) | | | | | | | | |
| Baseline* | 84 (85) | 57 (81) | 139 (20) | 2 (100) | 120 (23) | 25 (93) | 148 (26) | 0.063 |
| 6 months | 84 (85) | 56 (80) | 133 (18) | 2 (100) | 115 (13) | 26 (96) | 143 (24) | 0.048† |
| 12 months | 88 (89) | 62 (87) | 136 (25) | 2 (100) | 109 (20) | 24 (89) | 139 (20) | 0.226 |
| DBP (mmHg) | | | | | | | | |
| Baseline* | 84 (85) | 57 (81) | 75 (14) | 2 (100) | 70 (4) | 25 (93) | 77 (12) | 0.741 |
| 6 months | 84 (85) | 56 (80) | 75 (18) | 2 (100) | 72 (2) | 26 (96) | 71 (16) | 0.577 |
| 12 months | 88 (89) | 62 (87) | 75 (16) | 2 (100) | 70 (6) | 24 (89) | 67 (13) | 0.099 |
| GR (mmol/L) | | | | | | | | |
| Baseline* | 46 (47) | 22 (31) | 5.8 (0.9) | 2 (100) | 8.9 (0.1) | 22 (82) | 11.0 (4.3) | < 0.001† |
| 6 months | 40 (40) | 16 (23) | 5.6 (1.3) | 2 (100) | 10.3 (4.0) | 22 (82) | 8.8 (4.0) | 0.010† |
| 12 months | 32 (33) | 11 (16) | 5.6 (1.2) | 2 (100) | 13.8 (3.2) | 20 (74) | 9.0 (3.8) | 0.003† |
| Miscellaneous | | | | | | | | |
| Feet exam | 1 (1) | NI | NI | 0 (0) | NA | 1 (4) | NA | NA |
| Eye exam | 3 (3) | 1 (1) | NA | 0 (0) | NA | 2 (7) | NA | NA |
| Urine dipstick | 2 (2) | 0 (0) | NA | 1 (50) | NA | 1 (4) | NA | NA |
| BMI ($kg/m^2$) | 12 (12) | 10(14) | 31 (5.2) | 0 (0) | NA | 2 (7) | 35 (0.2) | 0.402 |
| Laboratory | | | | | | | | |
| eGFR | 82 (83) | 59 (84) | NA | 2 (100) | NA | 21 (78) | NA | NA |
| HBA1c (%) | 18 (18) | NI | NI | 2 (100) | 8.9 (0.6) | 16 (59) | 8.7 (2.4) | 0.771 |
| TC (mmol/L) | 63 (64) | 40 (57) | 5.0 (1.3) | 2 (100) | 4.8 (1.8) | 21 (78) | 4.7 (0.9) | 0.696 |
| TG (mmol/L) | 57 (58) | 32 (46) | 1.5 (1.1) | 2 (100) | 2.4 (0.4) | 23 (85) | 1.3 (0.6) | 0.302 |

*Baseline = first month of the study period

†Statistically significant

Abbreviations: SPB = Systolic blood pressure, DBP= Diastolic blood pressure, GR = Glucometer reading, BMI = Body mass index, HBA1c = Hemoglobin A1c, NA = Not available, NI = Not indicated, eGFR = Estimated glomerular filtration rate, TC = Total cholesterol, TG = Triglyceride.
Data are expressed as frequency count (%) or mean (SD).
P-values are generated using the one-way analysis of variance. Significant level is $p < 0.05$.

Of all patients with DM (n=29), 25 (86%) were on metformin, 13 (45%) were on sulphonylurea, and 9 (31%) were on insulin therapy. Of all patients with HTN (n = 97), 88 (91%) were on diuretics, 66 (68%) were ACEI, 55 (57%) were on CCB, and 19 (20%) were on beta-blockers. Of the ones on ACEI inhibitors (n = 55), 19 (35%) had DM. Statins were prescribed in 23 and Aspirin (ASA) in 7 (7%).

Of the study population (n=99), cerebrovascular accident/transient ischaemic attack (CVA/TIA) was documented in 4, nephropathy in 10, ischaemic heart disease/coronary heart disease (IHD/CAD) in 2, and cataract in 1. Of the patients with CVA/TIA (n = 4), 1 (25%) was on a statin, and 2 (50%) were on ASA; and of the ones with IHD/CAD (n = 2), statins and ASA were prescribed in both (100%).

Of all patients in this study (n = 99), BP was not done by the clinician in seven at baseline, six at 6 months, and seven at 12 months. Eight patients did not present for their review at baseline, nine at 6 months, and four at 12 months (**Table 3**).

**Table 3: Compliance with blood pressure monitoring (n = 99)**

| **Variables** | **Number of patients in whom blood pressure was monitored** | | |
|---|---|---|---|
| | **Baseline** | **6 months** | **12 months** |
| Test done | 84 | 84 | 88 |
| Test not done | 15 | 15 | 11 |
| By the clinician | 7 | 6 | 7 |
| Patient not present | 8 | 9 | 4 |

All data expressed as frequency count

In all patients with DM (n = 29), glucose monitoring was not done in 5 at baseline and six months, and seven at 12 months; all related to patients not being present for their visits (**Table 4**).

**Table 4: Compliance with glucose monitoring using a glucometer (n = 29)**

| **Variables** | **Number of patients in whom blood sugar was monitored** | | |
|---|---|---|---|
| | **Baseline** | **6 months** | **12 months** |
| Test done | 24 | 24 | 22 |
| Test not done | 5 | 5 | 7 |
| By the clinician | 0 | 0 | 0 |
| Patient not present | 5 | 5 | 7 |

All data expressed as frequency count

In patients living with HIV infection (n = 22), all (100%) were on ART. The annual HIV viral load was done in 19 (86%) and was suppressed in all. Twenty (91%) had HTN, and 2 (9%) had HTN and DM. eGFR was evaluated in 16 of those with HTN; and was < 15 mL/min/1.73 $m^2$ in 1, between 30 -59 mL/min/1.73 $m^2$ in another one, and ≥ 60 mL/min/1.73 $m^2$ in 14. Of the two patients who had HTN and DM, eGFR was evaluated in both and was 60 ≥ mL/min/1.73 $m^2$ (**Table 5**).

**Table 5: Diagnosis and estimated glomerular filtration rate in HIV infected (n = 22)**

| **Diagnosis** | **eGFR done** | **eGFR (mL/min/1.73 $m^2$)** | | | |
|---|---|---|---|---|---|
| | | **≥60** | **30 - 59** | **15 -29** | **<15** |
| HTN (n = 20) | 16 | 14 | 1 | 0 | 1 |
| HTN and DM (n = 2) | 2 | 2 | 0 | 0 | 0 |

Abbreviations: HTN = Hypertension, DM = Diabetes mellitus, eGFR = Estimated glomerular filtration rate

**Discussion**

Compliance with PC 101 guidelines has never been reported before. This study assessed PHC clinician compliance with screening and managing cardiovascular complications in patients with HTN and DM. Patients in this study were older with a mean (SD) of 60 (12) years; two-thirds were aged 55 years and older, and none were younger than 35 years. None of the patients in the study had documented secondary causes of Hypertension. Blacks and female patients represented the majority of the study population. Hypertension was more prevalent than DM. The predominance of black patients can explain these findings in this cohort as the population at risk of developing HTN due to propensity to salt sensitivity and suppressed plasma renin leading to sodium retention and predisposition to HTN (31). Of those with DM, most (93%) had HPT. Similar observations have been reported in other studies where patients with DM had at least a 2-fold increased risk of developing HTN after being diagnosed with DM (32-34). In addition, DM and HTN co-existence are suggestive insulin resistance or metabolic syndrome (35, 36). This suggests that almost one-third (27%) in this cohort could have metabolic syndrome. However, further studies are required to confirm and evaluate these findings.

Blood pressure (BP) and glucometer reading (GR) monitoring were suboptimal in this cohort. This is contrary to a study done in the Cape peninsula where 98% of patients had their BP and blood glucose monitored and recorded (37). In our study, the more affected patients were those who were treated for HTN (n = 70), with BP measured in 81% at first month, 80% at 6 months, and 87% at 12 months visit) compared to those treated for both HTN and DM (n = 27), BP was done in 93% at first month, 96% at 6 months, and 89% at 12 months). Glucometer reading monitoring (31% at first month, 23% at 6 months, and 16% at 12 months) in those with HTN (but no DM) was not regarded as non-compliance with the guideline, which suggests that blood glucose should be checked yearly in patients with HPT since patients in this cohort were

not diagnosed at the same time and had different times that were regarded as annual visits. In patients with HTN and DM (n=27), GR monitoring was poor, done on 79% on average (82% at baseline and 6 months, and 74% at 12 months visits).

There was no difference in the mean for SBP and DBP in all the groups. The differences in mean (SD) for GR at baseline [5.8 (0.9) vs. 8.9 (0.1) mmol/L, $p < 0.001$] for those with HTN vs DM, and at 6 months [5.6 (1.3) vs 10.3 (4.0) mmol/L, p 0.010] is expected, since those with HTN did not have DM. At 12 months visit, the observed differences in the mean between the groups (p 0.03) reflect poor glycaemic control in those with DM only; mean (SD) of 9.0 (3.8), since target blood glucose should be less than 8 mmol/L according to the guidelines (13). These findings were supported by the mean (SD) HBA1c of 8.9% (0.6) in those with DM only. Suboptimal glycemic control was similarly seen in patients with DM in Tshwane district in a cluster-randomized trial of 12 primary health care clinics (38) and a study at a rural district in Hlabisa, Kwazulu-Natal (39).

Body mass index (BMI) was done in 12 patients, 83% of whom were had HTN (but not DM), and 17% had HTN and DM. Only one BMI reading was documented in these patients over 12 months. However, there are indications that BMI was above the ideal limit in most (mean (SD) BMI of 31 (5.2) $kg/m^2$ in those with HTN and 35 (0.2) $kg/m^2$ in those with HTN and DM, which warranted frequent monitoring of BMI as per guideline (13). It is essential to mention that some patients had their body weight measured but no documented height. Investigations for other cardiovascular risks, i.e., TC and TG, were also suboptimal, especially in those patients with HTN only than those HTN and DM. However, the reasons for these findings were not clear, and require further investigation and training of the clinician on the importance of performing these tests as recommended.

Cardiovascular complications were also reported, and nephropathy was the commonest, followed by CVA/TIA and IHD/CAD. Both patients with IHD/CAD were on aspirin and statins; however, only 50% of those with CVA/TIA were on aspirin, and 25% were on a statin with no documented reasons. This was not in keeping with guidelines that suggest aspirin and statin for life in ischaemic CVA/TIA (13). In DM patients, metformin was the most prescribed (86%), followed by sulphonylureas (45%), and then insulin (31%). In HTN patients, diuretics were prescribed in 91%, ACEI in 68%, and CCB in 57%. The clinician's failure to assess BMI, perform urine dipsticks analysis, eye and feet examination, and measure eGFR, serum lipids and HbA1c was the main reason below expected level of care in this cohort. However, patients not presenting for their visit was the main reason for non-compliance with blood glucose monitoring in those with DM.

HIV testing was done in 95% of the study population, and almost a quarter of the patients were HIV infected and all (100%) on ARTs. Viral load was done in 86% and noted to be lower than detectable in all (100%).

This was in line with the 90-90-90 goal, where 90% of people living with HIV should be aware of their HIV status, of whom 90% must be on ARTs and 90% virologically suppressed (25). Assessment of renal function including urine dipsticks in the HIV infected is essential, particularly in those on tenofovir, and renal dysfunction may complicate treatment for HTN (22). In addition, the renal disease may cause secondary HTN (21), and increase cardiovascular risk. Data for the ART regimen was not collected in this study, however it is important to mention that certain classes of drugs such as protease inhibitors (PIs) are associated with risk of metabolic disease development and increased cardiovascular risk (40). Eighteen (82%) HIV-infected patients had eGFR done, and 2 (11%) of those had eGFR of less than 60%. All HIV-infected patients had HTN, and only 2 had DM in this cohort; none had documented IHD.

**Study limitations**

The major limitations were poor record-keeping (incorrect diagnosis recorded on the register) and small sample size. In addition, though the weight was measured in most patients, no height was documented in the majority, hence the inability to calculate the BMI. Furthermore, though eGFR was done in most, the mean could not be determined since no specific values for eGFR greater than 60 mL/min/1.73m$^2$ were recorded. Urine dipsticks analysis was another major limitation in this study.

**Conclusion**

Compliance with PC101 guidelines to survey and manage patients with cardiovascular risk at this PHC was suboptimal in respect to BP monitoring at every visit; blood glucose monitoring in those with DM at every visit; BMI assessment, urine dipsticks analysis, eGFR and serum lipids measurements at least annually in patients with HTN or DM; and annual feet and eye examination in those with DM. Though clinician failure to perform the recommended examinations and tests was the main reason for below expected level of care, patients related factors (not presenting for follow-up) was also noted, and further studies are required to investigate reasons for non-compliance.

**Recommendation**: To reduce cardiovascular risk burden, it is important that all those at risk are screen and adequately monitored for control and prevention of complication at PHC level since it serves majority of the population, and to reduce the disease burden in the already strained secondary and tertiary level hospitals.

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## Appendix A: Research protocol

**TITLE OF THE STUDY:** Is there adequate routine clinical care management of diabetic, hypertensive patients as an identified population at risk of cardiovascular disease development and progression.

**AIM OF THE STUDY**

To determine clinician compliance with guidelines for the management of cardiovascular risk factors in patients with hypertension (HTN) and diabetes mellitus (DM).

**SPECIFIC OBJECTIVES**

- To determine clinician compliance of blood pressure monitoring on hypertensive and diabetic patients
- To determine clinician compliance of blood glucose monitoring of diabetic patients
- To determine clinician compliance of risk factor control on hypertensive and diabetic patients

**BACKGROUND AND LITERATURE**

Cardiovascular disease (CVD) is a subset of non-communicable diseases (NCD) which account for 63% of all deaths, with 80% of the global burden in low and middle-income countries (1). Current projects indicate that by 2020, the largest increases in NCD deaths will occur in Africa (2). Hypertension and DM are major risk factors (1, 3).

A collaborative effort of relevant stakeholders and policymakers is required to support and strengthen the primary health care system with the current drive in the implementation of Integrated Chronic Disease Managements; where interventions of primary and secondary prevention apply and result in improved health outcomes and thus reducing the costly burden of disease (4, 5). Primary health care promises to be a vital role in the health care system, servicing the majority of our South African population (6). Primary care (PC) 101 is a guide for doctors and nurses working at primary health care provided by the South African National Department of Health (NDOH) (7). The guide encompasses patient management as per approved South African clinical policies and guidelines. The guide is symptom-based and has algorithms and checklists to guide the healthcare user on managing common symptoms and chronic conditions in adults (7).

According to the World Health Organization (WHO) data, raised blood pressure (BP) is estimated to be responsible for 7.5 million deaths, which makes 12.8% of the total deaths (1). Hypertension is a major risk factor for coronary heart disease. This risk doubles for each BP increment of 20/10 mmHg in some

population groups. Reduction of BP to less than 140/90 mmHg is associated with reduced cardiovascular complications (1). The overall prevalence of raised blood pressure in adults between the age of 25 and above in 2008 was estimated to be around 40%, highest in Africa at a prevalence of over 46% (1). In patients with established HTN, treating and controlling systolic and diastolic blood pressure to target levels remains the primary objective (8). In addition, blood pressure control is a major priority in preventing premature cardiovascular events in patients with type 2 diabetes and hypertension (9).

The WHO data states that the global prevalence in adults above 18 years was 8.5% in 2014 and has risen more rapidly in middle and low-income countries (10). Diabetes Mellitus has long-term macrovascular and microvascular complications, including retinopathy, nephropathy, and neuropathy (11). In addition, diabetic patients are at an increased of developing cardiovascular disease, mainly stroke and ischemic heart disease(12, 13). The main goal of treating glycemia in diabetic patients is to reduce blood glucose adequately to prevent or delay the onset of complications (14). In order to achieve this, glycemic targets are set for glycemic control measured by glycated hemoglobin (HBA1c), and optimum blood glucose levels are required to achieve these targets (15).

Hypertension and diabetes are growing concerns in individuals living with human immunodeficiency virus/advanced immunodeficiency syndrome (HIV/AIDS), mainly because certain classes of drugs such as protease inhibitors (PIs) are associated with risk of metabolic disease development and increased cardiovascular risk (5).

## METHODS

### Study design

The study is a retrospective, observational study which will use a retrospective cohort of patients' charts on chronic care at Southport clinic, a primary health care center at Ugu Health district. The aim is to determine whether patients are screened and managed according to PC 101 to prevent complications and progression, such as chronic kidney disease. This retrospective study will reveal the outcome of current practice.

The study will use a data collection tool to document the findings of the study. The data will be assessed using regression analysis. This method used is better suitable for this study as it involves modelling and analyzing several variables. All variables are dependent on whether they have been assessed, but the variables are independent of each other.

- The validity of the research will be judged by the alternative criteria of judging qualitative research. The context of this research uses a primary health care which serves a catchment of urban and rural communities assumes transferability. In doing so, this study can serve as an illustration of the function or current practices at primary health care services under the jurisdiction of Ugu health District.
- The researcher will be responsible and accountable to describe all the changes that occurred during the study and how they have affected the study.
- A data audit examining the data collection and analysis procedures will be done so as to judge potential for bias or distortion.

The researchers will invite two collaborators, Dr F. Oloowokorun (Ugu Health District Family Physician) and Miss Thembakazi Ndlobeni (Ugu Health District Roving Team Pharmacist) to assist with assessing the credibility and confirm reliability and validity of the study.

**Inclusion and exclusion criteria**

***Inclusion criteria***

- Patients above the age of 18 years, already diagnosed with diabetes and/or hypertension and managed at Southport clinic from 1 June 2015 - 31 August 2016

***Exclusion criteria***

- Newly diagnosed and undiagnosed patients

**Sampling**

The population under study is a cohort of patients receiving chronic care for Diabetes, Hypertension care at Southport clinic, Ugu Health District, from 1 June 2016 -31 August 2016. This clinic services patients from both urban and rural areas as it is within easily accessible transport routes.

An estimation of 200 charts will be reviewed.

The sampling technique will be the stratified random sampling. The population studied will be divided into non-overlapping subgroups: namely Diabetes, Hypertensive, HIV ART patients.

**Possible confounding factors that may affect the study outcomes**

- Lack of implementation of pc101 due to inadequate training or lack of familiarity with the guidelines.

**DATA ANALYSIS**

The data collected will be captured and subsequently analyzed using Intercooled Stata version 13. Descriptive statistics such as frequencies and percentages will be used to summarize categorical data. Measures of central tendency, mean and median, and measures of dispersion such as standard deviation and interquartile range will be calculated for numerical variables. A value of one will be assigned to items where clinicians were compliant, and zero will be assigned where they were not compliant. Thereafter a score reflecting clinician compliance will be calculated by summing up items in the checklist. Box and Whisker plot will be used to present distribution of clinician compliance. The database will be managed through the use of a computerized database program: Microsoft EXCEL. Data will be managed with a computerized program, Microsoft Access. Data will be checked upon entry for accuracy:

1. The information documented on the tool is legible
2. All data elements documented
3. All data elements recorded

**STUDY LOCATION**

Ugu District, Southport Clinic, Southport Port Shepstone

**STUDY PERIOD**

01 June 2016-1 August 2016

**LIMITATIONS**

Data is dependent on documentation on file, which may be incomplete or inconclusive. The study is looking at one primary health care facility, which may not be a total reflection of all facilities'

**ETHICAL CONSIDERATIONS**

Ethics approval was obtained from the University of Kwa-Zulu Natal (UKZN) Biomedical Research Ethics committee. The necessary permission to conduct the study will be obtained from the Department of Health KwaZulu Natal.

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## Appendix B: Author guidelines for South African Medical Journal (SAMJ)

**Journal Manuscript submission**

*Guideline word limit: 4 000 words*

Research articles describe the background, methods, results, and conclusions of an original research study. The article should contain the following sections: *introduction, methods, results, discussion, and conclusion*, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text.

*Structured abstract*

- This should be 250-400 words, with the following recommended headings:
    - **Background:** why the study is being done and how it relates to other published work.
    - **Objectives:** what the study intends to find out
    - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
    - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
    - **Conclusion:** must be supported by the data, include recommendations for further study/actions.

- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

*Main article*

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g., primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g., smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc) that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

*Results*

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.

- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

*Discussion*

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g., what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

*Conclusions*

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

**Illustrations/photos/scans**

If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.

Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).

All images must be of high enough resolution/quality for print.
All illustrations (graphs, diagrams, charts, etc.) must be in PDF or jpeg form.

Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g., 0; 1.0; 2.0; 3.0; 4.0 etc.

Scans/photos showing a specific feature e.g. Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain). –include an arrow to show the tumour.

Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

**Tables**

Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.

Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author

Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.

Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.

Tables must be cell-based (i.e., not constructed with text boxes or tabs) and editable.

Ensure each table has a concise title and column headings, and include units where necessary.

Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for n and %:

Rather:

Combine into one column, n (%):
Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

**References**

NB: Only complete, correctly formatted reference lists in Vancouver style will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Endnotes must not be used.

Authors must verify references from original sources.

Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]

All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).

Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.

Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.

Volume and issue numbers should be given.

First and last page, in full, should be given e.g.: 1215-1217 not 1215-17.

Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:

On the Crossref homepage, paste the article title into the ‘Metadata search’ box.

Look for the correct, matching article in the list of results.

Click Actions > Cite

Alongside 'url =' copy the URL between (30).

Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

## Appendix C: Ethical approvals

### (i) Biomedical Research Ethics Committee (BREC) Approval

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

09 March 2018

Dr K Nqiwa (993217155)
Discipline of Medicine
School of Clinical Medicine
knqiwa@yahoo.com

Dear Dr Nqiwa

**Protocol: Is there adequate routine clinical care management of diabetic patients as an identified population at risk of cardiovascular disease development and progression. Degree: MMed**
**BREC reference number: BE020/17**

**EXPEDITED APPLICATION: APPROVAL LETTER**

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 21 December 2017.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 01 March 2018 to BREC correspondence dated 30 June 2017 has been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given **full ethics approval** and may begin as from 09 March 2018.

This approval is valid for one year from **09 March 2018.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its next meeting taking place on **10 April 2018.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

[redacted]

Professor V Rambiritch
Deputy Chair: Biomedical Research Ethics Committee

cc supervisor: [redacted] cc postgraduate administrator: [redacted]

**Biomedical Research Ethics Committee**
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## (ii) Biomedical Research Ethics Committee (BREC) Approval– Amended

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

**27 October 2021**

**Dr K Nqiwa (993217155)**
**Discipline of Medicine**
**School of Clinical Medicine**
knqiwa@yahoo.com

**Dear Dr Nqiwa**

**Protocol: Is there adequate routine clinical care management of diabetic patients as an identified population at risk of cardiovascular disease development and progression.**
**Degree: MMed**
**BREC reference number: BE020/17**
***New Title: Compliance with the guidelines for the management of cardiovascular risk factors in patients with hypertension and/or diabetes mellitus***

We wish to advise you that your application for amendments received on 15 October 2021 listed below for the above study has been **noted and approved** by a subcommittee of the Biomedical Research Ethics Committee.

Amendments noted and approved:

1. Change the title to the above new title
2. Add Dr Bavumile Mbanjwa as Co-Supervisor.

The committee will be notified of the above approval at its next meeting to be held on 14 December 2021.

Yours sincerely

[redacted]

Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

**(ii) Department of health approval**

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE:
Health Research & Knowledge Management

HRKM Ref: 014/18
NHRD Ref: KZ_2018001_02

Date: 14 February 2018
Dear Dr K. Nqiwa
UKZN

**Approval of research**

1. The research proposal titled 'Is there adequate routine clinical care management of Diabetic, Hypertensive patients as an identified population at risk of cardiovascular disease development and progression?' was reviewed by the KwaZulu-Natal Department of Health.

   The proposal is hereby **approved** for research to be undertaken at Southport clinic.

2. You are requested to take note of the following:
   a. Make the necessary arrangement with the identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

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

Yours Sincerely

[redacted]
**Dr E Lutge**
Chairperson, Health Research Committee
Date: 19/2/18

Fighting Disease, Fighting Poverty, Giving Hope

**Appendix D: Data collection tools**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NUMBER | | | | | | | | | | | | |
| AGE | | | | | | | | | | | | |
| SEX | | MALE | | | | | | FEMALE | | | | |
| RACE | | BLACK | | | WHITE | | | | | ASIAN | | |
| | | | | | | | | | | | | |
| **DIABETES** | | | | | | | | | | | | |
| DIABETES | | YES | | | | | | NO | | | | |
| DIABETES | | Type 1 | | | | | | Type 2 | | | | |
| RBS DONE | | YES | | | | | | NO | | | | |
| RBS RECORD | INTIAL | | | AT 6MO | | | AT 12 MO | | | | | |
| HBCA1c | at 3/12 | | | AT 6MO | | | AT 12 MO | | | | | |
| | | | | | | | | | | | | |
| **HYPERTENSION** | | | | | | | | | | | | |
| HYPERTENSION | | YES | | | | | | NO | | | | |
| BP DONE | | YES | | | | | | NO | | | | |
| SYSTOLIC BP | INITIAL | | | AT 6MO | | | AT12 MO | | | | | |
| DIASTOLIC BP | INITIAL | | | AT 6MO | | | AT 12MO | | | | | |
| TREATMENT | | | | | | | | | | | | |
| | | | | | | | | | | | | |
| **HIV** | | | | | | | | | | | | |
| HIV STATUS | | POSITIVE | | | | | | NEGATIVE | | | | |
| VL DONE | | AT 6MO | | | | | | AT 12 MO | | | | |
| VL RECORD | AT 6MO | | | | | | AT 12MO | | | | | |
| IN HAART | | YES | | | | | | NO | | | | |
| | | | | | | | | | | | | |
| **URINALYSIS** | | | | | | | | | | | | |
| URINALYSIS DONE | | | INITIAL | | | YES | | | NO | | | |
| | | | AT 6MO | | | YES | | | NO | | | |
| | | | AT 12MO | | | YES | | | NO | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| PROTENURIA | | | | INITIAL | | YES | | | NO | | |
| | | | | AT 6MO | | YES | | | NO | | |
| | | | | AT 12MO | | YES | | | NO | | |
| TREATMENT FOR PROTENURIA | | | | | | YES | | | NO | | |
| | | | | | | | | | | | |
| **BMI** | | | | | | | | | | | |
| HT | | | | | | | | | | | |
| WEIGHT | INITIAL | | | AT6MO | | | AT 12 ꟾO | | | | |
| | | | | | | | | | | | |
| eGFR DONE | | | BASELINE | | | | AT 12 ꟾO | | | | |
| eGFR RECORD | | | BASELINE | | | | AT 12 ꟾO | | | | |

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