IMPACT OF THE HEALTHY HEART AFRICA PROGRAM ON THE ADEQUACY OF BLOOD PRESSURE CONTROL IN KIAMBU COUNTY

GRACE WANGUI NGARIKO (B PHARM)

U51/87796/2016

A thesis submitted in partial fulfillment of the requirements for the award of the degree of Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance in the department of Pharmacology and Pharmacognosy of the University of Nairobi.

AUGUST 2021

UNIVERSITY OF NAIROBI DECLARATION OF ORIGINALITY

Name of student:	Grace Wangui Ngariko
Registration no.:	U51/87796/2016
College:	College of Health Sciences
School:	School of Pharmacy
Department:	Pharmacology and Pharmacognosy
Course Name:	Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance
Title of the work:	Impact of the Healthy Heart Africa on the adequacy of blood pressure control in Kiambu County.

DECLARATION

I, Grace Wangui Ngariko, declare that:

1. I understand what plagiarism is and am aware of the University's policy in this regard.

2. This thesis is my original work and has not been submitted elsewhere for examination, award of a degree, or publication. Where other people's work or my work has been used, this has properly been acknowledged and referenced per the University of Nairobi's requirements.

3. I have not sought or used the services of any professional agencies to produce this work.

4. I have not allowed and shall not allow anyone to copy my work to pass it off as his/her work.

5. I understand that any false claim regarding this work shall result in disciplinary action per the University Plagiarism Policy.

Signature  Date 17-8-2021

Grace Wangui Ngariko U51/87796/2016

SUPERVISORS' APPROVAL

This thesis has been submitted for examination with our approval as university supervisors.

DR. ERIC M. GUANTAI (PhD)

Department of Pharmacology and Pharmacognosy

School of Pharmacy

University of Nairobi

Signature…… 17th August 2021 …….. Date…17th August 2021……

DR. MARGARET N. OLUKA (PhD)

Department of Pharmacology and Pharmacognosy

School of Pharmacy

University of Nairobi

Signature…… …… Date…18-08-2021…….

PROF. FAITH A. OKALEBO (PhD)

Department of Pharmacology and Pharmacognosy,

School of Pharmacy

University of Nairobi

Signature…… …… Date17th August, 2021…….

DEDICATION

I dedicate this work to my dear husband, Reuben Kimani, and my daughters, Keisha and Hailey.

ACKNOWLEDGEMENT

I am grateful to the Almighty God for the gift of life and for giving me the strength to accomplish this work.

I am also grateful to the University of Nairobi Graduate School for awarding me a scholarship that enabled me to pursue my studies without any financial hustles.

Special thanks to the Newton Institutional Links Grant for funding the research.

Special thanks to my highly valued and able supervisors Dr. Eric M. Guantai, Prof Faith Okalebo, and Dr. Margaret Oluka, for their invaluable support and guidance throughout the study.

My sincere appreciation to the Kiambu County Department of Research, Medical superintendents, clinicians, pharmacists, and staff at the record's department in Ruiru and Tigoni hospitals for their invaluable support during data collection.

Finally, I wish to thank my classmates for walking this journey with me.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS AND ACRONYMS

ACEIs	Angiotensin-converting enzyme inhibitors
ADRs	Adverse Drug Reactions
AHA	American Heart Association
ALLHAT	Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
AMREF	African Medical and Research Foundation
ARBs	Angiotensin Receptor blockers
BP	Blood Pressure
BMI	Body Mass Index
CCBs	Calcium Channel Blockers
CVD	Cardiovascular diseases
CNS	Central Nervous System
DBP	Diastolic Blood Pressure
ESC	European Society of Cardiology
ESH	European Society of Hypertension
GERD	Gastroesophageal Reflux Disease
HCTZ	Hydrochlorothiazide
HCWs	Health Care Workers
HHA	Healthy Heart Africa

ISH	International Society of Hypertension
ISHIB	International Society on Hypertension in Blacks
JNC	Joint National Committee
LMIC	Low and Medium income countries
MEDS	Mission for Essential Drugs
MH	Mantel-Haenszel
NHIF	National Health Insurance Fund
NICE	National Institute for Health and Care Excellence
PPIs	Proton Pump Inhibitors
RAAS	Renin angiotensin Aldosterone System
SAHS	South Africa Hypertension Society
SBP	Systolic Blood Pressure
WHO	World Health Organization

DEFINITION OF TERMS

Adequate blood pressure control: Blood pressure levels below 140/90 mmHg.

Blood pressure: The force exerted by blood against the walls of arteries as a result of the pumping action of the heart

Diastolic blood pressure: The minimum arterial pressure during relaxation and dilatation of the heart ventricles when they are filled with blood.

Hypertension: Repeatedly elevated blood pressure with SBP of above 140mmHg and DBP of above 90mmHg.

Systolic blood pressure: The maximum arterial pressure during contraction of the left ventricle of the heart.

ABSTRACT

Background: Hypertension is one of the most important independent risk factors for cardiovascular disease worldwide. It has been steadily on the rise in Sub-Saharan Africa, where it is often insufficiently controlled in the vast majority of patients. In response to these problems, AstraZeneca, a British-Swedish Pharmaceutical Company, introduced the Healthy Heart Africa program to tackle the burden. The aim is to assess the impact of this program on the adequacy of blood pressure control.

Methods: Multisite analytical retrospective cross-sectional study of hypertensive patients enrolled in outpatient clinics of two sub-county hospitals.

Results: A total of 202 files were reviewed, 86 from the Healthy Heart Africa group and 116 from the non-HHA program group. The patients were predominantly female with a mean age of 59 years. Thiazide diuretics, Calcium channel blockers and Angiotensin-Converting Enzyme Inhibitors were the most prescribed class of antihypertensive drugs. Felodipine and lisinopril were the most frequently prescribed antihypertensive drugs in the Healthy heart program, whereas in the non-program group, nifedipine and enalapril were mostly preferred. Patients on the program drugs had fewer cases of CCF, peripheral neuropathy and hyperlipidemia compared to those on the non-program drugs.

The prevalence of adequately controlled BP was 40.1%. There was no statistically significant difference in the BP control between the HHA program and the non-program groups (p=0.67). Diabetic patients were more likely to have uncontrolled BP (OR:0.4, p=0.03). Patients with peptic ulcers had better-controlled blood pressure (OR:2.6, p= 0.03).

Conclusion: There was no significant difference in the prescribing patterns of antihypertensive drugs across the two hospitals. There was no statistically significant difference in the level of blood pressure control across patients on the HHA program's drugs and non-program drugs. Patients who were on the program drugs had a lower prevalence of end-organ complications of diabetes and cardiovascular complications.

CHAPTER 1: INTRODUCTION

1.1 Background

Hypertension is characterized by systolic blood pressure (BP) of≥ 140 mmHg and/or diastolic BP of ≥ 90 mmHg on repeated examination (1). Hypertension is a significant health challenge globally, mainly due to its high prevalence and association with cardiovascular and renal complications (2).

As per the 2013 World Health Organization (WHO) report on hypertension, around 40% of people above 24 years had hypertension in 2008 globally (3). The population living with hypertension rose from 600 million in 1980 to almost 1 billion in 2008 (3). National reports show that the prevalence of hypertension is growing in low and middle-income countries (LMIC) but is declining in high-income countries (4). Africa bears the highest burden of hypertension than other continents, with an estimated overall prevalence of between 10 to 30% (5) or even as high as 40% (4). An estimated 75 to 80 million Africans had hypertension in 2000, a number expected to double by 2025 (4).

Hypertension is a key modifiable risk factor for developing cardiovascular disease (CVD), including heart attacks and strokes. Lowering blood pressure has been proven beneficial in decreasing cardiovascular complications and preventing premature mortality in hypertensive individuals. The timing and intensity of interventions to manage blood pressure are determined by factors like the stage of hypertension, the patient's absolute CVD risk, and factors like the presence of end-stage organ damage (6).

Hypertension control refers to maintaining blood pressure levels below 140/90 mmHg for most patients (1,7). The management and the subsequent control of hypertension involve the use of both pharmacological and non-pharmacological interventions. Non-pharmacological approaches involve lifestyle modification like proper diet, weight control and regular physical exercises, low salt intake, quitting smoking, and reduction of alcohol consumption. On the other hand, pharmacological interventions include the use of antihypertensive drugs and treatment of other modifiable CVD risk factors. The main classes of antihypertensive drugs used are the β-blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), diuretics, and angiotensin II receptor blockers (ARBs) (1,6,8).

Globally the control of BP is poor. The poor control is a cause for concern, especially in high-risk populations, including Blacks, Asians, and other cardiovascular diseases or multiple risk factors (9). In the majority of the African setup, hypertension is unrecognized and undiagnosed. In addition, even with treatment, it remains largely uncontrolled in the vast majority of hypertensive patients (4). Approximately 40% of Africans with hypertension are undiagnosed; less than 30% of those diagnosed are on treatment, and less than 20% of those on treatment have well-controlled blood pressure (4). Factors that influence the adequacy of blood pressure control include the age and sex of the patient, comorbid conditions, choice of antihypertensive drug, and adherence to medications (3,6,10).

Optimal BP control is associated with a dramatic reduction in adverse health outcomes (11). It has been associated with a 50% reduction in heart failure, 40% reduction in strokes events, and a 20-25% reduction in myocardial infarction (12). The absolute benefits of optimizing the control of blood pressure are higher in populations that have a higher risk of BP-related cardiovascular events. These populations include Sub-Saharan Africans, African-Americans, and Eastern Asians (6,9).

1.2 The Healthy Heart Africa program

AstraZeneca came up with an innovative program - the Healthy Heart Africa (HHA), in response to the increasing prevalence, poor control of hypertension, and the increased burden of cardiovascular diseases across Africa. AstraZeneca is a British-Swedish pharmaceutical company that manufactures and distributes a wide range of pharmaceutical products.The program is a holistic approach to healthcare delivery. It builds on existing healthcare systems and supports three pillars: community education and awareness, provider training and guideline development, and improved access to affordable medicines. In collaboration with Mission for Essential Drugs (MEDs), AstraZeneca introduced three highly subsidized and quality drugs: Zestoretic® (lisinopril 20mg/Hctz 12.5 mg) and Plendil® (Felodipine) 5 mg and 10 mg.

HHA targets to reach 10 million hypertensive patients across Sub-Saharan Africa by the year 2025. This target aligns with the World Health Organization's global hypertension targets of reducing hypertension by 25% in 2025. Kenya is among the chosen pilot countries for the HHA program. In October 2010, the HHA program was rolled out in; Central, Coast, Nairobi, and Rift Valley provinces of Kenya. In Central Kenya, Kiambu and Kirinyaga counties have adopted and implemented the program.

1.3 Statement of the problem

The prevalence and poor control of hypertension have been steadily rising globally, especially in low-income countries like in sub-Saharan Africa. In most Africans, hypertension goes unrecognized and undiagnosed, and worse still, even with treatment, it remains uncontrolled (4).

In Kenya, studies to assess the adequacy of BP control have shown an overall poor control of BP, with the proportion of patients with controlled BP ranging from 7.4 to 48.3% (3,6,10,13). Treatment and optimal BP control are vital because uncontrolled BP is a major, independent risk factor for heart failure, stroke, and kidney failure (14). Effective management of these complications is a significant challenge in Sub-Saharan countries where resources are limited.

The Healthy Heart Africa (HHA) program was introduced in Africa by AstraZeneca, a British-Swedish pharmaceutical company, in collaboration with the Ministry of Health in response to the growing prevalence and increasing rates of uncontrolled hypertension. The success of the adoption and implementation of this interventional program and its impact in improving BP control has not been evaluated. Therefore, this study sought to compare the adequacy of blood pressure control among patients on the HHA program drugs and other classes of antihypertensive drugs in two hospitals in Kiambu County, Central Kenya. It also aimed to identify the challenges in the adoption and implementation of the program.

1.4 Research questions

1 Do patients on the HHA program drugs have better BP control compared to patients on other hypertension drugs?
2 What are the challenges in the adoption and implementation of the Healthy Heart Africa program in Kiambu County?

1.5 Study objectives

1.5.1 Broad objective

The main objective of this study was to compare the adequacy of blood pressure control among patients on the Healthy Heart Africa program drugs and non-program antihypertensive drugs in Ruiru and Tigoni hospitals in Kiambu County and to identify challenges in the implementation of the program.

1.5.2 Specific objectives

The specific objectives were to:

1. Identify the independent predictors of blood pressure control in the two hospitals in Kiambu County.
2. Compare the proportion of patients with controlled blood pressure among patients on the Healthy Heart Africa program drugs and those on non-program drugs in two hospitals in Kiambu County.
3. Identify the challenges in the adoption and implementation of the Healthy Heart Africa program in Kiambu County.

1.6 Study justification

Several studies that have been done in Kenya to assess the adequacy of blood pressure control have shown an overall poor control of BP, with the reported proportions of hypertensive patients with controlled BP ranging from 7.4% to 48.3% (3,6,10,13).

The HHA program was introduced in Africa and piloted in Kenya as an interventional program to tackle the rising prevalence of hypertension, the poor control of BP, and the associated risk of cardiovascular disease and increased mortality. In Central Kenya, Kiambu and Kirinyaga Counties had adopted and implemented the program. The contribution of this interventional program to the adequacy of blood pressure control in Kenya has not been assessed. This study aimed to establish the overall proportion of patients who had adequately controlled blood pressure following the program's introduction and how the HHA program had contributed to better control of hypertension in Kiambu county. Kiambu County was selected as a study site due to the ease of accessibility to the investigator.

Assessment of the adequacy of blood pressure control is essential in preventing mortality and complications associated with hypertension. Uncontrolled BP is a significant healthcare problem due to increased risk of cardiovascular diseases and sudden death (8). Results on the contribution of the HHA program to the adequacy of BP control will be used to provide feedback to AstraZeneca (Kenya) and Amref, especially on success rate and areas of improvement. Findings showing a favorable BP control profile with the HHA program may further support countrywide adoption of the program and incorporation into the country’s

hypertension treatment guidelines. The findings of this study will also be shared with the two hospitals to guide them on aspects of the program that require improvement.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology of hypertension

Hypertension in sub-Saharan Africa is a widespread problem of great economic importance due to its increasing prevalence, frequent under-diagnosis, overall poor control, and the severity of the associated complications (14). Effective management of hypertension is associated with reduced mortality and morbidity as it is one of the main modifiable risk factors for cardiovascular and renal diseases. The 2010 global estimates of hypertension showed that 31.1% of the population (approximately 1.39 billion people) had hypertension, including 28.5% in high-income countries and 31.5% in LMIC (2). In addition, according to the 2012 World Health Statistics, one in three adults of the worldwide population had a raised blood pressure (10).

An estimated 10 to 30% of all Africans are affected by hypertension. In the year 2000, 75 to 80 million Africans had hypertension, which is expected to double by 2025 (4). In separate surveys done in four rural and urban communities in Sub-Saharan Africa between 2009 and 2011, the prevalence of hypertension was estimated to be 21.4% in rural Kenya,23.7% in Dar es Salaam, Tanzania, 19.3% in rural Nigeria, and 38% in urban Namibia (15). In Cameroon, a study on prevalence, awareness, and treatment of hypertension done in 2012 found a prevalence of 47.5% (16).

Few population-based studies on the prevalence of hypertension have been conducted in Africa. According to the 2008 World Health Statistics, the prevalence of hypertension in Kenya was 38.9% for males and 35.1% for females, with pooled estimates of 35% (13). A cross-sectional household survey carried out in rural Kenya in Nandi District between 2009 and 2011 estimated the prevalence of hypertension at 21.4% (10,15). Moreover, a 2008 regional cross-sectional study focusing on individuals above 49 years in a rural Kenyan population showed a prevalence of 50.1% (17). In addition, a 2010 population-based household survey in Kibera slums reported an age-standardized hypertension prevalence of 22.8% (17).

2.2 Risk factors for hypertension

Anyone can develop high blood pressure. However, factors like age, gender, race, obesity, lifestyle habits, and a family history of high blood pressure increase the chances of an individual developing high blood pressure. Blood pressure tends to rise as an individual ages.

The prevalence of hypertension is age-related and is highest in over 50 years (18). A 2013 study by Wang et al. on the factors associated with prevalence, awareness, treatment, and control of hypertension in the Chinese population reported that old age was strongly associated with a higher prevalence of hypertension. Participants aged 45-59 years had 3.37 the odds of those aged 18-44 years of having hypertension, and those aged 60 years and above had 8.1 times the odds of those aged 18-44 years of having hypertension (19). A longitudinal study evaluating risk factors for hypertension and their relation to cardiovascular disease by Wenyu et al. (2006) showed that for the same sex, there was a significant age difference in the incidence of hypertension. In addition, participants aged ≤65 years had a 38% and a 62% higher incidence of hypertension than those aged 55 to 64 years and 45 to 54 years, respectively (20).

High blood pressure is more common in Africans compared to Caucasians and Hispanics. Furthermore, compared to other ethnic groups, Africans are more likely to develop high blood pressure earlier in life and less likely to achieve targeted blood pressure with treatment (4). Various studies have investigated this observation, such as a study on ethnic differences in hypertension which reported a higher prevalence in African-Americans than whites (60% vs. 38%). Prevalence in Hispanics (42%) and Chinese (39%) did not differ significantly from whites (21).

Various studies have investigated the association between high BMI and hypertension. Wenyu et al. reported different risks of developing hypertension among the various BMI subgroups. Obese participants had 1.9 times the odds of those with average weight of having hypertension. Moreover, overweight participants had 1.46 times the odds of those with normal weight of having hypertension (20). Generally, hypertensive patients are older with a higher BMI and waist circumference compared to individuals with normal blood pressure in each racial group (21).

There has been a positive association between lifestyle habits like smoking and alcohol consumption and the development of hypertension. The association between excessive alcohol intake and an increased risk of hypertension prevails regardless of the beverage type (22). A meta-analysis of randomized controlled trials on the effects of alcohol reduction on BP found that reducing alcohol consumption was associated with a significant decrease in mean SBP by 3.31mmHg and DBP by 2.04 mmHg (23). There was a dose-dependent relationship between

reduction of alcohol and mean BP reduction. In both men and women, consumption of more than two drinks daily was associated with an increased risk of developing hypertension (22).

There exists a relationship between smoking and hypertension. In a South Indian study, smokers had 1.66 times the odds of non-smokers of having hypertension (18). A 14-year longitudinal study in Japan demonstrated that smokers had 1.13 odds of non-smokers of developing hypertension (24).

2.3 Antihypertensive drugs

The main drug classes for lowering BP are diuretics, β- blockers, CCBs, ACEIs, and ARBs. Thiazide diuretics are the most evaluated agents. They show a higher reduction in morbidity and mortality.They are recommended as first-line agents by the World Health Organization/International Society of Hypertension (WHO/ISH) and Joint National Committee (JNC) guidelines (6,7). The most commonly used thiazide diuretic is hydrochlorothiazide (HCTZ). They are cheap, effective (even in blacks), and are well-tolerated in low doses. However, they are associated with side effects such as hypokalaemia, impaired glucose tolerance, slight elevation of low-density lipoprotein (LDL), cholesterol, triglycerides, and urate levels (25).

β-blockers are cost-friendly drugs. However, they are thought to be less effective in blacks. They include atenolol, propranolol, and carvedilol. They are associated with side effects such as lethargy, erectile dysfunction, impaired blood glucose control, and worsening of dyslipidemia (25).

Calcium channel blockers include drugs such as nifedipine, amlodipine, verapamil, and felodipine. They are effective in lowering BP, especially in blacks, and are well tolerated. They are also used in the management of angina and arrhythmia. Side effects of calcium channel blockers include tachycardia, flushing, and ankle edema (26).

Angiotensin-converting enzyme inhibitors include drugs such as enalapril and lisinopril, while ARBs include drugs such as losartan and valsartan. These drug classes are useful in reducing morbidity and mortality in heart failure and halts the progression of renal disease in diabetes mellitus. However, there is a poor response in black patients when used as monotherapy (27,28). Their side effects include angioedema and dry cough, which is more prevalent with ACEs than ARBs (29).

2.4 Guidelines for the management of hypertension

There are various guidelines developed for the management of hypertension. These guidelines give recommendations on identification, classification, diagnosis, and associated risk factors of hypertension. They also provide recommendations on treatment initiation, management strategies (pharmacological, lifestyle modification), blood pressure targets, and preferred antihypertensive drug.

The USA Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, has published reports and guidelines over the years through its panel members appointed to the various JNC committees. Their latest report, JNC-8 on evidence-based guidelines for the management of hypertension, was published in 2014 (7). The Joint Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) issued three guidelines in 2003,2007, and the latest in 2013 (10,30). Other guidelines include the National Institute for Health and Care Excellence (NICE) guideline, which was last updated in 2016, and the WHO-International Society of Hypertension (ISH) guidelines issued in 1999 and 2003. All these international guidelines offer the best practice evidence-based advice on the management of hypertension. Furthermore, expert opinions and recommendations are relied on in the absence of evidence.

The international guidelines recommend a target BP of 140/90mmHg for patients below 80 years of age and 150/90 mmHg for those above 80 years. However, a target BP of 130/80mmHg is recommended in patients with CVD risk and chronic renal disease. Non-pharmacological therapy is indicated for patients with mild hypertension. However, if target BP is not achieved, a thiazide diuretic is indicated as first-line monotherapy. In patients with diabetes, an ACEI or CCB is preferred as monotherapy. For patients with moderate to severe hypertension, non-pharmacological therapy is given in combination with pharmacological therapy consisting of a combination of two drugs. In blacks, a diuretic or a CCB should be used initially as they have better outcomes (7,27,28).

Most African countries have adopted the international guidelines, mainly the JNC-7 and NICE guidelines. However, South Africa has developed its own guidelines. The latest version was published in 2014 by the South African Hypertension Society (SAHS) (28). The Kenya National Guidelines for Cardiovascular Disease Management were developed in 2018 based

on an extensive review of up to date, evidence-based practices (31). According to the Kenyan guidelines, hypertension is diagnosed when the BP reading is greater than 140/90 mmHg on three separate occasions. The management goal is to reduce BP to <140/90mmHg in individuals with uncomplicated hypertension and <130/90mmHg in those with complications. The guidelines also highlights the pharmacological and non-pharmacological approaches for managing hypertension. Non-pharmacological therapy is recommended for mild hypertension (SBP 140-159 and DBP 90-99 mmHg). However, if the BP target is not achieved within three months, monotherapy with either a CCB or a thiazide diuretic should be initiated. A second drug (CCB/thiazide+ ACEI/ARB) is added if target BP is not achieved with monotherapy. A two-drug pharmacological therapy with a CCB/thiazide+ ACEI/ARB is initiated in moderate to severe hypertension (SBP of more than 160mmHg and DBP of more than 100 mmHg). If target BP is not achieved, three-drug combination therapy should be initiated; CCB+thiazide+ ACEI/ARB. Recommendations of the Kenyan guidelines are consistent with other international guidelines (7,28,32).

2.5 Management of hypertension in the African population

There is a great need for individualized therapy of hypertension in Africans (27). Compared to other races, hypertension in Africans is often more severe, more resistant to treatment leading to earlier end-organ damage, higher rates of cardiovascular events and premature death (27). Response to antihypertensive drug classes may differ across age and race subgroups. This has an impact on the choice of antihypertensive drug(s).

Black and elderly patients demonstrate a better BP response to thiazide diuretics and/or long-acting CCBs, as long as they do not have a compelling indication for an ACEI or an ARB such as heart failure or chronic kidney disease (33). In African patients, diuretics are among the most effective BP-lowering drugs. However, evidence indicates that in patients with high baseline diastolic pressures (higher than 110mmHg), CCBs are more effective (27,34). Overall, patients of African descent have a better response to CCBs and diuretics. However, response to β blockers and ACEIs is reduced especially in monotherapy (3,33). The CREOLE study that compared dual therapies for lowering BP in Black Africans found that combinations of amlodipine with either hydrochlorothiazide or perindopril were more effective than perindopril plus hydrochlorothiazide in reducing both ambulatory SBP and office BP (35)

A meta-analysis by Palla et al. (2017) comparing the effects of renin-angiotensin system(RAS) inhibitors and other drug classes in blacks found that the incidence of stroke was significantly increased in patients treated with RAS inhibitors compared with CCBs and diuretics but not β-blockers (33). The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) found that there was a 51% higher risk (relative risk 1.51;95% CI 1.22-1.86) of stroke in black persons with the use of an ACEI as initial therapy compared with the use of a CCB. ACEIs are less effective in reducing BP in black individuals compared to CCBs (7,36). In contrast, younger white patients respond better to ACEI or ARBs. Patients of European ancestry on ACEI have a systolic/diastolic BP reduction of 12.8/11.4mmHg compared to those of African ancestry with a reduction of 8.5/8.0mmHg (27). The observed differences may be as a result of a lower plasma renin activity in hypertensive blacks. A repressed renin-angiotensin-aldosterone system (RAAS) occurs mainly in persons of African descent (33).

A meta-analysis on inter-racial differences in response to treatment showed that β blockers and ACEI inhibitors resulted in a more significant reduction of SBP/DBP among whites compared to blacks. conversely, diuretics and CCBs resulted in more significant reductions among blacks compared to whites (34). The inter-racial differences in response to ACEI and β blockers disappear when these drugs are combined with diuretics. CCBs show the most consistent response in blacks compared to other classes of drugs used as monotherapy (27,28,35).

A study carried out in Nyeri Provincial general hospital in Kenya on blood pressure control in hypertensive patients found that CCBs were positively associated with good BP control. In addition, patients on twice-daily CCB dosing had even better controlled BP than patients on a diuretic (3).

2.6 Treatment targets and adequacy of hypertension control

The target blood pressure for most patients with uncomplicated hypertension is<140/90mmHg. A more stringent goal of <130/80mmHg is recommended for patients with established CVD, diabetes, or chronic kidney disease (7,28,32). The treatment goals of hypertension, according to the Kenya National Guidelines for Cardiovascular Disease Management (31) and the HHA program guidelines (37), is a BP of<140/90mmHg for all adult patients and 150/90mmHg for those aged above 80 years.

Poor rates of BP control have been widely reported globally. Most of the reported levels of BP control fall below the WHO recommended 50% for community control (6,38). Poor BP control

is a primary concern, especially in high-risk groups such as Africans, patients with cardiovascular diseases, or an increased risk of other complications associated with uncontrolled BP. An Italian study on adherence to antihypertensive treatment and blood pressure control reported the proportion of patients with adequate control of BP at 48.1% (39). In addition, the prevalence of good BP control has been reported as low as 53.1% in the US; 41% in Canada; 33.6% in Germany and 29.2% in the UK (39). African studies evaluating the level of BP control reported varying proportions of patients with a well-controlled BP ranging from 1.7% to 39.8% (40–43).

Several studies that have been done in Kenya to assess the adequacy of blood pressure control have shown varying levels of good BP control ranging from 7.4% to 48.3% (3,6,10,13). Adequate control of blood pressure is an essential element in preventing mortality and complications associated with hypertension. Uncontrolled BP is a significant challenge in the healthcare system because of its association with increased risk of cardiovascular diseases and sudden death (38). The higher the BP, the greater the risk of coronary artery disease, heart failure, cerebrovascular accidents, and kidney disease (7,9).

2.7 Factors affecting adequacy of blood pressure control

One of the main contributors to poor control of BP is poor compliance with pharmacological and non-pharmacological treatment (6). One of the possible contributing factors to non-compliance is the complexity of the medication regimen. Generally, BP control requires more than one antihypertensive drug, and the frequency of dosing of the various medications may vary; this complexity significantly affects compliance. Once-daily dosing improves compliance.

In addition, unacceptable adverse effects of medications in a largely asymptomatic disease may contribute to non or partial compliance (44). Treatment of hypertension may result in side effects such as dry cough, dizziness, nausea, headache, and sexual dysfunction depending on the drug used, which may significantly affect a patient's adherence (45).

Knight et al. (2001) found an association between poor blood pressure control and adverse events. Patients who attributed a specific side effect to a specific antihypertensive medication had two times the odds of those who did not of having a higher blood pressure (46). Another study showed that patients who were on CCBs had better compliance to therapy than those who were on thiazide diuretics, possibly because the former may have fewer side effects (13). In

Ghana, 33% of the patients cited medication side effects as a reason for non-compliance (47). Most of the side effects were intolerable headaches and sexual dysfunction in men associated with nifedipine which was the commonly prescribed drug.

In Sub-Saharan Africa, the unavailability and unaffordability of essential antihypertensive medicines negatively affect patient compliance to treatment. Antihypertensive drugs within the same class and between classes have different prices, and the cost of managing of hypertension is often borne by the patient as an out-of-pocket expenditure (48). This observation has been supported by various studies evaluating the effect of drug cost on compliance to treatment (47,49,50).

Other patient factors that influence BP control include age, gender, obesity, and lifestyle modification strategies like low salt diet and smoking cessation. Old age is associated with overall poor control of BP (3,51). The male gender has been associated with poorly controlled blood pressure. This could be attributed to poor health-seeking behavior by males compared to females (1,52). Overweight and obese patients are less likely to have a well-controlled BP than patients with normal weight (53,54). Low salt intake and smoking cessation have been associated with a well-controlled BP (51,53)

Comorbidities like diabetes and dyslipidemias have been associated with poor control of blood pressure. Hypertensive patients with diabetes are less likely to have a well-controlled BP than nondiabetic hypertensive patients (3,53). Hyperlipidemia is negatively associated with adequate control of BP (52).

In Nyeri Provincial General Hospital, old age, having diabetes, and being on three or more antihypertensive drugs were strongly associated with poor control of BP (3).

2.8 The Healthy Heart Africa program

The HHA program is a holistic approach to healthcare delivery introduced by AstraZeneca to tackle the burden of uncontrolled hypertension in Africa. The initiative builds on existing health systems, and supports three pillars of activities: community awareness and education, provider training and guideline development ,and access to quality and affordable medicines.

Patient education and awareness were carried out by conducting awareness-raising activities in communities to encourage people to seek hypertension screening, diagnosis, and treatment.

Provider training and guidelines development focused on training health care workers to provide comprehensive and appropriate hypertension care, based on a guideline developed in collaboration with Kenya's MOH, HHA partners, and Kenyan cardiologists.

Hypertension treatment access and affordability entails equipping facilities to provide screening services and ensuring a consistent supply of quality antihypertensives at a significantly reduced price. This aimed at addressing the availability of hypertension medicines, which varied considerably at different levels of health care systems. HCTZ was one of the more consistently available antihypertensives. However, 70% of the 148 facilities surveyed did not have CCBs, β-blockers, and ACEI in stock. Three drugs were introduced, namely felodipine (Plendil® 5 mg and Plendil® 10 mg) and lisinopril 20 mg/HCTZ 12.5 mg (Zestoretic®).

The HHA program's guideline borrowed heavily from the South African and NICE guidelines (37). It gives a protocol for the identification and management of hypertension in adults in primary care. In this protocol, hypertension should be confirmed in all patients with an SBP higher than 140mmHg and/or DBP higher than 90mmHg for at least three separate occasions within two months. Therapy needs to be initiated in all patients aged 18 to 79 years (SBP >140 & DBP >90mmHg) and in patients older than 80 years(SBP>150 & DPB > 90mmHg). In patients with mild hypertension (SBP 140-159 and/or DPB 90-99mmHg) with no comorbidities, lifestyle modification should be instituted for three months. If the goal BP is not achieved, monotherapy with a long-acting CCB or a thiazide diuretic should be initiated. For patients with mild hypertension and comorbidities, antihypertensive therapy with a long-acting CCB or thiazide diuretic is indicated. For moderate to severe hypertension (SBP >160 and/or DBP >100 mmHg a combination therapy is recommended of a CCB+Thiazide diuretic or an ACEI +Thiazide diuretic or an ACEI+CCB. All patients should be reviewed at the clinic at least every 4-6 months, and at every visit, education on lifestyle modification and compliance to treatment should be emphasized. Dipstick urine and random blood sugar are indicated at the first visit and repeated after that if clinically needed.

A post hoc analysis of cross-sectional survey data obtained from a population of Kenyan adults enrolled in the HHA program was conducted through a partnership between the Ministry of health and AstraZeneca from February 2015 to October 2018. The prevalence of prehypertension and hypertension was reported at 54.5 and 2.8% respectively. Male gender and rural residence were independently associated with prehypertension (55).

2.6 Conceptual framework

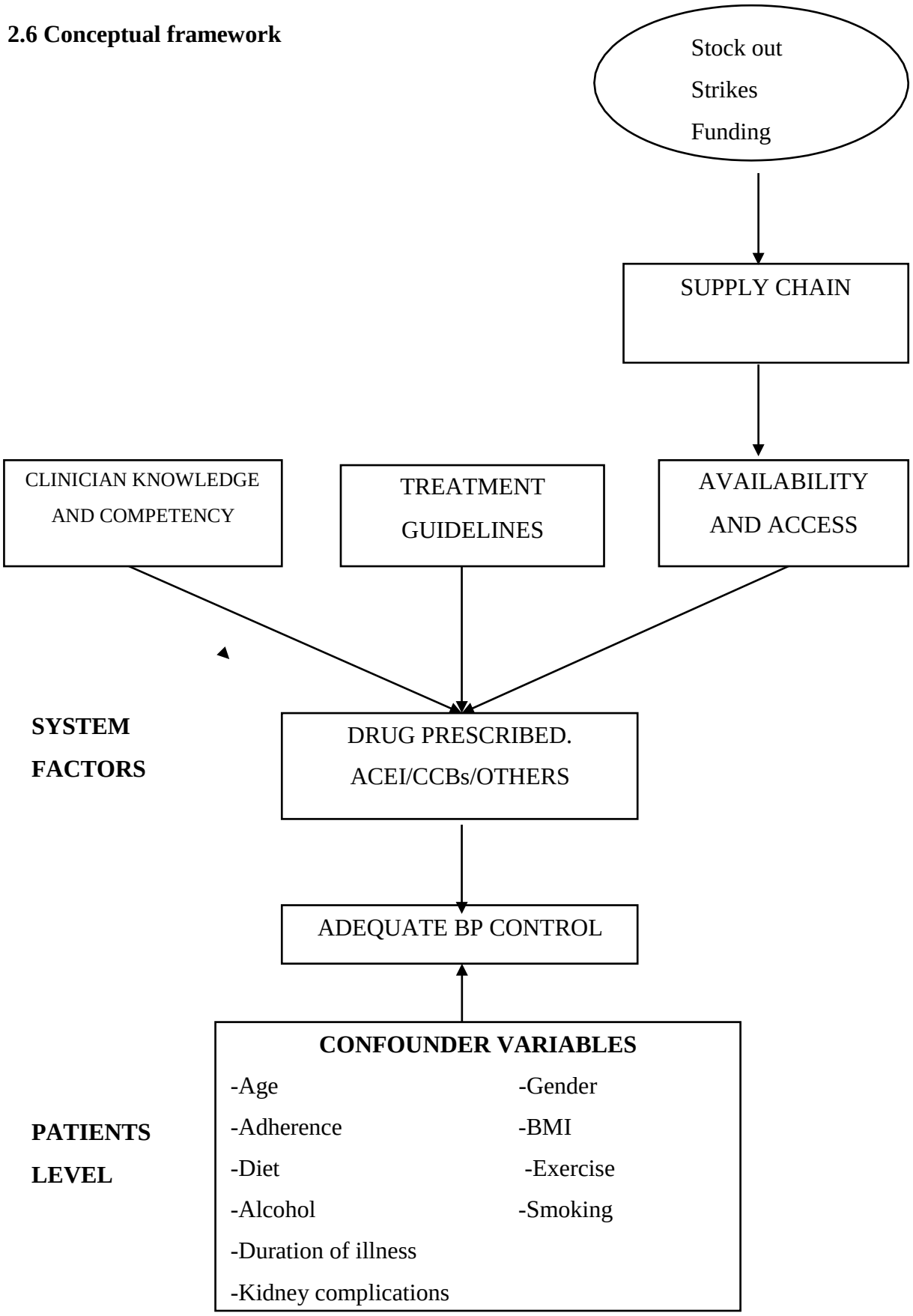

Figure 1 Conceptual framework for the factors affecting the success of the Healthy Heart Program

In this framework, adequate BP control is influenced by both system and patient factors. System factors include the type of drug prescribed, which in this study can be an ACEI, CCB, or any other class of antihypertensive medications. The choice of drug is determined by clinician knowledge and competency, existing treatment guidelines, and availability and access to the specific drug. The availability of antihypertensive drugs is further influenced by supply chain factors such as funding and stock-outs.

Patient's factors that influence the adequacy of BP control include: age and sex of the patient, with advanced age and male sex being associated with poor control. Patients with higher BMI have poor controlled BP compared to those with lower BMI. A healthy and low sodium diet and regular exercise lead to better BP control. Patients who have had hypertension for an extended period and with complications like kidney disease tend to have poorly controlled BP. Smoking and alcohol consumption is also associated with poor BP control.

CHAPTER 3: METHODS

This study was divided into two parts. The first part was a quantitative study assessing and comparing the adequacy of BP control among patients who were on the HHA program drugs and those who were on non-program drugs in two-level four hospitals in Kiambu County. The second part was a qualitative study that involved interviewing clinicians and pharmacists on the prescribing practices and the overall success of implementation and challenges of the HHA program.

3.1 Control of blood pressure in two-level four hospitals

3.1.1 Study design

This was a multisite analytical retrospective cross-sectional study. All files of hypertensive patients who met the eligibility criteria were assessed, and data were extracted using a standardized data collection tool.

3.1.2 Study site

The study was conducted in two-level four hospitals in Kiambu County (Ruiru and Tigoni sub-county hospitals). Kiambu and Kirinyaga counties were piloted for the HHA program in Central province.

3.1.3 Study population

The target population was adult patients with hypertension in Kenya on the HHA program drugs and other antihypertensive drugs regimens. The study population was adult hypertensive patients on the HHA program and other antihypertensive drugs attending medical outpatient clinics in Tigoni and Ruiru hospitals between January and April 2018.

3.1.4 Inclusion and exclusion criteria for patients

Participants were included if they met all of the following criteria:

1. Adults 18 years and older with a diagnosis of hypertension.
2. Patients on the respective antihypertensive treatments for at least one year at the time of the study.
3. Patients receiving their hypertension management from one of the 2 study sites.

Participants were excluded if they did not meet the inclusion criteria, did not have at least three independent BP readings taken at least four weeks apart during the last year of treatment, or had incomplete records.

3.1.5 Sample size determination.

To determine the appropriate sample size, the following formula was used.

$$n = \frac{2\,[\,(a + b)^2\,\alpha^2]}{(\mu_1 - \mu_2)^2}$$

Where:

n= the sample size in each of the groups

u_1= population mean in treatment Group 1

u_2= population mean in treatment Group 2

u_1-u_2 = the difference the investigator wished to detect

α^2= population variance (SD)

a= 1.96. The conventional multiplier for alpha=0.05

b=0.842. The conventional multiplier for power=0.80

This was a comparative study with equal sample sizes in each arm. The main outcome variable was categorical (56). A previous publication on BP control levels in patients on standard hypertension treatment in Ruiru Sub-county hospital reported a mean SBP of 141.5 mmHg

with a standard deviation of 20.5 mmHg. It was assumed that the addition of felodipine and lisinopril-HCTZ improved the mean SBP by at least 7.5mmHg with an effect size (u_1-$u_{2)}$ of 7.5. A small effect size of 7.5mmHg was selected because studies designed to find differences between drugs of the same therapeutic categories generally show a small difference.

The formula gave a sample size (n) of 117. Therefore a total of 117 patients' files for patients on the HHA program drugs and 117 files for patients on the other antihypertensive drugs were targeted for review and data extraction from the two hospitals.

3.1.6 Sampling procedure for hospitals and patients

Purposive sampling was employed to select Tigoni and Ruiru hospitals as they had the highest number of patients enrolled in the HHA program. Patients' files with a diagnosis of hypertension were obtained from the records department The files were examined to ascertain if patients met the eligibility criteria using the eligibility checklist in appendix 1. In each hospital, universal sampling was employed to select patients who were on non-program drugs. This involved sampling patients' files who met the inclusion criteria starting from the last clinic day preceding the commencement date of data collection and working backward in time until the calculated sample size was achieved.

A pilot study conducted in Ruiru and Tigoni hospitals showed that the number of patients on the HHA program drugs was relatively small. Therefore, universal sampling for patients on the HHA program drugs was employed to attain the desired sample size. All patients on this program and who meet the eligibility criteria were included in the study.

3.1.7 Data collection

The Data Collection Form for the abstraction of patient records (Appendix 1) was pre-tested on ten records in Ruiru before the commencement of the study to ensure its validity and reliability. Files for patients who attended medical outpatient clinics (MOPC) between January and April 2018 were sampled from the attendance register to achieve the desired sample size of 116. This number translated to 60 participants from Ruiru and 56 from Tigoni on the hospitals' standard regimens.

Files for all patients on the HHA program were reviewed, and a total of 86 participants met the inclusion criteria (49 in Ruiru and 37 in Tigoni hospital). The target sample size of 117 was

not met due to the lower than anticipated uptake of the HHA program. In addition, most participants were on the program drugs for less than one year. Therefore, the total number of study participants was 202.

Information that was abstracted from the records included the patient's demographic characteristics like age, sex, education level, marital status and occupation, weight, height, and duration of treatment. Antihypertensive drugs, comorbidities, concomitant long-term treatments and at least three latest independent BP readings taken at least four weeks apart during the last year of treatment were also recorded.

3.1.8 Variables

The main outcome/dependent variable for this study was the adequacy of BP control. The main independent/predictor variable was the HHA drugs vis-a-vis other drugs like CCBs, ACEI, and other antihypertensive drugs. The potential confounding variables included age, gender, BMI, diet, exercise, alcohol, study site, duration of illness, smoking, and adherence to treatment.

3.1.9 Case definition

Patients with well-controlled blood pressure were those with the last three BP readings taken at least four weeks apart, below 140/90 mmHg according to the latest JNC-8 guidelines on the management of hypertension (7).

3.1.10 Data management

Patient information was extracted from the patient records which were obtained from the records department during working hours. Unique patient identifiers were used to ensure confidentiality. Any document that linked collected data to the patients' files was kept under lock and key and only accessed by the researcher. All raw data were entered into Epi Info Version 7, and a database was created. Data entered were double-checked by the investigator to ensure accuracy and completeness. Data backup was done on a flash disk on a weekly basis. Upon completing the study, the data collection forms were archived for at least the next ten years according to the Kenyan law on handling research materials.

3.1.11 Data analysis

Quantitative data were entered into Epi Info Version 7. Stata® version 13(Stata Corp, USA) was used for analysis. Summary descriptive analysis was carried out for each demographic variable. Normally distributed continuous variables were presented as mean and standard deviation, whereas not normally distributed were presented as the median and interquartile range (IQR). Categorical variables were presented as frequencies and percentages. The results were also presented as graphs, tables, or pie charts.

Exploratory data analysis to establish patterns within and between the various variables was carried out and presented graphically in bar charts and scatter plots. Comparative analysis of patients with controlled BP and patients with uncontrolled BP was carried out. Unpaired t-test was used to compare the distribution of normally distributed continuous variables across the two arms. In contrast, the rank-sum test was used for continuous variables which were not normally distributed. Pearson's chi-square test was used to compare the distribution of the categorical variables across the two arms. The level of significance was set at 0.05. Forward stepwise logistic regression analyses were carried out to identify the key predictor variables that influenced the control of BP.

3.2 Assessment of the progress of the Healthy Heart Africa program

3.2.1 Study design

This was a descriptive cross-sectional study entailing in-depth interviews of key informants.

3.2.2 Study site and study population

The study was carried out in the Tigoni and Ruiru hospitals in Kiambu County. The study participants included key informants comprising of two hospital pharmacists in-charges, five medical officers, and one consultant.

3.2.4 Sampling procedure and recruitment.

Purposive sampling was used to select the key informants. The hospital pharmacists and clinicians working at the Medical Outpatient Clinics in both study sites were identified through the help of the medical superintendents.

3.2.5 Data collection

The selected participants were approached after clinic hours and presented with the Consent Form (Appendix 2), and the purpose, methods, and benefits of the study were explained to them. They were also informed why they were included in the study, the expected duration of the interview, voluntary participation, and information confidentiality. Questions were administered using a semi-structured interview guide (Appendix 3), and notes were taken by the interviewer, who was the investigator. The interview notes were transcribed within 24 hours, and the original scripts were destroyed. The interview guide was designed to collect information on prescribers' biodata and information on the availability and use of hypertension guidelines and explore the success of the implementation of the HHA program and the challenges and barriers associated with the implementation of the program.

3.2.6 Data analysis

The data obtained from the interviews were analyzed manually. A descriptive thematic approach was used to analyze the qualitative data. The data were examined for key and meaningful themes/patterns and interpreted by triangulating all the provided information.

3.3 Ethical considerations

Approval to carry out the study was obtained from Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UoN-ERC) before the commencement of the study. The approval number KNH-ERC/Mod&SAE/284 is attached (Appendix 4). At the County, approval was sought from the Kiambu County Department of Health Research (Appendix 5).

Patients were identified using patients' codes to ensure privacy and confidentiality. Informed consent was also obtained from the key informants and codes were used as identifiers.

CHAPTER 4: RESULTS

This chapter presents the results of the descriptive, inferential and logistic regression analysis. In addition, it describes the sociodemographic characteristics of the study population, the prescribing patterns of antihypertensive drugs, and co-medications, and patients' comorbidities.

4.1 Sociodemographic characteristics of the study population

Summary data analysis was carried out on data collected from the 202 patients' files. The sociodemographic characteristics of the patients were compared both by the hospital and by the program. In both hospitals, more females were sampled (78% in Ruiru & 72% in Tigoni) compared to male patients (22% in Ruiru & 28% in Tigoni). The median age of patients in Ruiru hospital was 56 years with a range of between 45 and 67 years. However, in Tigoni hospital, the median age was 61 years, with a range of between 52 and 70 years. The sociodemographic and other characteristics are summarized in Table 1. Although the median number of visits per year was the same for the two hospitals, in Ruiru, there were about nine patients who visited the facility very frequently (over seven times in one year). In Tigoni, some outliers had a very long duration between visits hence the statistically significant difference in duration between visits.

Table 1: Sociodemographic characteristics of hypertensive patients in Ruiru and Tigoni hospitals

Characteristic	Ruiru n (%)	Tigoni n (%)	Total	P-value
Sex				
Male	24 (22)	26 (28)	50 (24.8)	0.33
Female	85 (78)	67 (72)	152 (75.2)	
Age (years)				
20-34	1 (0.9)	3 (3.3)	4 (2)	0.012
35-49	33 (30)	15 (16.3)	48 (23.8)	
50-64	35 (31.8)	38 (41.3)	73 (36.1)	
65-79	37 (33.7)	30 (32.6)	67 (33.2)	
>79	4 (3.6)	6 (6.5)	10 (4.9)	
Total	**110**	**92**	**202**	
Body mass index				
Underweight	1 (0.9)	2 (2.1)	3 (1.5)	0.399
Normal	27 (24.5)	24 (26.1)	51 (25.2)	
Overweight	42 (38.2)	40 ((43.5)	82 (40.6)	
Obese	40 (36.4)	26 (28.3)	66 (32.7)	
Total	**110**	**92**	**202**	
Marital status				
Married	89 (81.7)	72 (77.4)	161 (79.7)	0.201
Single	13 (11)	15 (17.2)	28 (13.9)	
Divorced	2 (1.8)	0 (0.0)	2 (1.0)	
Unknown	6 (5.5)	5 (5.4)	11 (5.4)	
Total	**110**	**92**	**202**	
Occupation				
Unemployed	39 (35.8)	2 (2.2)	41 (20.3)	0.383
Self-employed	30 (27.5)	3 (3.2)	33 (16.3)	
Employed	18 (16.5)	0 (0.0)	18 (8.9)	
Unknown	23 (20.2)	87 (94.6)	110 (54.5)	
Total	**110**	**92**	**202**	
Number of visits Median (Range)	4 (4,5)	4 (3,4)	4 (3,4)	**0.003**
Total	**110**	**92**	**202**	
The duration between visits (weeks) Median (Range)	12 (12,12)	12 (12,16)	12 (12,16)	**0.007**
Total	110	92	202	

There were more female patients in the non-HHA program 86 (74.1%) compared to 66 (76.7%) in the HHA program. Similarly, there were more males in the non-HHA program as compared to the HHA program. The mean age for patients in the program was 58.5 years, while for non-program was 59 years. There was no statistically significant difference in most of the sociodemographic characteristics across the two groups. However, there was a statistically significant difference in the number of visits and duration between visits ($p<0.001$). The findings across the programs are summarized in Table 2.

Table 2: Sociodemographic characteristics of hypertensive patients on the HHA and non-HHA program

Characteristic	HHA program n (%)	Non-program n (%)	Total	P-value
Sex				
Male	20 (23.3)	30 (25.9)	50 (24.8)	
Female	66 (76.7)	86 (74.1)	152 (75.2)	0.67
Total	**86**	**116**	**202**	
Age (years)				
20-34	3 (3.5)	1 (0.9)	4 (2)	
35-49	19 (22.1)	29 (25)	48 (23.8)	0.756
50-64	31 (36)	42 (36.2)	73 (36.1)	
65-79	29 (33.7)	38 (32.7)	67 (33.2)	
>79	4 (4.7)	6 (5.2)	10 (4.9)	
Total	**86**	**116**	**202**	
Body mass index				
Underweight	1 (1.2)	2 (1.7)	3 (1.5)	
Normal	19 (22.1)	32 (27.6)	51 (25.2)	0.595
Overweight	39 (45.3)	43 (37.1)	82 (40.6)	
Obese	27 (31.4)	39 (33.6)	66 (32.7)	
Total	**86**	**116**	**202**	
Marital status				
Married	69 (80.2)	92 (79.3)	161 (79.7)	0.98
Single	12 (14.0)	16 (13.8)	28 (13.9)	
Divorced	1(1.2)	1(0.9)	2(1.0)	
Unknown	4 (4.6)	7 (6.0)	11 (5.4)	
Total	**86**	**116**	**202**	
Occupation				
Unemployed	25 (29.1)	16(13.8)	41 (20.3)	
Self-employed	13 (15.1)	20 (17.2)	33 (16.3)	0.091
Employed	12 (13.9)	6 (5.2)	18 (8.9)	
Unknown	36 (41.9)	74 (63.8)	110 (54.5)	
Total	**86**	**116**	**202**	
Number of visits				
Median (Range)	4 (3,4)	4 (4,5)	4 (3,4)	
Total	**86**	**116**	**202**	**<0.001**
Duration between visits (weeks)				
Median (Range)	12 (12,12)	12 (12,16)	12 (12,16)	**< 0.001**
Total	**86**	**116**	**202**	

4.2 Comorbidities amongst hypertensive patients in Ruiru and Tigoni hospital

In the two hospitals, the most prevalent comorbidity was arthritis (21.4%), followed by peripheral neuropathy (20.9%) and diabetes (17.4%). A summary of the comorbidities is shown in Table 3.

Table 3: Comorbidities in the study population

Comorbidity	N	%
Arthritis	43	21.4
Peripheral neuropathy	42	20.9
Diabetes	35	17.4
Peptic ulcers	25	12.4
Hyperlipidemia	22	10.9
Asthma	9	4.5
Congestive cardiac failure	9	4.5
HIV	2	1
Mental illness	1	0.5

The comorbidities were compared both by the hospital and by the program. The prevalence of diabetes was higher in Tigoni compared to Ruiru (28.3% versus 8.3%). Peripheral neuropathy was more prevalent in Ruiru than in Tigoni (28.4% versus 12%). Other conditions that were more prevalent in Ruiru included peptic ulcers, arthritis, and hyperlipidemia. Statistically significant differences were noted in the number of patients with diabetes ($p<0.001$), peripheral neuropathy ($p=0.004$), and ulcers ($p=0.02$). The differences in the prevalence of comorbidities across the two hospitals are summarized in Table 4.

Table 4: Comorbidities in hypertensive patients in Tigoni and Ruiru hospitals

Comorbidity	Ruiru n (%)	Tigoni n (%)	Total	P-value
Comorbidities due to metabolic syndrome				
Diabetes	9 (8.3)	26 (28.3)	35	**<0.001**
CCF	4 (3.7)	5 (5.4)	9	0.547
Peripheral neuropathy	31 (28.4)	11 (12)	42	**0.004**
Hyperlipidemia	16 (14.7)	6 (6.5)	22	0.061
Other comorbidities				
Asthma	5 (4.6)	4 (4.4)	9	0.935
Mental illness	0	1 (1.1)	1	0.278
Peptic Ulcers	19 (17.4)	6 (6.5)	25	**0.02**
HIV	1 (0.9)	1 (1.1)	2	0.904
Arthritis	26 (23.6)	17 (18.5)	43	0.355

CCF-Congestive Cardiac Failure

4.3 Comorbidities in hypertensive patients on the HHA program and on non-HHA program drugs

Patients on non-program drugs had a higher prevalence of peripheral neuropathy, congestive cardiac failure, and arthritis, as presented in Table 5. There was a statistically significant difference in the number of patients with peripheral neuropathy across the programs (p=0.001).

Table 5: Comorbidities in hypertensive patients by program

Comorbidity	HHA program n (%)	Non-HHA program n (%)	Total	P-value
Comorbidities due to metabolic syndrome				
Diabetes	16 (19.3)	19 (16.1)	35	0.559
Congestive cardiac failure	1 (1.2)	8 (6.9)	9	0.06
Peripheral neuropathy	8 (9.6)	34 (28.8)	42	**0.001**
Hyperlipidemia	8 (9.6)	14 (11.8)	22	0.633
Other comorbidities				
Asthma	3 (3.61)	6 (5.1)	9	0.62
Mental illness	1 (1.2)	0 (0.0)	1	0.23
Peptic ulcers	10 (12.1)	15 (12.7)	25	0.888
HIV	0	2 (1.7)	2	0.233
Arthritis	14 (16.9)	29 (24.6)	43	0.189

4.4 Medication history of hypertensive patients

4.4.1 Classes of antihypertensive drugs prescribed

The various antihypertensive drugs prescribed in the two hospitals were expressed as percentages, as shown in Table 6. Thiazide diuretics were the most frequently prescribed drugs (81.7%), followed by CCBs (55.5%) and ACE inhibitors (52.9%). Felodipine and nifedipine were the most widely prescribed CCBs, while enalapril and lisinopril were the most prescribed ACEIs. On the other hand, atenolol was the most commonly used β- blocker.

Table 6: Classes of antihypertensive drugs prescribed for the study population

Drug name	n	%
Thiazide diuretics		
Hydrochlorothiazide	165	81.7
CCBs		
Felodipine	46	22.8
Nifedipine	42	20.8
Amlodipine	24	11.9
Total	**112**	**55.5**
ACE inhibitors		
Enalapril	55	27.2
Lisinopril-HCTZ	52	25.7
Total	**107**	**52.9**
ARBs		
Losartan-HCTZ	31	15.4
Losartan	14	6.9
Total	**45**	**22.3**
β- BLOCKERS		
Atenolol	24	11.9
Carvedilol	7	3.5
Propranolol	1	0.5
Total	**33**	**15.9**
Other diuretics		
Furosemide	6	3
Spironolactone	2	1
Total	**8**	**4**
Miscellaneous		
Methyldopa	1	0.5
Hydralazine	1	0.5
Total	**2**	**1**

There were clear apparent differences in the prescribing patterns across the two hospitals. Felodipine was the most frequently prescribed CCB in Ruiru, while nifedipine and amlodipine were the commonly prescribed CCBs in Tigoni. Enalapril was more likely to be prescribed in Tigoni hospital compared to Ruiru. Lisinopril use was also higher in Tigoni. β- blockers were rarely prescribed in Tigoni than Ruiru. Methyldopa, propranolol, and hydralazine were prescribed only in Tigoni, while Spironolactone was prescribed exclusively in Ruiru.

Table 7: Antihypertensive drugs prescribing patterns in Ruiru and Tigoni hospitals

Drug name	Ruiru n (%) N=109	Tigoni n (%) N=93	P-Value
Thiazide diuretics			
Hydrochlorothiazide	90 (82.6)	75 (80.7)	0.429
CCBs			
Nifedipine	15 (13.8)	27 (29)	**0.008**
Felodipine	41 (37.6)	5(5.4)	**<0.001**
Amlodipine	3 (2.8)	21 (22.6)	**<0.001**
ACE inhibitors			
Enalapril	22 (20.2)	33 (35.5)	0.015
Lisinopril-HCTZ	22 (20.2)	30 (32.3)	**0.05**
ARBs			
Losartan	9 (8.3)	5 (5.4)	0.422
Losartan-HCTZ	21 (19.3)	10 (10.8)	0.094
β- Blockers			
Atenolol	22 (20.2)	2 (2.2)	**<0.001**
Carvedilol	6 (5.5)	1 (1.1)	0.086
Propranolol	0 (0)	1 (1.1)	0.278
Other diuretics			
Furosemide	4 (3.7)	2 (2.2)	0.526
Spironolactone	2 (1.8)	0 (0)	0.189
Miscellaneous			
Methyldopa	0 (0)	1 (1.1)	0.278
Hydralazine	0 (0)	1 (1.1)	0.278

Table 8: **Antihypertensive drugs prescribing patterns in the HHA and Non-HHA program**

Drug name	HHA program n (%)	Non-program n (%)	P-Value
Thiazide diuretics			
Hydrochlorothiazide	73 (84.3)	92 (79.3)	**<0.001**
CCBs			
Nifedipine	0 (0.0)	42 (36.2)	**<0.001**
Felodipine	46 (53.5)	0 (0.0)	**<0.001**
Amlodipine	11 (12.8)	13 (11.2)	0.731
Total	**57 (66.3)**	**55 (47.4)**	
ACE inhibitors			
Enalapril	5 (5.8)	50 (43.1)	**<0.001**
Lisinopril-HCTZ	52 (60.5)	0 (0.0)	**<0.001**
Total	**57 (66.3)**	**50 (43.1)**	
ARBs			
Losartan-HCTZ	2 (2.3)	29 (25)	**<0.001**
Losartan	3 (3.5)	11 (9.5)	0.097
Total	**45**	**22.3**	
β- BLOCKERS			
Atenolol	8 (9.3)	16 (13.8)	0.329
Carvedilol	2 (2.3)	5 (4.3)	0.466
Propranolol	0 (0.0)	1 (0.9)	0.388
Total	**10 (11.6)**	**22 (19)**	
Other diuretics			
Furosemide	2 (2.3)	4 (3.5)	0.642
Spironolactone	0 (0.0)	2 (1.7)	0.221
Miscellaneous			
Methyldopa	0 (0.0)	1 (0.9)	0.388
Hydralazine	1 (1.2)	0 (0.0)	0.244

A comparison of the prescribing patterns of antihypertensive drugs across the two programs. Statistically significant differences were observed between thiazide diuretics, CCBs (nifedipine and felodipine), ACE inhibitors, and fixed-dose combinations of losartan and hydrochlorothiazide. There was a greater propensity to prescribe diuretics in patients on the non-HHA program drugs. Patients on the non-program drugs were more likely to receive enalapril.

4.4.2 Number of antihypertensive drugs per patient

Figure 2 shows the number of antihypertensive drugs per patient. A large proportion of the patients were on a two-drug regimen (57%), followed by a three-drug regimen (34%). In contrast, monotherapy and a four-drug regimen were least prescribed.

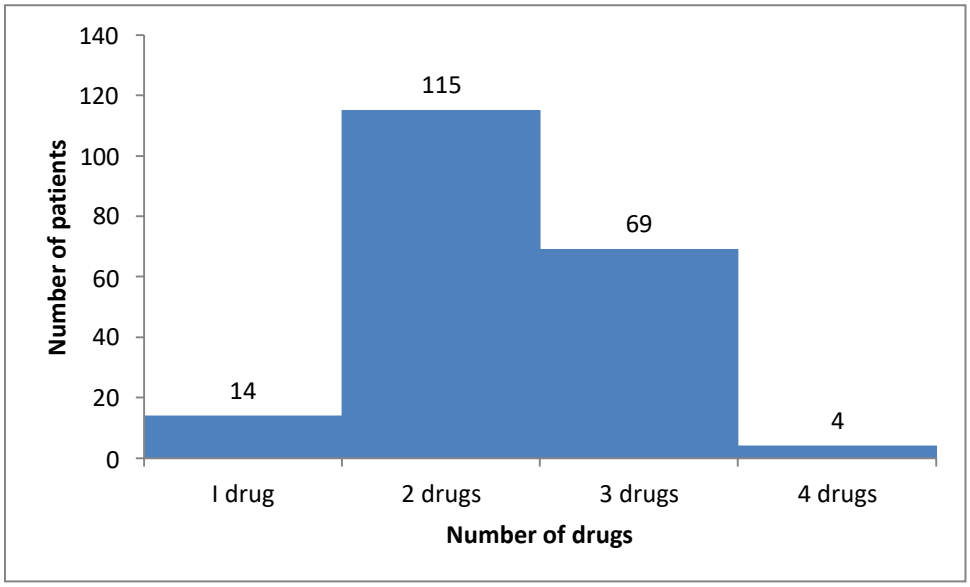

Figure 2: Number of antihypertensive drugs per patient

Table 9 shows a comparison of the number of antihypertensive drugs per patient in the program and non-program groups. Across the two groups, the two-drug regimen was the most prescribed, followed by a three-drug regimen, and the least prescribed was a four-drug regimen. The differences in the number of antihypertensive drugs prescribed were statistically significant between the two groups (p=0.033).

Table 9: Number of antihypertensive drugs prescribed per patient between the programs

Number of drugs	HHA Program n (%)	Non-HHA program n (%)	P-Value
1	5 (5.8)	9 (7.8)	**0.033**
2	46 (53.5)	69 (59.5)	
3	33 (38.4)	36 (31)	
4	2 (2.3)	2 (1.7)	

4.4.3 Specific antihypertensive regimens prescribed

The most commonly prescribed regimen was a two-drug combination of an ACE inhibitor and a thiazide diuretic (19.8 %), followed by a three-drug combination of a CCB, an ACE inhibitor, and a thiazide diuretic (18.8%). Regimens containing a β- blocker was the least frequently prescribed.

Table 10: Specific antihypertensive regimens prescribed

Regimen	n	%
Monotherapy		
CCB	7	3.5
ACE inhibitor	6	3
Thiazide diuretic	1	0.5
2-drug combination therapy		
ACE inhibitor+ Thiazide diuretic	40	19.8
CCB+ Thiazide diuretic	29	14.4
ARB+ Thiazide diuretic	22	10.9
CCB+ ACE inhibitor	9	4.5
CCB+ BB	4	2
CCB+ ARB	3	1.5
ACE inhibitor+ BB	3	1.5
ACE inhibitor+ loop diuretic	2	1
Thiazide+ BB	1	0.5
ARB+BB	1	0.5
ACE inhibitor+ methyldopa	1	0.5
3-drug combination therapy		
CCB+ACE inhibitor+ Thiazide diuretic	38	18.8
CCB+ ARB+Thiazide	11	5.4
CCB+ BB+ Thiazide diuretic	7	3.5
ARB+ BB+ Thiazide diuretic	6	3
ACE inhibitor+ BB+ Thiazide diuretic	2	1
ACE inhibitor+BB+ other diuretics	2	1
CCB + ACE inhibitor+ other diuretics	1	0.5
BB+ Thiazide diuretic+ other diuretics	1	0.5
ACE inhibitor+ Thiazide diuretic+ hydralazine	1	0.5
4-drug combination therapy		
CCB + ACE inhibitor+Thiazide diuretic+BB	2	1.5
CCB+ ARB+Thiazide diuretic+ BB	1	0.5
ARB+Thiazide diuretic+BB+spirinolactone	1	0.5

ACE= Angiotensin-converting enzyme, ARB= Angiotensin receptor blocker,
BB= β- blockers, CCB= calcium channel blocker,

4.4.4 Designation of the prescribers

In the two hospitals, hypertensive patients attending the MOPC were treated by either a medical officer or a consultant. A total of 90.6% of all the prescriptions were generated by medical officers, while consultants generated 9.4% of the prescriptions.

4.5 Prescribing patterns of long term co-medications

Concomitant long-term medications were compared both by the hospital and by the program. As shown in Table 11, more classes of long-term medications (NSAIDS, anti ulcers, antiasthmatics, antiarthritics, cardiac glycosides, and statins) were prescribed in Ruiru compared to Tigoni Hospital. The use of antidiabetics was much higher in Tigoni than in Ruiru.

Table 11: Long term co-medications for patients in Ruiru and Tigoni hospitals

Drug	Ruiru n(%)	Tigoni n (%)	Total	P-Value
NSAIDs				
Meloxicam	17 (5.5)	4 (4.3)	21	
Celecoxib	9 (8.3)	2 (2.2)	11	0.29
Antidiabetics				
Insulin	2 (1.9)	6 (6.5)	8	0.1
Glibenclamide	5 (3.7)	14 (15.1)	19	**0.023**
Metformin	6 (5.5)	19 (19.4)	25	**0.005**
Pioglitazone	0 (0)	6 (6.5)	6	**0.007**
Anti ulcers				
Omeprazole	14 (12.8)	4 (4.3)	18	**0.019**
Esomeprazole	6 (5.5)	1 (1.1)	7	
Antiasthma				
Salbutamol	5 (4.6)	2 (2.2)	7	0.36
Fluticasone/Salmeterol	0 (0.0)	1 (1.1)	1	
Supplements				
Calcium supplements	6 (5.5)	1 (1.1)	7	0.146
Vitamin supplements	16 (14.7)	8 (8.6)	24	0.183
Cardiac glycosides				
Digoxin	4 (3.7)	1 (1.1)	5	0.237
Statins				
Atorvastatin	14 (12.8)	6 (6.5)	20	0.129
CNS drugs				
Antipsychotics	0 (0)	1 (1.1)	1	0.278
Amitryptilline	8 (7.3)	0 (0.0)	8	**0.008**
Thyroid drugs				
Levothyroxine	0 (0)	1 (1.1)	1	
Carbimazole	0 (0)	1 (1.1)	1	0.306
Others				
ARVs	1 (0.9)	1 (1.1)	2	0.91
Aspirin	6 (5.5)	5 (5.4)	11	0.968
Pregabalin	8 (7.3)	4 (4.3)	12	0.363

There were systematic differences in the use of long-term drugs across program and non-program patients. Generally, the non-program patients had a higher prevalence of use of most drugs except glibenclamide, metformin, and aspirin. There were no program patients on digoxin. In addition, most of the patients on vitamin supplements were not on the program drugs. The findings are summarized in Table 12.

Table 12: Long term co-medications for patients in the HHA and non-HHA program

Drug	HHA program n (%)	Non-program n (%)	Total	P-Value
NSAIDs				
Meloxicam	10 (1.2)	21 (7.6)	31	0.154
Celecoxib	3 (3.6)	8 (6.7)	11	
Antidiabetics				
Insulin	2 (2.4)	6 (5.1)	8	0.339
Glibenclamide	10 (12.0)	9 (7.6)	19	0.304
Metformin	14(16.9)	11 (8.4)	25	0.137
Pioglitazone	1 (1.2)	5 (4.2)	6	0.217
Antiulcers				
Omeprazole	6 (7.2)	12 (10.1)	18	
Esomeprazole	4 (4.8)	3 (2.5)	7	0.55
Antiasthma				
Salbutamol	1 (1.2)	6 (5.0)	7	
Fluticasone/Salmeterol	1 (1.2)	0 (0.0)	1	0.17
Supplements				
Calcium supplements	0 (0.0)	7 (5.9)	7	**0.055**
Vitamin supplements	2 (2.4)	22 (18.5)	24	**0.001**
Cardiac glycosides				
Digoxin	0 (0.0)	5 (4.2)	5	**0.059**
Statins				
Atorvastatin	9 (10.8)	11 (9.2)	20	0.708
CNS drugs				
Antipsychotics	1 (1.2)	0 (0.0)	1	0.23
Amitriptylline	3 (3.6)	5 (4.2)	8	0.833
Thyroid drugs				
Levothyroxine	0 (0.0)	1(0.84)	1	
Carbimazole	0 (0.0)	1(0.84)	1	0.494
Others				
ARVs	0 (0.0)	2 (1.7)	2	0.235
Aspirin	8 (9.6)	3 (2.5)	11	**0.028**
Pregabalin	4 (4.8)	8 (6.7)	12	0.573

4.6 Blood pressure control

Three latest BP readings were used to determine the adequacy of blood pressure control. Systolic blood pressure control was considered adequate if the mean of the last three readings was <140mmHg. A mean SBP above 140mmHg was considered inadequate. Using this outcome definition, 40.1% of all patients had well-controlled blood pressure, whereas 59.9% had uncontrolled blood pressure

In the HHA program, 33 (38.4%) patients had a well-controlled BP, while 53 (61.6%) had uncontrolled blood pressure. In the non-program group, 48 (41.4%) patients had a well-controlled BP, whereas 68 (58.6%) had uncontrolled blood pressure

4.6.1 Relationship between blood pressure control and sociodemographic characteristics of the study population

Bivariate comparative analysis was carried out to find the association between BP control and the other study variables. The rank-sum test was used to analyze the continuous variables and the Pearson's chi-square test for the categorical variables. Blood pressure control was compared with sociodemographic and other patients' characteristics. A summary of the findings is shown in Table 13. In Ruiru hospital, 46 (42.2%) had adequately controlled BP compared to 35 (37.6%) in Tigoni hospital. The difference in the control of BP across the two hospitals was not statistically significant (p=0.51). Blood pressure was adequately controlled in 20 (40%) males than 61 (40.1%) females. However, the gender difference was not statistically significant (p=0.99). Age was also not significantly associated with good BP control (p=0.33). Other variables not significantly associated with BP control included treatment duration, marital status, and weight of the patients. The participants' program was also not significantly associated with good blood pressure control (p=0.67).

Table 13: Association between blood pressure control, sociodemographic characteristics, and other study variables

Variable	Total	Controlled BP (%)	Uncontrolled BP (%)	COR 95% CI	P-Value
Hospital					
Ruiru	109	46 (42.2)	63 (57.8)	0.8 (0.47-0.51)	0.51
Tigoni	93	35 (37.6)	58 (62.4)		
Sex					
Male	50	20 (40)	30 (60)	1 (0.52-1.93)	0.99
Female	152	61 (40.1)	91 (59.9)		
Age					
<55 years	79	35 (44.3)	44 (55.7)	0.8 (0.42-1.33)	0.33
>=55 years	123	46 (37.4)	77 (62.6)		
Treatment duration					
1 year	9	3 (33.3)	6 (66.7)	1 (0.94 – 1.07)	0.97
>1 year	193	48 (40.4)	115 (59.6)		
Program					
HHA	86	33 (38.4)	53 (61.6)	0.9 (0.49-1.56)	0.67
Non-HHA program	116	48 (41.4)	68 (58.6)		

4.6.2 Relationship between blood pressure control and patients' clinical characteristics

The clinical characteristics considered were the antihypertensive drugs prescribed, comorbidities, and long-term co-medications. The association between BP control and clinical characteristics was examined. Statistically significant associations were found between blood pressure control and the number of antihypertensive drugs prescribed, having diabetes and peptic ulcers, and using omeprazole. There was a negative association between being diabetic and control of blood pressure. Patients who were diabetic had 0.4 times the odds of those without diabetes of having a well-controlled blood pressure (p=0.03). A positive association was noted between having peptic ulcers, being on omeprazole, and better control of blood pressure. Patients who had ulcers had 2.6 times the odds of those who did not have ulcers of having a well-controlled blood pressure (p=0.03). There was an association between blood pressure control and the number of antihypertensive drugs prescribed. Patients who were on one or two drugs had a better controlled BP compared to those who had three or four drugs (p=0.03). As the number of drugs increased, the proportion of patients who had uncontrolled blood pressure increased. There was no statistically significant association between specific antihypertensive drugs and control of blood pressure. These findings are summarized in Table 14.

Table 14: Association between blood pressure control and clinical characteristics of the study population

Variable	Total	BP controlled n (%)	BP uncontrolled n (%)	OR (95% CI)	P-Value
No. of anti-hypertensives					
1	14	8 (53.6)	6 (46.4)	0.5 (0.34 -0.79)	**0.03**
2	115	45 (39.3)	70 (60.7)		
3	69	16 (23.7)	53 (76.3)		
4	4	2 (50)	2 (50)		
Diabetic					
Yes	35	8 (22.9)	27 (77.1)	0.4 (0.17-0.92	**0.03**
No	166	72 (43.4)	94 (56.6)		
Peptic Ulcers					
Yes	25	15 (60)	10 (40)	2.6(1.09-6.03)	**0.03**
No	176	65 (36.9)	111 (63.1)		
Omeprazole					
Yes	25	14 (56)	1 (44)	1 (0.99-1.06)	**0.05**
No	177	67 (37.9)	110 (62.1)		
Enalapril					
Yes	55	17 (30.9)	38 (69.1)	0.6 (0.3-1.12)	0.10
No	147	64 (43.5)	83 (56.5)		
Lisinopril					
Yes	52	21 (40.4)	31 (59.6)	1 (0.53-1.93)	0.96
No	150	60 (40)	90 (60)		
Felodipine					
Yes	46	18 (39.1)	28 (60.9)	0.9(0.48-1.86)	0.88
No	156	63 (40.4)	93 (59.6)		
Amlodipine					
Yes	24	9 (37.5)	15 (62.5)	0.88(0.37- 1.17)	0.78
No	178	72 (40.5)	106 (59.5)		
Hydrochlorothiazide					
Yes	82	28 (34.1)	54 (65.9)	0.16 (0.37-1.17)	0.15
No	120	53 (44.2)	67 (55.8)		

4.6.3 Independent predictors of blood pressure control

Multivariate logistic regression analysis was carried out to identify independent predictors of BP control. Diabetes was an independent predictor of poor control of BP (COR=0.4; 95% CI 0.17-0.92). Participants who were diabetic had 0.4 times the odds of those without diabetes of having a well-controlled blood pressure (AOR=0.5; 95% CI 0.2-1.12).

Ulcers were an independent predictor of adequate BP control (COR=2.6; 95% CI (1.09-6.03). Participants who had ulcers were twice as likely to have a well-controlled BP than those without ulcers (AOR=2.3; 95% CI (0.95-5.49).

The use of hydrochlorothiazide was an independent predictor of poor control of BP (AOR=0.5; 95% CI 0.28-1.00). Participants on hydrochlorothiazide had 0.5 times the odds of those who were not using it of having a well-controlled blood pressure.

4.6. Diabetic status and effectiveness of individual antihypertensive drugs

Multivariable logistic regression analysis reported the effectiveness of enalapril and amlodipine to vary with the diabetic status of the patient. This relationship was not observed with either felodipine or lisinopril. Diabetic patients on enalapril had four times the likelihood of having a well-controlled blood pressure compared to non-diabetic patients on enalapril (AOR= 3.96; 95% CI 0.76-20.66). This observation was an effect measure modification. The Mantel-Haenszel (MH) test for homogeneity of the measure of association confirmed the effect measure modification (p=0.019). Figure 3 shows the relationship between the effectiveness of enalapril and the diabetic status of the participants.

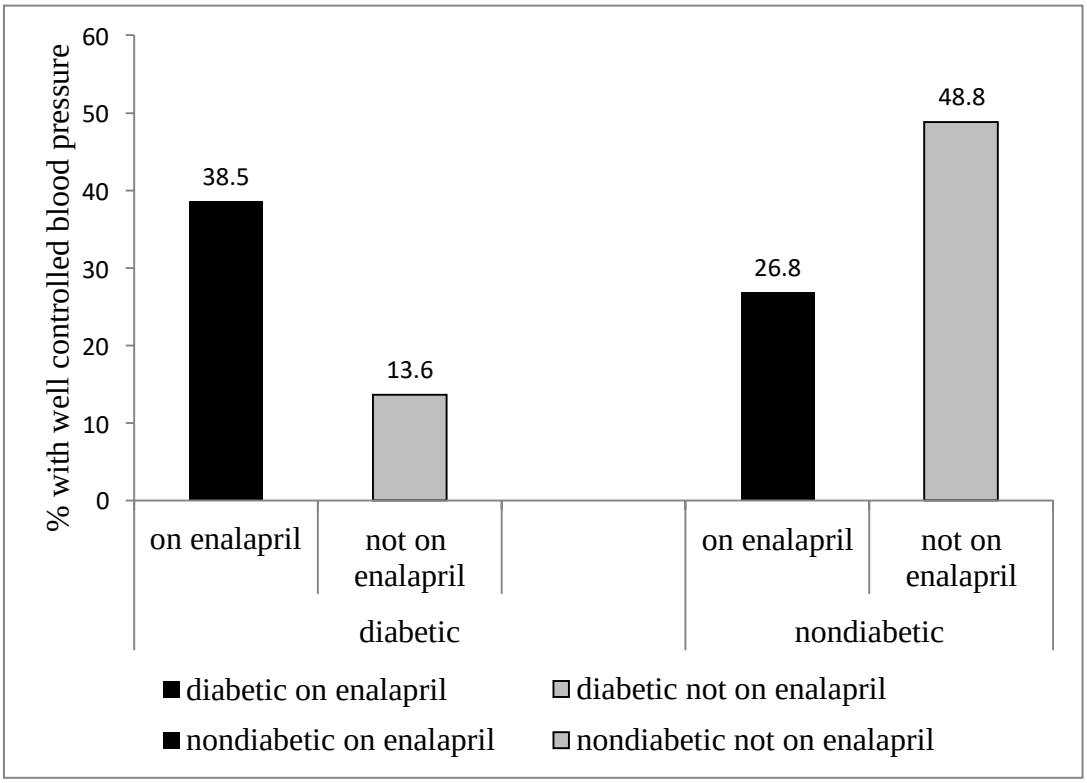

Figure 3: Relationship between enalapril and diabetic status

Amlodipine was also more effective among diabetic patients (AOR=5.8; 95% CI 1.00-32.95). Diabetic patients on amlodipine had five times the odds of non-diabetics on amlodipine of having well-controlled blood pressure. This relationship is illustrated in Figure 4. The MH test for homogeneity of the measure of association confirmed effect measure modification (p=0.023).

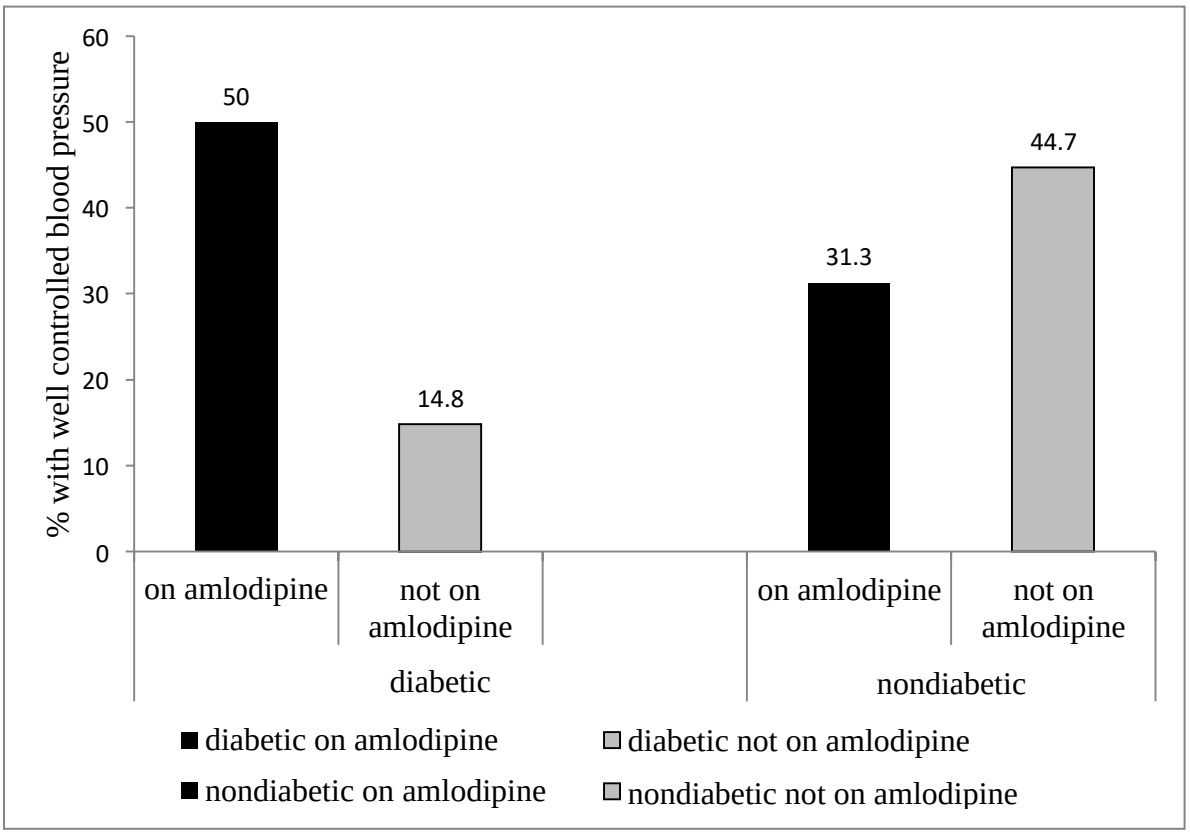

Figure 4: Relationship between amlodipine and diabetic status

4.6.5 Relationship between gender and effectiveness of enalapril

The effectiveness of enalapril was found to vary with the patient's gender. Male participants on enalapril had four times the odds of females on enalapril of having a well-controlled blood pressure (AOR=4.2; 95% CI 0.47-36.73). The MH test for equality of odds confirmed effect measure modification (p=0.065). This relationship is illustrated in Figure 5

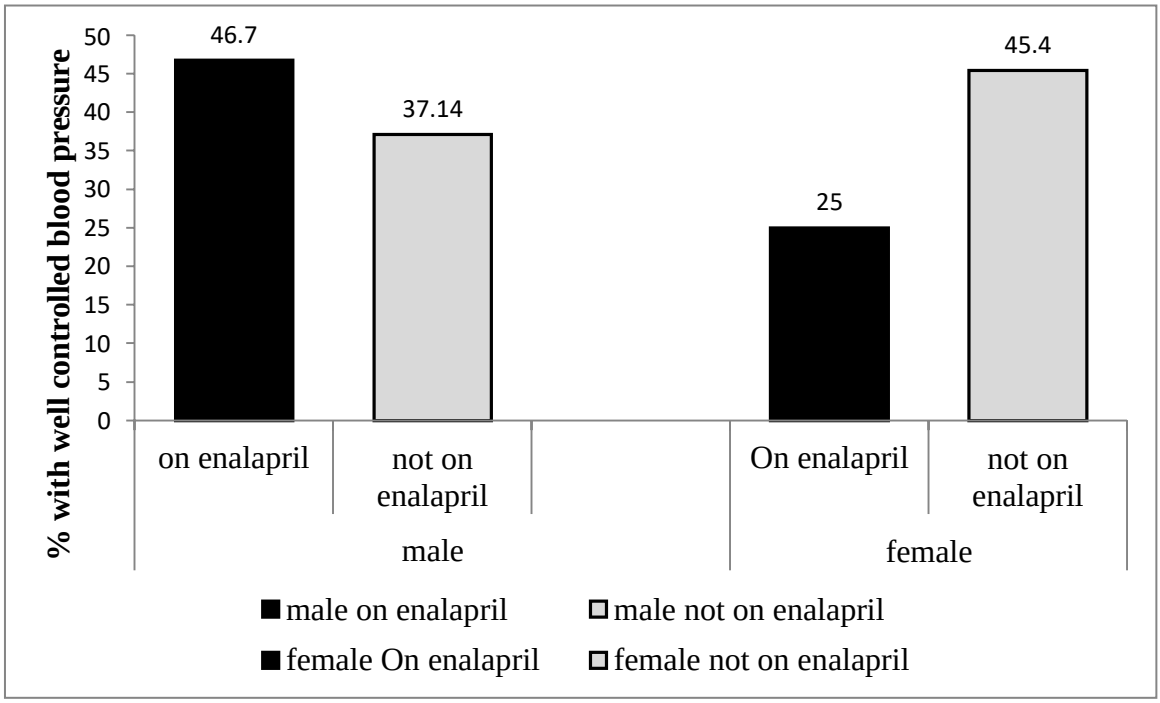

Figure 5: Influence of gender on the effectiveness of enalapril

4.7 Hypertension management and HHA program progress

A key informant interview was conducted to establish what informed the prescribing patterns of the antihypertensive drugs and evaluate the success and challenges in implementing the HHA program. A total of eight respondents were interviewed, six of whom were clinicians, and two were pharmacists. Their ages ranged from 26 to 46 years, with a mean of 32 years. Three of the participants were males, while five were females. The average duration of practice was 6.7 years.

4.7.1 Determinants of drug selection for hypertension management

Most of the clinicians stated that drug selection for hypertension management was based on the stage of hypertension and comorbidities such as diabetes. There was general concordance amongst clinicians that severity of hypertension and comorbidities were the major criteria for treatment selection. Only one respondent stated that he used pregnancy as a determinant for drug selection. Similarly, one respondent stated that the availability of drugs in the hospital was a key determinant for drug selection. Pregnancy and drugs availability did not seem to be major criteria for drug selection.

Only two respondents stated the criteria they were using to initiate therapy. They said they initiate therapy in patients aged above 60 years whose BP is >150/90 and in patients aged below 60 years with a BP of 140/90. Four clinicians mentioned that since all the patients were black, they used a CCB+ a thiazide diuretic as first-line treatment. The other clinicians reported using a CCB+ACEI/ARB as the first-line treatment. There was variation in the type of 1st line drugs but the overwhelming majority initiated with a CCB. The second drug that was given with the CCB was either a diuretic or an ACEI.

The most frequently mentioned comorbidities were diabetes and renal impairments. However, the treatment approaches for patients with these comorbidities were not provided by the respondents. One respondent pointed out that he avoided ACEI and ARBs in patients with renal impairments. Most clinicians did not mention the treatment targets, but one mentioned that he evaluated blood pressure monthly, and if the target was not achieved, he adjusted therapy. A second clinician also mentioned adjustments that he made in cases where treatments targets were not achieved. These adjustments included increasing the dose or adding a second drug.

4.7.2 Knowledge, access, and use of hypertension treatment guidelines

Five out of the six clinicians stated that they were aware of the JNC8 guidelines. There was very little knowledge of the NICE guidelines for managing hypertension. Only one respondent mentioned the NICE guidelines. Moreover, there was very poor knowledge of ESH/ESC, ISH, and ISHIB guidelines. Four clinicians stated they were aware of the AHA guidelines, while three knew of the WHO treatment guidelines. Only three out of the six clinicians were aware of the HHA guidelines.

Clinicians had access to eight guidelines, which can lead to confusion as the guidelines might have conflicting information in some areas. Some guidelines were more popular than the others, with JNC 8, AHA, and HHA guidelines being most widely used by the clinicians. The clinicians seemed to appreciate that there were different guidelines for black patients, with four mentioning that they focused on guidelines specific for blacks that recommend initiating with a CCB+ Diuretic.

All six clinicians believed that the guidelines were useful and applicable in their setup. However, one respondent found the guidelines useful only in patients with mild and moderate hypertension. Some of the reasons given in favor of the guidelines were that the guidelines had well-stipulated drugs and doses, and were easy to use and apply. One stated he had noticed

patients had a positive response, while another stated the guidelines "*Eliminate trial and error*" and "*are based on patients' parameters."* All the respondents stated that the guidelines were applicable in their clinical setting. *"The drugs were readily available, affordable and efficacious."*

None of the respondents stated any deviations from the guidelines. Their overall opinion was that the guidelines were very helpful, but *"more local data was needed for the black African population."*

4.7.3 In-service training on management of hypertension

Only three respondents had ever received any post-qualification training on hypertension management. Two of the respondents had received training from AstraZeneca, while one received training from the Kenya Cardiology Society.

4.8 Knowledge and training of the healthy heart program

All eight respondents said they knew and understood the objectives of the HHA program. It is a program by AstraZeneca in collaboration with MOH, with Jhpiego and AMREF as the implementing partners. They mentioned the three objectives as "*patients' education and awareness, improved access to quality affordable drugs and clinicians training*." The clinicians reported their roles in the program as diagnosis, prescribing, and patient education on risk factors and lifestyle modifications. The pharmacists' roles were reported as procurement, dispensing, drug information, and monitoring of ADRs.

Four out of the eight respondents stated that they had received training on the various aspects of the program. The four reported having received training on the protocol for identification and management of hypertension, use of the HHA treatment guidelines, and the drugs used in the program. Those who stated they had never received any training said they relied on knowledge acquired from undergraduate and postgraduate studies to implement the program. One respondent said she had learned about the program on the job from her fellow clinicians.

Four out of the eight respondents reported having used the treatment guideline, while four had not. One of the respondents said he uses the Kenyan guidelines interchangeably with the JNC-8 guidelines. One respondent gave a summary of the guideline recommendation as for mild hypertension lifestyle modification was recommended, moderate hypertension- use of a CCB

or a thiazide diuretic or both. The recommended baseline tests were reported as random blood sugar, ECG, and urinalysis.

4.8.1 Opinion on the success of adoption and implementation of the program

The respondents had mixed opinions on the success of the program. Five respondents said it was a success with varying supporting reasons. The drug supply was fairly constant and improved health outcomes for some patients and BP control. One of the respondents said, *"The program has enhanced patients' awareness, provided continuous HCWs education and constant supply of high-quality affordable drugs."*

Two respondents said that the program had some success. However, several challenges like inadequate training of HCWs, erratic supply of drugs, and inadequate BP monitoring tools were reported. One respondent believed that the program adoption and implementation had failed. *"Frequent stock-outs of drugs and the program drugs are too expensive in the chemist,"* he also cited *"Most of my patients prefer non combined generics which are more affordable."*

Six respondents agreed that the program had a positive impact on the control of blood pressure. *"Some patients' BP has markedly improved after using the program's interventions."* One respondent was not sure of the impact. *"There is need to analyze data to determine the impact."* One of the respondents said that the program had both positive and negative impacts. *"Some patients have had marked improvements while others had a worsening of the condition due to non-compliance*."

4.8.2 Challenges in the implementation of the program

Five of the respondents strongly agreed that their institution did not support the program. They cited erratic supply of drugs, lack of enough BP monitoring tools, underfunding of patients outreach activities, and staff shortage as the main areas where the institutions had failed. Three respondents felt the institutions had supported the program through frequent CMEs and a fairly constant supply of drugs, especially in Tigoni hospital. The frequent stock out of the drugs had led to poor compliance, switching to other drugs, or patients are forced to buy the drugs from the retail pharmacies, which placed a heavy economic burden on the already poor patients.

There was a universal agreement among the respondents that the program drugs had documented adverse drug reactions (ADRs) on some patients. Lisinopril-HCTZ was associated

with angioedema, intractable cough, and increased micturition. Felodipine was associated with bilateral limb oedema and persistent headaches. These ADRs had led to poor compliance and a switch to other drug classes.

Additional challenges were: poor BP taking methods and techniques, patients defaulting to medical outpatient clinics, lack of social support for poor patients through NHIF, and prohibitive drug prices outside the government facilities.

4.8.3 Respondents recommendations on improvement of the Healthy Heart Africa program

Six respondents suggested the provision of a non-combined lisinopril and hydrochlorothiazide pill, intensified training, and availing the guideline to all HCWs. Also, *"Provide a variety of drugs from the two drugs classes to choose from."* They also recommended more drugs to be added into the program, ensure availability at all times, and further subsidization of the drugs to cater for the very poor. The respondents unanimously agreed that more work needs to be done on the training of clinicians on the use of the program's guidelines and identification and screening through regular seminars and CMEs.

The respondents recommended that institutions need to support the program through the provision of more trained staff, additional modern BP monitoring tools, and ensuring availability of drugs at all times by lobbying for more funding and consistent disbursements. Additionally, the institutions should subsidize the charges for the recommended baseline tests. One respondent added that *"There is a need to recruit more researchers to the program and improve partnership with the county government to improve outreach capacity."*

CHAPTER 5: DISCUSSION

The main objective of this study was to compare the proportion of patients with controlled BP among patients on the HHA program drugs and other antihypertensive drugs. In addition, the study aimed to explore the challenges in the adoption and implementation of the Healthy Heart Africa program in Kiambu County.

5.1 Characteristics of the patients

The ratio of males to females was 1:3. This ratio was consistent with findings from studies in other parts of the country (3,6). In a study carried out in Ruiru hospital in 2014, the ratio of males to females was 1:7 (10). This gender difference can be attributed to differences in health-seeking behavior among males and females, with females being more likely to visit health facilities than males (57).

The median age of the participants from the two hospitals was 58.5 years, with Ruiru and Tigoni having a median age of 56 years and 61 years, respectively. The median age was comparable to findings from other studies carried out in the region (3,6,10). Patients in Tigoni were older and taller than those in Ruiru. This could be explained by the fact that Ruiru is a more cosmopolitan area, has a younger population, and has more people who have migrated from other parts of the country. On the other hand, Tigoni hospital is in a rural setup.

In the two hospitals, arthritis was the most prevalent comorbidity at 21.4%, followed by peripheral neuropathy at 20.9% and diabetes at 17.4%. Peripheral neuropathy and arthritis were more common in Ruiru than in Tigoni, while diabetes was more common in Tigoni. Patients in Tigoni were older and, therefore, may have been more prone to diabetes. These findings were in contrast to various studies that showed diabetes to be the most prevalent comorbidity among hypertensive patients. A 2014 study carried out in Ruiru hospital found diabetes to be the most common comorbidity with a prevalence of 37%, while a study done in Central Kenya found the prevalence of diabetes to be 42% (3,10).

Patients who were on the program drugs had a lower prevalence of end-organ complications of diabetes and cardiovascular complications. The distribution of the other non-CVS conditions was almost equal across the two groups. This finding could be attributed to confounding by indication whereby patients with fewer comorbidities were more likely to be treated with program drugs. In addition, patients on the program drugs could have increased care and,

therefore, decreased comorbidities. To elucidate the true reason for this difference, analysis should be repeated using propensity scoring to adjust for confounding by indication.

5.2 Prescribing patterns of the antihypertensive drugs and co-medications

Thiazide diuretics were the most prescribed class of antihypertensive drugs in the two hospitals, followed by CCBs and ACEIs. This could be explained by the use of the various guidelines which recommend use of a thiazide diuretic or a CCB or both as first-line agents in a black population (7,27,28,31). Hydrochlorothiazide (a thiazide diuretic) is readily available and affordable compared to the other antihypertensive drugs in our setup. There were apparent differences in the prescribing patterns of the specific drugs from each of the three drug classes across the two hospitals. Felodipine was the most prescribed CCB in Ruiru, whereas nifedipine was the most preferred CCB in Tigoni. Lisinopril was more prescribed in Tigoni compared to Ruiru. Enalapril was the most preferred ACEI in Ruiru. These differences could be attributed to the availability of the various drugs. During the study period, it was observed that lisinopril was held in larger stocks in Tigoni compared to Ruiru. On the other hand, felodipine was held in large stocks in Ruiru compared to Tigoni hospital. Generally, in the HHA program, lisinopril-hydrochlorothiazide and/or felodipine were the most prescribed drugs. Patients on the HHA program with very poor blood pressure control had a third or fourth non-program drug in their regimen. A large proportion of the patients were on a two drugs regimen and three drugs regimen. This finding is comparable to the findings by Jarari et al. that reviewed the prescribing patterns of antihypertensive drugs(58). A study done in 2014 at Ruiru hospital reported a 60% prevalence of combination therapy (1).

A two-drug combination of an ACE inhibitor and a thiazide diuretic was the most prescribed. This finding contrasts with the Kenya National Guidelines for Cardiovascular Diseases Management that recommends a two-drug combination of a CCB and a thiazide diuretic (31). This was followed by a three-drug combination of a CCB, an ACE inhibitor, and a thiazide diuretic. This complies with the Kenyan and the recent JNC 8 guidelines that recommend a three-drug combination of CCBs, ACE inhibitors, and thiazide diuretics (7,31,58).

The most prescribed long-term co-medications in the two hospitals were antidiabetics followed by NSAIDs and high-dose vitamin supplements. Systematic differences were observed in the prescribing patterns of the co-medications across the two hospitals, with NSAIDs and vitamin

supplements being prescribed more in Ruiru and antidiabetics being prescribed more in Tigoni. The observed differences could be attributed to varying disease patterns across the hospitals.

5.3 Blood pressure control

The overall prevalence of well-controlled BP was 40.1%. However, the prevalence in Ruiru was 42.2% and 37.6% in Tigoni hospital. A previous study carried out in Ruiru hospital reported a prevalence of 46% (10). However, the prevalence of well-controlled blood pressure in this study was higher than other similar studies carried out in the region. A 2009 study in KNH found a low prevalence of BP control of 26%, which was comparable to 33% good BP control reported in Nyeri PGH by Mutua et al.(3,6). The poor control of BP among patients in Tigoni hospital could be attributed to a larger proportion of the participants having diabetes compared to Ruiru. Having diabetes was negatively associated with blood pressure control (OR 0.4, p=0.03).

There was no statistically significant difference in the adequacy of BP control between patients who were on the HHA program drugs and other antihypertensive drugs (p=0.67). This finding is consistent with findings of studies designed to find a difference in effectiveness among drugs of the same therapeutic categories that generally show a small or no difference(12,59,60). The frequent stock-outs of program drugs could have led to poor compliance to treatment hence poor control of BP than would have been expected.

Predictors of good BP control were having peptic ulcers and being on omeprazole. Patients who had ulcers and on omeprazole were more likely to have a well-controlled blood pressure compared to those without peptic ulcers (p=0.03 and 0.05, respectively). This finding is consistent with findings of a study done in the Chinese population that showed that proton pump inhibitors (PPIs) had a blood pressure-lowering effect in hypertensive patients with gastroesophageal reflux disease (GERD). Specifically, omeprazole therapy resulted in a statistically significant reduction of the mean, daytime, and nighttime BP (61).

The use of enalapril was not statistically significantly associated with better control of BP. However, multivariate logistic regression analysis revealed that the effectiveness of enalapril varied with the sex and diabetic status of the patient. Enalapril was found to be more effective in males and diabetic patients. These are novel findings and have not been documented in any previous publication.

Predictors of poor BP control in this study were diabetic status and the number of antihypertensive drugs. Non-diabetic patients had 0.4 times the odds of diabetic patients of having well-controlled blood pressure. A higher proportion of uncontrolled blood pressure was reported in patients on a higher number of antihypertensive drugs. This finding was comparable to the findings of a study done in 2014 on the predictors of poor BP control in a regional referral hospital in Central Kenya that showed diabetes, old age, and use of three or more drugs to be significant predictors of poor blood pressure control (3). The use of a high number of antihypertensive drugs might not have caused poor control of blood pressure. Rather, the clinicians could have prescribed more antihypertensive drugs in poorly controlled blood pressure.

5.4 Knowledge and use of treatment guidelines by clinicians

There was a general concordance amongst the clinicians that the selection of antihypertensive drugs was based on hypertension disease staging, comorbidities, and the availability of the drugs in the hospitals. Generally, the prescribers had access to eight different hypertension guidelines. However, the JNC-8, AHA, and the HHA guidelines were mostly used interchangeably. The use of multiple guidelines can lead to confusion in areas where the guidelines have conflicting information. Most of the respondents had not received any post-qualification training on hypertension management which implies a gap in in-service support for the management of hypertension.

Some of the respondents had scanty knowledge of the guidelines' recommendations on criteria for initiating therapy, first-line treatments, and treatment targets. This indicates a need for continuous training on the latest guidelines for hypertension management. All the respondents believed that the guidelines were useful and applicable in their setup.

5.5 Adoption and implementation of the Healthy Heart Africa program

There was a noticeable knowledge gap that required to be addressed immediately by training all the healthcare workers. This was clear as some of the clinicians had never been trained on the various aspects of the program.

The respondents had mixed opinions on the success of adoption and the implementation of the program. The majority felt that the program had improved health outcomes. This was supported with information collected from the patients' files whereby the BP readings markedly improved

after being switched to the program drugs. Worsening of BP control was also evident in some patients on the HHA program drugs. The clinicians attributed the poor BP control to non-compliance.

Lack of institutional support was one of the major challenges highlighted. It was strongly agreed that the hospitals did not fully support the program. An erratic supply of drugs was evident from the patients' files as some patients had been switched to other drugs classes. Only one outdated BP recording machine was available at the clinic, and monitoring was mainly done by the support staff as there was a severe shortage of nurses in the two hospitals. There were no reported patients outreach activities in the preceding years due to a lack of finances.

The respondents recommended that the hospital provide more trained staff, especially nurses and clinicians, additional modern BP monitoring tools, and ensure availability of drugs by lobbying for more funding and consistent disbursements.

Some patients had documented ADRs with the program drugs leading to poor compliance and a switch to other drug classes. Lisinopril-hydrochlorothiazide was associated with angioedema, intractable cough, and increased micturition. However, felodipine was associated with bilateral limb edema and persistent headaches. This finding was consistent with documented ADRs associated with these drug classes (25).

Treatment adherence was also reported to be a major challenge. It was attributed to frequent drug stock-outs and unaffordability of the drugs in the hospital and retail pharmacies. Consequently, this had a negative impact on BP control.

5.6 Limitations of the study

The target sample size of 117 in the HHA program was not achieved mainly because most patients were on treatment for less than one year while others had been switched to other non-program regimens. The small sample size could have limited the power of the study to detect the association between adequacy of BP control and being on a particular treatment regimen.

The retrospective data used in this study was not always complete. The study design did not allow the collection of data on patient factors such as adherence, smoking, and exercise, which also impact the level of BP control. Moreover, the in-depth interviews conducted in clinicians and pharmacists were prone to information bias. To mitigate this limitation, the researcher tried

to appropriately pose and rephrase questions to the participants in a manner that would encourage them to give honest responses.

5.7 Conclusion

There was no statistically significant difference in the prescribing patterns of antihypertensive drugs across the two hospitals. Thiazide diuretics and CCBs were the most prescribed classes of antihypertensive drugs. This is consistent with various guidelines recommending the use of a thiazide diuretic or a CCB as first-line treatment in the black population.

There was no statistically significant difference in the prevalence of well-controlled BP between participants on the HHA program drugs and other antihypertensive drugs. However, it was noted that patients on the program drugs had a lower prevalence of end-organ complications of diabetes and cardiovascular complications. The antihypertensive drugs prescribed did not influence the adequacy of BP control. However, diabetic patients on enalapril or amlodipine had a well-controlled BP.

The main gaps in the adoption and implementation of the HHA program in Kiambu County were an erratic supply of the program's drugs, inadequate blood pressure monitoring tools, and inadequate training of health care workers.

5.8 Recommendations

5.8.1 Recommendations to improve the Healthy Heart Africa program

Recommendations to improve the HHA program were to strengthen the supply of the drugs by lobbying for more funding and consistent disbursements, continuous training, and reviewing the program's performance. There was a need to add more drug classes into the program and further subsidize their prices to cater to the poor.

5.8.2 Recommendations for policy and practice

1. Mandatory continuous training of HCWs should be implemented to ensure that they keep abreast with the changing trends and emerging new evidence in the management of hypertension.

5.8.3 Recommendations for further research

1. Further investigations on the effect measure modification of gender and the diabetic status on the effectiveness of enalapril and amlodipine should be carried out using larger sample sizes.
2. Further studies to investigate how peptic ulcers and proton pump inhibitors are associated with better blood pressure control should be carried out.
3. A systematic review needs to be done that compares the effectiveness of amlodipine versus felodipine and lisinopril versus enalapril using database data.
4. Further research should be carried out to establish the association of lisinopril and felodipine with a lower prevalence of end-organ complications of diabetes and cardiovascular complications.

REFERENCES

1. Mbui JM, Oluka MN, Guantai EM, Sinei KA, Achieng L BA, Jande M, Masselle A GB. Prescription patterns and adequacy of blood pressure control among adult hypertensive patients in Kenya; findings and implications. Expert Rev Clin Pharmacol. 2017;10(11):1263–71.

2. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearny PM, Reynolds K CJ. Global disparities of hypertension prevalence and control. Circulation. 2016;134(6):441–50.

3. Mutua EM, Gitonga MM, Mbuthia B, Muiruri N, Cheptum JJ MT. Level of blood pressure control among hypertensive patients on follow-up in a Regional Referral Hospital in Central Kenya. Pan Afr Med J. 2014;18:278.

4. Onen CL. Epidemiology of ischaemic heart disease in sub-Saharan Africa: review article. Cardiovasc J Afr. 2013;24(2):34–42.

5. Addo J, Smeeth L, Leon DA. Hypertension in sub-Saharan Africa: A systematic review. Hypertension. 2007;50(6):1012–8.

6. Achieng' L, Joshi M, Ogola E, Karari E. Adequacy of blood pressure control and level of adherence with antihypertensive therapy. East Afr Med J. 2009;86(11):499–506.

7. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults. Jama. 2014;311(5):507.

8. Gu Q, Dillon CF, Burt VL, Gillum RF. Association of hypertension treatment and control with all-cause and cardiovascular disease mortality among US adults with hypertension. Am J Hypertens. 2010;23(1):38–45.

9. Murray CJL, Lopez AD. Mortality by cause for eight regions of the world : Global Burden of Disease Study. Lancet. 1997;349:1269–76.

10. Muthoni J. Treatment of hypertension in adult patients in Ruiru Sub-County Hospital. MPharm thesis. 2015;(November).

11. Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, et al.

Health Outcomes Associated With Various Antihypertensive Therapies Used as First-Line Agents. Jama. 2003;289(19):2534.

12. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. Bmj. 2009;338(may19 1):b1665–b1665.

13. Kimuyu B. Factors associated with adherence to antihypertensive treatment in Kiambu District Hospital. MPH Thesis. 2014

14. Kayima J, Wanyenze RK, Katamba A, Leontsini E, Nuwaha F. Hypertension awareness , treatment and control in Africa: a systematic review. BMC Cardiovasc Disord. 2013;13:54.

15. Hendriks ME, Wit FWNM, Roos MTL, Brewster LM, Akande TM, de Beer IH, et al. Hypertension in Sub-Saharan Africa: Cross-sectional surveys in four rural and urban communities. PLoS One. 2012;7(3).

16. Dzudie A, Kengne AP, Muna WFT, Ba H, Menanga A, Kouam CK, et al. Prevalence , awareness , treatment and control of hypertension in a self- selected sub-Saharan African urban population: a cross-sectional study. BMJ Open. 2012;

17. Joshi MD, Ayah RN, Kaharo E, Kayima J, Njeru K, Kennedy E WR, KK M. Prevalence of hypertension and associated cardiovascular risk factors in an urban slum in Nairobi, Kenya: A population-based survey. BMC Public Health. 2014;14.

18. CS Shantirani et al. Prevalence and Risk Factors of Hypertension in a Selected South Indian Population - The Chennai Urban Population Study. Japi. 2003;51:20–7.

19. Wang H, Zhang X, Zhang J, He Q, Hu R, Wang L, et al. Factors Associated with Prevalence , Awareness , Treatment and Control of Hypertension among Adults in Southern China: A Community-Based , Cross-Sectional Survey. PLoS One. 2013;8(5).

20. Wang W, Lee ET, Fabsitz RR, Devereux R, Best L, Welty TK, et al. A longitudinal study of hypertension risk factors and their relation to cardiovascular disease: The strong heart study. Hypertension. 2006;47(3):403–9.

21. Kramer H, Han C, Post W, Goff D, Diez-roux A, Cooper R, et al. Multi-Ethnic Study of Atherosclerosis (MESA). 2017;(October):963–70.

22. Sesso HD, Cook NR, Buring JE, Manson JE, Gaziano JM. Alcohol consumption and the risk of hypertension in women and men. Hypertension. 2008;51:1080–7.

23. Xin X, He J, Frontini MG, Ogden LG, Motsamai OI, Whelton PK. Effects of Alcohol Reduction on Blood Pressure: A Meta-Analysis of Randomized Controlled Trials. Hypertension. 2001;38(5):1112–7.

24. Dochi M, Sakata K, Oishi M, Tanaka K, Kobayashi E, Suwazono Y. Smoking as an independent risk factor for hypertension: a 14-year longitudinal study in male Japanese workers. Tohoku J Exp Med. 2009;217(1):37–43.

25. RPS. British National formulary. 70th ed. 2015.

26. Dustan HP. Calcium Channel Blockers;Potential medical benefits and side effects. Hypertension. 1989;13:137–41.

27. Brewster LM, Seedat YK. Why do hypertensive patients of African ancestry respond better to calciumblockers and diuretics than to ACE inhibitors and β-adrenergic blockers? Asystematic review. BMC Med. 2013;11(1):141.

28. Seedat YK, Rayner BL. South African hypertension guideline 2011. South African Med J. 2012;102(1):60–83.

29. Moholisa RR, Rayner BR, Owen EP, Schwager SLU, Stark JS. Association of B2 Receptor Polymorphisms and ACE Activity With ACE Inhibitor – Induced Angioedema in Black and Mixed-Race South Africans. J Clin Hypertens. 2013;15(6):413–9.

30. Agabiti-rosei E, Mancia G, Ambrosioni E, Burnier M, Caulfield MJ, Cifkova R, et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. J Hypertens. 2009;1–38.

31. Ministry of Health. Kenya National Guidelines for Cardiovascular Diseases Management Division of Non-Communicable Diseases. Minist Heal Kenya. 2018;24–42.

32. Hypertension in adults: diagnosis and management. Nice. 2016;(August 2011).

33. Palla M, Ando T, Androulakis E, Telila T, Briasoulis A. Renin-Angiotensin System Inhibitors vs Other Antihypertensives in Hypertensive Blacks: A Meta-Analysis. J Clin Hypertens. 2017;19(4):344–50.

34. Sehgal AR. Overlap between Whites and Blacks in Response to Antihypertensive Drugs. Hypertension. 2004;43(3):566–72.

35. Ojji DB, Mayosi B, Francis V, Badri M, Cornelius V, Smythe W, Kramer N BF, Damasceno A, Dzudie A, Jones E, Mondo C, Ogah O, et al. Comparison of Dual Therapies for Lowering Blood Pressure in Black Africans. 2019;2429–39.

36. The ALLHAT Officers. Major Outcomes in High-Risk Hypertensive Patients Randomized to or Calcium Channel Blocker vs Diuretic. J Am Med Assoc. 2002;288(23):2981–97.

37. HHA. Protocol for the identification and management of hypertension in adults in primary care. 2015.

38. Emmanuel A, Kofi OI, C NB. Blood Pressure Control Status of Hypertensive Patients Attending an Out-Patient Specialist Clinic in Ghana. Open Sci. 2016;4(5):28–34.

39. Di Martino M, Veronesi C, Degli Esposti L, Scarpa F, Buda S, Didoni G, et al. Adherence to antihypertensive drug treatment and blood pressure control: a real practice analysis in Italy. J Hum Hypertens. 2008;22(1):51–3.

40. Okwuonu CG, Ojimadu NE, Okaka EI, Akemokwe FM. Patient-related barriers to hypertension control in a Nigerian population. Int J Gen Med. 2014;7:345–53.

41. Rayner B, Schoeman HS. A cross-sectional study of blood pressure control in hypertensive patients in general practice (the I-TARGET study). Cardiovasc J Afr. 2009;20(4):224–7.

42. Addo J, Agyemang C, Smeeth L, de-Graft Aikins a, Edusei a K, Ogedegbe O. A review of population-based studies on hypertension in Ghana. Ghana Med J. 2012;46(June):4–11.

43. Cappuccio FP, Micah FB, Emmett L, Kerry SM, Antwi S, Martin-Peprah R, et al. Prevalence, Detection, Management, and Control of Hypertension in Ashanti, West Africa. Hypertension. 2004;43(5):1017–22.

44. Thrall G, Lip GYH, Lane D. Compliance with pharmacological therapy in hypertension: can we do better , and how ? 2004;595–7.

45. Benson J, Britten N. Patients' decisions about whether or not to take antihypertensive drugs: qualitative study. BMJ. 2002;325(7369):873.

46. Knight EL, Bohn RL, Wang PS, Glynn RJ, Mogun H, Avorn J. Predictors of Uncontrolled Hypertension in Ambulatory Patients. 2001;

47. Buabeng KO, Matowe L, Plange-Rhule J. Unaffordable drug prices: The major cause of non-compliance with hypertension medication in Ghana. J Pharm Pharm Sci. 2004;7(3):350–2.

48. Seedat YK, Y.K. S. Why is control of hypertension in sub-Saharan Africa poor? Cardiovasc J Afr. 2015;26(4):193–5.

49. Ilesanmi OS, Ige OK, Adebiyi AO. The managed hypertensive: the costs of blood pressure control in a Nigerian town. Pan Afr Med J. 2012;12:96.

50. Maimaris W, Paty J, Perel P, Legido-Quigley H, Balabanova D, Nieuwlaat R, et al. The Influence of Health Systems on Hypertension Awareness, Treatment, and Control: A Systematic Literature Review. PLoS Med. 2013;10(7).

51. Animut Y, Assefa AT, Lemma DG. Blood pressure control status and associated factors among adult hypertensive patients on outpatient follow-up at university of gondar referral hospital, northwest ethiopia: A retrospective follow-up study. Integr Blood Press Control. 2018;11:37–46.

52. Okai DE, Manu A, Amoah EM, Laar A, Akamah J, Torpey K. Patient-level factors influencing hypertension control in adults in Accra, Ghana. BMC Cardiovasc Disord. 2020;20(1):1–7.

53. Goverwa TP, Masuka N, Tshimanga M, Gombe NT, Takundwa L, Bangure D, et al. Uncontrolled hypertension among hypertensive patients on treatment in Lupane District,

Zimbabwe, 2012. BMC Res Notes. 2014;7(1):1–8.

54. Mwengi EM, Nyamu DG, Njogu PM, Karimi PN. Antihypertensive therapy and adequacy of blood pressure control among adult hypertensive diabetic patients with chronic kidney disease in a tertiary referral hospital. Hosp Pract (1995). 2019;47(3):136–42.

55. Mecha JO, Kubo EN, Odhiambo CO, Kinoti FG, Njau K, Yonga G, et al. Burden of prehypertension among adults in Kenya: a retrospective analysis of findings from the Healthy Heart Africa (HHA) Programme. 2020;4–9.

56. Florey C Du. Sample size for beginners. BMJ. 1993;306(6886):1181–4.

57. Mufunda E, Albin B, Hjelm K. Differences in Health and Illness Beliefs in Zimbabwean Men and Women with Diabetes. 2012;117–25.

58. Jarari N, Rao N, Peela JR, Ellafi KA, Shakila S, Said AR, et al. A review on prescribing patterns of antihypertensive drugs. Clin Hypertens. 2016;1–8.

59. Fretheim A, Odgaard-jensen J, Brørs O, Madsen S, Njølstad I, Norheim OF, et al. Comparative effectiveness of antihypertensive medication for primary prevention of cardiovascular disease: systematic review and multiple treatments meta-analysis. 2012;1–14.

60. Schellberg D, Henning F, Tobias T, Grundtvig M, Goode K, Corletto A, et al. Comparative effectiveness of enalapril , lisinopril , and ramipril in the treatment of patients with chronic heart failure: a propensity score-matched cohort study. 2018;82–92.

61. Li Z, Ji F, Han X, Wang L. The Role of Gastroesophageal Reflux in Provoking High Blood Pressure Episodes in Patients With Hypertension. 2018;52(8):685–90.

APPENDIX 1: PATIENT'S DATA EXTRACTION FORM

Hospital's name……

Date……. Outpatient number…….

ELIGIBILITY CHECKLIST

1. Age above 18 years Yes ☐ No ☐

2. Hypertensive Yes ☐ No ☐

3. On treatment for at least 1 year Yes ☐ No ☐

4. Receiving hypertension management from study site Yes ☐

No ☐

Age (years)…….

Sex Male ☐

Female ☐

Height (cm)…… Weight (Kg)……

Marital status…… Married ☐ Single ☐ Divorced ☐

Education level Primary ☐

Secondary ☐

Tertiary ☐

Others (specify) ☐

Occupation…… Employed ☐

Self-employed ☐

Unemployed ☐

Hypertension management

Date of diagnosis…….. Duration ……

BP reading at diagnosis…….

Number of visits during the last 1 year……..

Duration between visits during the last 1 year (weeks)….……

……

Latest BP readings: 1……. Date……. 4……. Date…….

2……. Date……. 5……. Date…….

3……. Date……. 6……. Date…….

Antihypertensive drugs at diagnosis/initiation of treatment

Date of commencement: ……

Drug name	**Dosage**	**Frequency**

Current antihypertensive drugs (if different from initiation regimen)

Date of commencement of current regimen: ……

Reason(s) for change to current regimen:

……

……

Drug name	**Dosage**	**Frequency**

Previous antihypertensives regimens (between initiation and current)

Date of commencement of regimen: ……

Reason(s) for change to regimen:

……

Drug name	**Dosage**	**Frequency**

(*continue at the back if more space is needed*)

Comorbidities present and their duration in years.

Diabetes ☐

Renal disease ☐

Heart failure ☐

Congestive cardiac failure ☐

Asthma ☐

Ulcers ☐

HIV ☐

Arthritis ☐

Peripheral neuropathy ☐

Epilepsy ☐

Mental illness ☐

Others

1…….

2…….

Other concomitant long term treatment medications

Analgesics/NSAIDs	**Dosage**	**Frequency**
Diclofenac		
Meloxicam		
Paracetamol		
Ibuprofen		
Piroxicam		

Anti ulcers	**Dosage**	**Frequency**
Omeprazole		
Magnesium trisilicate		
Ranitidine		

Peripheral neuropathy	**Dosage**	**Frequency**
Gabapentin		
Amitriptyline		
Carbamazepine		

Others	**Dosage**	**Frequency**	**Indication**

Designation of the prescriber

Clinical Officer ☐

Medical Officer ☐

Consultant ☐

Other (specify): ……..

Any other relevant information

……

……

……

……

……

(*Continue at the back if more space is needed*)

APPENDIX 2: CONSENT EXPLANATION FORM

Title of the study

Adoption of the Healthy Heart Africa program and its contribution to the adequacy of blood pressure control: Case of Kiambu County.

Principal investigator: Dr. Grace Wangui Ngariko.

Institution: Department of Pharmacology and Pharmacognosy, School of Pharmacy, University of Nairobi.

Introduction

My name is Dr. Grace Wangui Ngariko. I am the principal researcher in this study on assessing adequacy of blood pressure control in two level four hospitals in Kiambu County. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens when you participate, the possible risks and benefits, your rights as a volunteer, and anything else about the research that is not clear. The following principles will apply to all participants who choose to willingly participate in this study: Your decision to participate is entirely voluntary, you may withdraw from the study at any time without giving reasons for your withdrawal, and we will provide you a copy of this form for your records.

Aim of the study

The main objective of this study is to compare the adequacy of blood pressure control in hypertensive patients in two level four hospitals in Kiambu County, Central Kenya, and to identify challenges in the implementation of the Healthy Heart Africa program.

What will happen if you decide to be in this research study?

If you agree to participate in this study, you will be interviewed by the principal investigator in a private and comfortable area. The interview will last approximately 30 minutes. The interviewer will cover topics on the prescribing patterns of antihypertensive drugs and the success and challenges of implementation of the Healthy Heart Africa program.

Risks and Benefits associated with the study

There are no anticipated direct benefits or risks to you for participating in the study. You will not be compensated for participating in this study.

Assurance of confidentiality

Your participation in this study could potentially lead to a loss of privacy. However, we will keep any information you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database, and all our paper records will be kept in a locked cabinet.

Contacts

If you have further questions or concerns about participating in this study, please contact Dr. Grace Wangui on 0713297698 or if you have any questions concerning your rights as a research participant, you can call the KNH/UoN-ERC chairperson on 2726300 Ext 44102.

Statement of consent

Participant's statement

I have read and understood the information provided regarding the study, and my questions have been satisfactorily addressed. I willingly consent to participate in this study.

Name of the participant……

Signature…….. Date……..

Researcher's statement

I have fully explained the relevant details of this research study to the participant, and I believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's name……...

Signature……... Date……..

APPENDIX 3: INTERVIEW GUIDE FOR THE PRESCRIBERS/KEY INFORMANTS

SECTION 1: BIODATA

Age (years)…….

Sex Male ☐

Female ☐

Designation Consultant ☐

Medical Officer ☐

Clinical Officer ☐

Pharmacist ☐

Other ☐

Years of Practice……..

SECTION II: HYPERTENSION MANAGEMENT

1. What do you base your drug selection for hypertension management on?

Patient's age ☐

Stage of hypertension ☐

Comorbidities ☐

Others (specify) ☐

……

……

……

2. Which hypertension treatment guidelines do you know of?

……

……

……

……

3. Which hypertension guidelines do you use?

……
……
……
……
……
……

4. Did you undergo any post-qualification training on these guidelines? Yes ( ) No ( )

……

5. How/by whom was the training done (specify)…….....

……
……
……

6. What are the general recommendations of the guidelines that you use?

……
……
……
……
……

7. Are the guidelines useful in making decisions on individual patient management?

Yes ( ) No ( )

(Briefly elaborate): ……....
……
……
……

8. Are the guidelines applicable in your setting?

Yes ( ) No ( )

(Briefly elaborate): ……....

……

……

……

9. Do you deviate from the guidelines?

Yes ( ) No ( )

10. If yes above, briefly explain the kinds and reasons for deviation.

……

……

……

……

……

11. What is your overall opinion of the recommended guideline(s)?

……

……

……

……

……

SECTION 3: THE HEALTHY HEART AFRICA PROGRAM.

1. Have you heard of the Healthy Heart Africa Program? Yes ( ) No ( )

2. If yes in 1 above:

a) What is your understanding of the HHA program?

……
……
……
……

b) What are the objectives of the program?

……
……
……
……

c) What is your role in the achievement of the program's objectives?

……
……
……
……

2. Have you received any training on the program? Yes ( ) No ( )

3. If yes above:

a) Were you trained on the protocol for the identification and management of hypertension?

……
……

b) Did you receive training on the use of the HHA recommended treatment guideline?

……
……
……

c) Were you trained on the hypertension drugs to be used in this program?

……

……

……

4. Have you used the program's guidelines and recommendations in the management of your patients? Yes ( ) No ( )

   If Yes, briefly elaborate

……

……

……

……

5. Would you say the adoption and the implementation of the program has been successful in your setting? Yes ( ) No ( )

(Briefly elaborate): ……....

……

……

……

6. Do you think the program has had an impact on tadequate control of blood pressure?

Yes ( ) No ( )

(Briefly elaborate): ……....

……

……

……

7. Have you faced any of the following challenges in the implementation of the program?

a) Lack of program's support from your institution? Yes () No ()

(Briefly elaborate): ……....

……

……

……

b) Unavailability of the program's drugs? Yes () No ()

(Briefly elaborate): ……....

……

……

……

c) Adverse drug reaction with the program's drugs? Yes () No ()

(Briefly elaborate): ……....

……

……

……

d) Patients non-adherence to treatment Yes () No ()

(Briefly elaborate): ……....

……

……

……

e) Worsening of patients' condition on the program drugs? Yes () No ()

(Briefly elaborate): ……....

……

……

……

f. Any other challenges (List)

……

……

……

8. Briefly highlight your overall recommendations on the following aspects of the program:

a) Improvement of the recommended standard treatment guideline for the program.

……

……

……

b) Choice of drugs used in the program and their availability

……

……

……

c) Training on the protocol of identification and management of hypertension and the recommended
guideline……

……

……

……

d) Institutional support of the HHA program…….....

……

……

……

e) Any other additional recommendation(s) (List)

……

……

……

APPENDIX 4: ETHICAL APPROVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

KNH-UoN ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/ Mod&SAE/284

August 30, 2018

Grace Wangui Ngariko
U51/87796/2016
Dept. of Pharmacology and Pharmacognosy
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Grace

Re: Approval of modifications – study titled "Adoption of the Health Heart Africa Program and its contribution to adequacy of blood pressure control: Case of Kiambu County (P24/01/2018)

Your communication dated August 8, 2018 refers.

The request touches on change of the study site from Kiambu to Tigoni due to low accrual of study participants. It is noted that the new study site is still in Kiambu County and all other study procedures remain unchanged.

The amendment is therefore approved.

Yours sincerely,

PROF M.L. CHINDIA
SECRETARY, KNH-UON ERC

c.c. The Principal, College of Health Sciences, UoN
The Director CS, KNH
The Chair, KNH-UoN ERC
The Dean, School of Pharmacy, UON
The Chair, Dept. of Pharmacology and Pharmacognosy, UON
Supervisors: Dr.Eric M. Guantai, Dr. Margaret N. Oluka, Prof.Faith A. Okalebo

Protect to discover

Scanned by CamScanner

APPENDIX 5: COUNTY APPROVAL

COUNTY GOVERNMENT OF KIAMBU
DEPARTMENT OF HEALTH SERVICES

All correspondence should be addressed to
HEAD HRDU – HEALTH DEPARTMENT
Email address: mndiritu@gmail.com
mkwasa@live.com
Mobile: 0721641516
0721974633

HEALTH RESEARCH AND DEVELOPMENT UNIT
P. O. BOX 2344 - 00900
KIAMBU

Ref. No: KIAMBU/HRDU/AUTHO/2018/04/09/Ngariko GW

Date: 09 Apr 2018

TO WHOM IT MAY CONCERN,

RE: CLEARANCE TO CONDUCT RESEARCH IN KIAMBU COUNTY

Kindly note that we have received a request by **Dr. Grace Wangui Ngariko** of **University Of Nairobi** to carry out research in Kiambu County, the research topic being on ***"Adoption Of Healthy Heart Africa And Its Contribution To Adequacy Of Blood Pressure Control"***.

We have duly inspected her documents and found that she has been cleared by **Kenyatta National Hospital-University Of Nairobi Ethical Review Committee** until **12 Mar 2019**. She thus does not need any further clearance with another regulatory body in order to conduct research within the county of Kiambu.

However, it is incumbent upon the facility in which the research is being carried out to ensure that they are conversant with the remit of the study and operate in line with their institutional norms on conducting research. This note also accords her the duty to provide feedback on her research to the county at the conclusion of her research.

DR. M. NDIRITU NDIRANGU
COUNTY HEALTH RESEARCH DEVELOPMENT UNIT
KIAMBU COUNTY