Uncontrolled Hypertension and Associated Factors in Hypertensive Patients at the Primary Healthcare Center Luis H. Moreno, Panama: A Feasibility Study

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Uncontrolled Hypertension and Associated Factors in Hypertensive Patients
at the Primary Healthcare Center Luis H. Moreno, Panama: A Feasibility Study

by

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A thesis submitted in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
Department of Epidemiology and Biostatistics
College of Public Health
University of South Florida

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Keywords: Primary hypertension, antihypertensive protocols, high blood pressure, cardiovascular disease, risk factor

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DEDICATION

I dedicate this effort to my mom and dad – Marisol and Ramon – who were the cornerstones on which I supported myself every day of this long journey. Thank you for keeping me going even when the light at the end of the tunnel seemed to be far away. I love you both.

To my beloved wife and friend – Lissie – who walked beside me and kept reminding me that every minute was worthwhile and helped me to embrace hope. Thanks for all the love you gave me and give me every day. To my son, Aang, for his time that was sacrificed and for being the person that brings meaning to our lifes.

To my brothers – Ramon, Randy and Eric – who were there in my absence and as a support voice that made the time pass by more quickly. To my family friends, who, in one way or another, helped me overcome this challenge.

Finally and foremost, to God, for carrying me in the moments of weakness and giving me strength to keep going, and to keep fighting for my goals.

To all of you, thanks.
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I want to make a special recognition to all the people at the University of South Florida (USF), professors and staff, and also to my classmates, especially the Panamanians; without their support this project wouldn’t be possible.

I want to express my deepest gratitude to my USF advisors Dr. Amy Alman and Dr. Heather Stockwell, for their unflagging recommendations and suggestions in every aspect of this research project, and for their encouragement to look for answers instead of giving them to me. To my Panamanian advisor, Dr. Cesar Cuero, for his clinical advice in this research project.

To Dr. Deanna Wathington, who opened USF’s doors and without her invaluable support, assistance and guidance, this program would have been way more difficult to achieve. I also want to thank Annette Chilton, for her friendship and for showing us the path through every process and paperwork that needed to be done. To Dr. Kate Wolfe-Quintero, for her unconditional support and for showing us how a second language can be use in the same way we used our native language.

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# TABLE OF CONTENTS

List of Tables ........................................................................................................... iii

Abstract .................................................................................................................... iv

Chapter One: Uncontrolled Hypertension and Associated Risk Factors ............... 1
Hypertension Epidemiology ....................................................................................... 1
Hypertension Classification and Control ................................................................. 2
Benefits in Controlling Hypertension ..................................................................... 3
Improving Hypertension Control .......................................................................... 4

Chapter Two: Research Objectives ......................................................................... 5
Objectives ................................................................................................................ 5

Chapter Three: Methodology .................................................................................. 6
Study Design ............................................................................................................. 6
Eligibility Criteria .................................................................................................... 7
Study Sample and Sample Selection ..................................................................... 7
Operational Definition of Variables .................................................................... 9
Demographic Variables ......................................................................................... 9
Clinical Variables .................................................................................................. 9
Assessment of Treatment Compliance with Antihypertensive Protocols ............. 10
Assessment of lifestyle modification recommendations .................................... 10
Assessment of pharmacological treatment adherence with antihypertensive protocols ................................................................. 11
Assessment of Blood Pressure Control Status .................................................. 12
Data Collection Procedures ............................................................................... 13
Statistical Analysis ................................................................................................. 15

Chapter Four: Results ............................................................................................. 17
Univariate Analysis – Patients Characteristics .................................................... 17
Demographic Variables ....................................................................................... 17
Clinical Variables ................................................................................................. 17
Bivariate Analysis .................................................................................................. 20
Demographic Variables ....................................................................................... 20
Clinical Variables ................................................................................................. 20
Multivariate Analysis ............................................................................................. 23
Chapter Five: Discussion

Key Findings ............................................................................................................ 26
Limitations and Strengths ..................................................................................... 26
Conclusions .............................................................................................................. 29
Recommendations .................................................................................................. 31

Chapter Six: List of References ............................................................................. 33

Appendices ................................................................................................................ 37
Appendix A: Electronic Data Entry Form ................................................................. 38
Appendix B: Classification in Appropriately and Inappropriately Treated
Hypertension According to the Guidelines of the Pan American Health
Organization – Republic of Panama ........................................................................ 40
Appendix C: University of South Florida’s Institutional Review Board
Letter of Approval ..................................................................................................... 41
Appendix D: University of South Florida’s Institutional Review Board
Letter of Approval of Amendment 1 ........................................................................ 43
Appendix E: Panama’s Institutional Review Board Letter of Approval
(Spanish) .................................................................................................................. 44
Appendix F: Panama’s Institutional Review Board Letter of Approval
(Translation) ............................................................................................................... 45
LIST OF TABLES

Table 3.1: Assessment of Treatment Compliance with Antihypertensive Protocols ................................................................. 12

Table 3.2: Pressure Level Goals According to Treatment Category .............................. 13

Table 4.1: Baseline Characteristics of Study Population ...................................................... 18

Table 4.2: Treatment Characteristics of Study Population .................................................. 19

Table 4.3: Patients Characteristics by Blood Pressure Control Status .............................. 21

Table 4.4: Crude and Adjusted Odds Ratios for Physician Adherence to Antihypertensive Protocols and Covariates ................................................................. 23

Table 4.5: Interaction Terms with Variables Included in the Model .............................. 24

Table 4.6: Stratified Model by Age as a Potential Modifier .......................................... 24

Table B.1: Treatment Classification According to the Guidelines of the Pan American Health Organization ......................................................... 40
ABSTRACT

According to the World Health Organization (WHO), hypertension is a major risk factor for cardiovascular disease (CVD), renal impairment, peripheral vascular disease, and blindness. In Panama, a recent study estimated the prevalence of hypertension at 38.5% in the two main provinces of the country, with a rate of uncontrolled hypertension of 47.2%. The aims of this study were to assess the feasibility of the study design and to describe the characteristics of the hypertensive population and the physician’s adherence to Panamanian antihypertensive protocols and their relationship with uncontrolled hypertension.

This is a cross-sectional study of adult hypertensive patients attending a primary healthcare facility in Panama City. Clinical charts from eligible participants were examined to describe the demographic and clinical characteristics related to uncontrolled hypertension and the use of antihypertensive protocols by medical doctors. Descriptive and central tendency statistics were used to characterize the study population. Bivariate relationships between demographic and clinical characteristics, and uncontrolled hypertension were explored using specific test for no association. Logistic regression modeling was used to examine the association between physician’s adherence to antihypertensive protocols and the presence of uncontrolled hypertension.

In this study the mean age was 56.7 years (±13.6); 58.1% of participants were females; 71.3% of participants had body mass index >25.0kg/m2; and 53.0% of
participants had stage 2 hypertension. Uncontrolled hypertension was present in 66.7% of
the study sample. 82.9% of participants had one or more comorbidities. The medical
doctors were compliant with antihypertensive protocols in 43.6% of participants,
primarily due to lower compliance with lifestyle modification recommendations. In the
multivariate analysis, a significant interaction was found with age, suggesting that age is
a potential effect modifier.

The rate of uncontrolled hypertension was high among this study population.
Nearly half of the attending physicians did not follow the recommendations given by
current antihypertensive protocols. Further research is necessary to explore the
relationships between subject characteristics, such as age, number of comorbidities, and
the presence of diabetes mellitus with uncontrolled hypertension.
CHAPTER ONE: UNCONTROLLED HYPERTENSION AND ASSOCIATED RISK FACTORS

Hypertension Epidemiology

Hypertension (High Blood Pressure, HBP) is defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mm Hg, the use of antihypertensive medication, or being told at least twice by a physician or other health professional that one has HBP (Roger et al., 2012).

According to the World Health Organization (WHO), hypertension is a major risk factor for cardiovascular disease (CVD, excluding congenital CVD) as well as renal impairment, peripheral vascular disease, and blindness. Hypertension is estimated to cause 7.5 million deaths worldwide annually, about 12.8% of the total deaths (Mendis, Puska, & Norrving, 2011). In the same report, WHO estimates the prevalence of hypertension in high-income countries as 35% for both genders, while in low, lower-middle and upper-middle income countries the prevalence is around 40%. Hypertension prevalence estimates from a study in seven Latin-American cities range from 13% to 29%, with an overall prevalence of 18% (Schargrodsky et al., 2008). However, in a recent study developed by the WHO in six middle-income countries around the world (including a Latin American country), the prevalence of hypertension was 37% (Basu & Millett, 2013).
In Panama, a study estimated the prevalence of hypertension at 38.5% in the two main provinces of the country (McDonald et al., 2012). In 2009, according to the Ministry of Health of Panama, primary hypertension (under the codes of the Tenth Edition of the International Classification of Diseases; World Health Organization [WHO], 2010) was the fourth reason for seeking care in those aged 20-59; while for those aged 60 and older, it was the leading cause (Ministerio de Salud, 2010).

**Hypertension Classification and Control**

There are two main hypertension classifications: the European Society of Hypertension/European Society of Cardiology (ESH/ESC) classification (Mancia et al., 2007), and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure of the National Heart, Lung, and Blood Institute (JNC 7 Report) classification (Chobanian et al., 2003). Both are based on at least two blood pressure measurements using a sphygmomanometer, recording as systolic blood pressure phase I Korotkoff sounds, and as diastolic blood pressure phase V Korotkoff sounds (Chobanian et al., 2003; Mancia et al., 2007). Both classifications use >140/90 mmHg as the cut point to diagnose hypertension.

According to the WHO, approximately one billion persons are living with uncontrolled hypertension worldwide (Mendis, Puska, & Norrving, 2011). In the United States, the prevalence of uncontrolled hypertension is estimated to be 53.5% of those with hypertension, affecting approximately 35.8 million persons (Centers for Disease Control and Prevention [CDC], 2012a). In a recent study in middle income countries it
was found that approximately 33.3% of hypertensive patients were uncontrolled (Basu & Millett, 2013). In Panama among hypertensive patients who receive medication, the rate of uncontrolled hypertension was 47.2% (McDonald et al., 2012).

**Benefits in Controlling Hypertension**

Several studies had shown the relationship between blood pressure and the risk of a cardiovascular event. As was stated by Chobanian et al. (2003), for each increase of 20 mmHg in systolic blood pressure and 10 mmHg in diastolic blood pressure the risk of ischemic heart disease and stroke is doubled. In the same report it was also established that the relationship between blood pressure and risk of cardiovascular disease (heart attack, heart failure, stroke, and kidney diseases) is continuous, consistent and independent of other risk factors, such as high cholesterol, low levels of high-density lipoprotein, smoking, diabetes and left ventricular hypertrophy.

The benefits of blood pressure level reduction were demonstrated in the VALUE study (Weber et al., 2004), in which a lower incidence of cardiovascular disease and mortality was observed in those with controlled hypertension compared to those with uncontrolled hypertension (blood pressure >140/90mmHg). In addition, in the FEVER study (Liu et al., 2005) a 28% reduction in coronary disease, stroke and cardiovascular mortality was demonstrated in those randomized to active antihypertensive treatment, compared to those randomized to placebo.
Improving Hypertension Control

Hypertension control is a complex issue which, to be achieve, needs active cooperation between physicians, patients, healthcare personnel and healthcare systems (Chobanian et al., 2003; Mancia et al., 2007). The fist step to address the uncontrolled hypertension problem is to develop local comprehensive hypertension prevention and treatment guidelines based in well-designed studies. However, these guidelines need to be accepted by all medical societies to facilitate their implementation. Medical doctors need to be informed about guidelines recommendations but also is necessary an audit process that could assess the implementation phase appropriately (Mancia et al., 2007).

Patient treatment compliance is a complicated problem that is influenced by factors such as cultural behaviors and beliefs, and previous experiences in the healthcare systems (Chobanian et al., 2003). The healthcare system plays a central role in the hypertension control, and is the responsible to provide the necessary tools and audit to guarantee the correct guidelines implementation (Mancia et al., 2007).

The Panamanian national health authorities (Ministry of Health and the Social Security Fund), to tackle the hypertension problem developed a structured program to address hypertension in cooperation with the Pan American Health Organization in 2009 (Organización Panamericana de la Salud, 2009). This is a comprehensive program which encompass several aspects in hypertension prevention and treatment, however there are scarce published data regarding the status of patients treated in primary healthcare settings in Panama.

This study aims to provide information about the feasibility to conduct a larger study, and to describe and analyze selected aspects of the hypertensive population.
CHAPTER TWO: RESEARCH OBJECTIVES

Objectives

This study was designed as a feasibility study to assess the current treatment practices and to describe select demographic and clinical characteristics of hypertensive adults attending the primary healthcare center Luis H. Moreno in Panama City, Republic of Panama.

The main research question was whether physician adherence to antihypertensive protocol recommendations would be associated with patient’s blood pressure control status.
CHAPTER THREE: METHODOLOGY

Study Design

This is a cross-sectional study of adult hypertensive patients who attended a primary healthcare facility in Panama City, Republic of Panama and received treatment for hypertension during the year 2012. Clinical charts from eligible participants were examined to describe the demographic and clinical characteristics related to uncontrolled hypertension and physician’s adherence to antihypertensive protocols. Descriptive and central tendency statistics were used to characterize the study population. Bivariate relationships between demographic and clinical characteristics, and uncontrolled hypertension were explored using the chi-square or the Fisher’s exact test for categorical distributions, the t-test for parametric continuous distributions, and the Wilcoxon sum-rank test for non-parametric continuous distributions. Finally, logistic regression modeling was used to examine the association between the physician’s adherence to antihypertensive protocols and uncontrolled hypertension after adjusting for other factors. Prior to data collection, approvals from the University of South Florida’s Institutional Review Board (IRB) and from the authorized Panamanian IRB (Punta Pacifica Hospital’s IRB) were obtained.
Eligibility Criteria

Eligible subjects were all adult patients (>18 years old), who were treated in the center between January 1st, 2012 and December 31, 2012 and had a diagnosis of primary hypertension (WHO, 2010). Patients with a diagnosis of primary hypertension made during the year 2009 or later, and those initially diagnosed before 2009 who had not taken hypertensive medication for at least 6 months and re-entered treatment in 2009 or later; were included in the study.

Criteria for exclusion included clinical charts with missing information on the appointment at which the antihypertensive pharmacological treatment was initiated, and those for which inadequate information was available to establish whether appropriate treatment was received and whether blood pressure control was obtained. Additional exclusion criteria included patients who had kept regular hypertension control appointments for less than six months, and pregnant women (since the treatment and classification of hypertensive pregnancy disease is different from primary hypertension) (Mancia et al., 2007).

Study Sample and Sample Selection

The needed sample size to develop the study was obtained using the formula developed by Cochran (1963) for proportions in large populations:

\[ n = \frac{Z^2 P(1-P)}{d^2} \rightarrow n \approx 383 \text{ participants} \]

Where: \( n \) = sample size; \( Z \) = \( Z \) statistics for the level of confidence of 95% (1.96 for two tailed test); \( P \) = Prevalence of uncontrolled hypertension in Panama (0.472); \( d \) = Precision (0.05).
For the sample size calculation, the prevalence of uncontrolled hypertension was obtained from a previous study (McDonald et al., 2012) that found that 47.2% of hypertensive patients receiving treatment did not achieve blood pressure goals.

A simple random sample of 383 clinical charts were selected for review, from the existing electronic log of all patients who attended the study center between January 1, 2012 and December 31, 2012 with a diagnosis of primary hypertension (WHO, 2010). Demographic data collected included age and gender. Race/ethnicity was not available in the charts and could not be collected. The clinical data that were collected included: date at which the pharmacological treatment was initiated (hereafter “treatment appointment”), date of follow-up (hereafter “follow-up appointment”), height (meters) and weight (kilograms) at the first appointment, blood pressure from the first and second appointments, presence of comorbidities, prescribed antihypertensive medication, type of attending physician (general practitioner and specialist), and if any recommendation of lifestyle modification was made during the treatment appointment (Appendix A). The clinical chart of each patient was reviewed, and those that met the additional eligibility criteria (diagnosis in 2009 or later, and those with a diagnosis prior to 2009 with at least 6 months of no antihypertensive therapy who had re-entered treatment in 2009 or later) were included in the study. Of the 383 clinical charts that were examined, only 117 clinical charts met the eligibility criteria for inclusion in the study.
Operational Definition of Variables

Demographic Variables. Age: the age of the patient at the treatment appointment, calculated based on the date of birth and date of the treatment appointment.

Gender: Female or male, as recorded in the clinical chart.

Clinical Variables. Treatment Appointment: the appointment at which the antihypertensive pharmacological treatment was initiated, or was re-initiated for those previously receiving treatment.

Follow-up Appointment: the appointment recorded as the hypertension follow-up appointment or the appointment in which the first antihypertensive medication refill was made, whichever occurred first.

Height and Weight: the height (meters) and weight (kilograms) to calculate the body mass index (BMI) category [CDC, 2012b].

Blood Pressure: systolic and diastolic blood pressure as recorded by the attending physician at both the treatment and follow-up appointments.

Presence of Comorbidities: the comorbidities noted in the chart at the treatment appointment that are listed in the Pan American Health Organization Guidelines (PAHO; Organización Panamericana de la Salud, 2009) as comorbidities to be considered in the protocol for hypertension treatment (Appendix B).

Lifestyle Modifications: recorded as “Yes” if there were any notes in the clinical chart regarding recommendations following the PAHO Guidelines for lifestyle modifications during the treatment appointment.
Antihypertensive Medication: all antihypertensive medications prescribed at the treatment appointment.

Type of Physician: the specialty of the attending physician: general practitioner or specialist.

Assessment of Treatment Compliance with Antihypertensive Protocols

In 2009, the Pan American Health Organization (PAHO), in cooperation with the Panamanian health authorities (Ministry of Health and the Social Security Fund), issued the Comprehensive Guidelines for the Hypertensive Population Treatment (PAHO Guidelines; Organización Panamericana de la Salud, 2009). This report established the procedures for prevention, detection, diagnosis and treatment of high blood pressure within the country. These guidelines were used to assess adherence to treatment protocols by attending physician.

The guidelines state that the antihypertensive treatment should consist of both lifestyle modifications and pharmacological treatment. These two variables were used together to establish physician’s adherence to antihypertensive protocols, as described in the two following sections.

Assessment of lifestyle modification recommendations. The lifestyle modification variable was recorded as “Yes” if there was a note recommending any of the suggested lifestyle modifications listed in the PAHO Guidelines for the non-pharmacological treatment of hypertension. The lifestyle modifications considered were: physical activity, stress reduction, tobacco cessation, limiting of alcohol use, weight
control, reducing sources of sodium, cholesterol and triglycerides in the diet, and adequate rest (six to eight hours daily).

**Assessment of pharmacological treatment adherence with antihypertensive protocols.** From clinical data abstracted in the treatment appointment, patients were classified based on the categories of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 Report) of the National Heart, Lung, and Blood Institute (Chobanian et al., 2003).

The pharmacological treatment was determined by the blood pressure level during the first appointment. If the blood pressure measure was greater than or equal to 140/90 mmHg, the initiation of pharmacological treatment was indicated. If the blood pressure level was less than 140/90 mmHg, the pharmacological treatment was indicated only if diabetes mellitus, cardiovascular disease, or renal disease were present as comorbidities (Organización Panamericana de la Salud, 2009). The PAHO Guidelines explicitly list diabetes mellitus and renal disease as independent cardiovascular disease risk factors.

Pharmacological treatment adherence with antihypertensive protocols by physicians was assessed at the treatment appointment in the following manner: patients were classified as “Yes” (appropriately treated) or “No” (inappropriately treated) according to the prescribed antihypertensive medication, and listed comorbidities (Appendix B). For example, if a patient with hypertension and no associated comorbidities was treated with a β-blocker, angiotensin-converting enzyme inhibitor (ACEI), angiotensin-receptor blocker (ARB) or calcium-channel
blocker (CCB), either alone or in combination (up to 2 agents) then he/she was classified as treated appropriately. If this treatment was not prescribed, then he/she was classified as inappropriately treated.

Finally, if a patient received both lifestyle modifications recommendations and received pharmacological treatment following antihypertensive protocols, the variable “treatment adherence to antihypertensive protocols” was classified as “Yes” (Table 3.1). If either of the two variables were classified as “No”, the variable “treatment adherence to antihypertensive protocols” was classified as “No”.

### Table 3.1

<table>
<thead>
<tr>
<th>Lifestyle Modifications</th>
<th>Pharmacological Treatment</th>
<th>Treatment Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*Note.* The variable Treatment Adherence is a combination of the variables Lifestyle Modifications and Pharmacological Treatment.

**Assessment of Blood Pressure Control Status**

The follow-up appointment was used to assess if the patient reached their blood pressure goal, as specified in Table 3.2. To fully consider the impact of comorbidities, the goal blood pressure level recommendations from the PAHO Guidelines and from the JNC 7 Report were used. Finally, for the remaining patient categories, a blood pressure goal level of <140/90 mmHg was used, based on a previous study in Panama in which the prevalence of uncontrolled hypertension was estimated (McDonald et al., 2012).
Data Collection Procedures

Once the 383 participants were identified, the clinical record identification number (CRIN) was collected and a study identification number (Study_ID) was assigned to each clinical chart. The study identification number went from 001 to 383. This code was stored in electronic format, encrypted using the encryption software Mac OS X version 10.8.3, and password-protected on the principal investigator’s personal computer. Only the principal investigator has access to this file and to the personal computer where it is stored. No other identifier was collected, such as name, personal identification number, social security number and/or participant's home address.

Table 3.2

Pressure Level Goals According to Treatment Category

<table>
<thead>
<tr>
<th>Category</th>
<th>Blood Pressure Goals</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT alone, Stage 1 or 2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>≤140/90</td>
<td>JNC 7 Report&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Late adulthood (&gt;55 years old)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>≤140/90</td>
<td>PAHO Guidelines&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + African American</td>
<td>≤140/90</td>
<td>Gorgas Study&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + DM</td>
<td>≤130/80</td>
<td>PAHO Guidelines&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Chronic Kidney Disease</td>
<td>≤130/80</td>
<td>PAHO Guidelines&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + DM + Nephropathy</td>
<td>≤130/80</td>
<td>PAHO Guidelines&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Coronary Heart Disease</td>
<td>≤140/90</td>
<td>JNC 7 Report&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Heart Failure</td>
<td>≤140/90</td>
<td>JNC 7 Report&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + LVH</td>
<td>≤140/90</td>
<td>Gorgas Study&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Obesity</td>
<td>≤140/90</td>
<td>Gorgas Study&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Dyslipidemia</td>
<td>≤140/90</td>
<td>Gorgas Study&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>HT + Asthma</td>
<td>≤140/90</td>
<td>Gorgas Study&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>Note</sup>. HT = Hypertension; DM = diabetes mellitus; LVH = left ventricular hypertrophy; JNC = Joint National Committee; PAHO = Pan American Health Organization. <sup>a</sup>As defined in “The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC Report,” by A. V. Chobanian et al., 2003, *The Journal of the American Medical Association*, 289(19), 2560-2572. <sup>b</sup>As defined in “Guías para la atención integral de las personas con hipertensión arterial [Comprehensive guidelines for the treatment of hypertensive patients],” by Organización Panamericana de la Salud [Pan American Health Organization], 2009. Republic of Panama. <sup>c</sup>As defined in “Prevalencia de factores de riesgo asociados a Enfermedad Cardiovascular [Prevalence of cardiovascular disease risk factors],” by Mc Donald et al., 2012. Republic of Panama.
An electronic data entry form was developed in Microsoft® 2012 Excel Software to capture the study variables (Appendix A) directly from the clinical chart, without any paper-based abstraction materials. The data collection was conducted by the principal investigator. Within the clinical chart, the demographic variables were abstracted from the “Demographic Information Section” and the clinical variables from the “Medical Information and Follow-up Section.” Then, when all data were collected, they were imported to Statistical Analysis System Software (SAS) Version 9.2 and to IBM SPSS Statistics Software for the analysis.

In order to test reliability and assure the quality of the data, re-abstraction of approximately 20% of the sample was performed. The following variables were abstracted: date of birth, age, systolic and diastolic blood pressures during the first and second appointments, lifestyle modification recommendations during first appointment, medications prescribed in the first appointment and existing comorbidities. Race/ethnicity was not referenced in the clinical chart and therefore, could not be abstracted. A research assistant did the re-abstraction and these data were compared with the data collected by the principal investigator using the same clinical charts. To assess the level of agreement between the two abstractors, a kappa statistic was used for categorical variables and the intraclass correlation coefficient for continuous variables. The kappa coefficient ranged from 0.854 to 1.000 and the intraclass correlation coefficient ranged from 0.940 to 0.996, showing very good to excellent agreement between abstractors (Byrt, 1996).

When all data analysis is completed, all files generated will be moved to an external storage drive (flash drive) and deleted from the principal investigator’s
personal computer. The external storage disk will be stored and locked in the facilities of the University of South Florida at the City of Knowledge in Panama, where it will remain for five years. After five years, the disk will be destroyed using the services of a certified company. The principal investigator will attend the disc destruction and receive a certificate that guarantees that the full process was executed.

**Statistical Analysis**

In the univariate analysis, for continuous variables Q-Q plots were used to assess if the variable was normally distributed. For those variables which were normally distributed, the mean and standard deviation were used as descriptive statistics; and for those that were not normally distributed the median and interquartile range (IQR) were used. For categorical variables, the results were presented as frequencies and proportions.

A bivariate analysis was performed to compare demographic and clinical variables with the dependent variable “Blood Pressure Control Status (Uncontrolled, Controlled)”. An independent sample t test was used for continuous normally distributed variables, Wilcoxon Sum-Rank test for continuous non-normally distributed variables, and Fisher’s exact test or chi-squared test for categorical variables, depending if the observed frequencies in any cell was less than five or not. To assess if the change in the blood pressure between both treatment and follow-up appointment was significant, a pair t test was performed. For all comparisons an alpha of 0.05 was used as level of statistical significance.
Finally, to investigate the relationship between the physician’s adherence to antihypertensive protocols and the presence of uncontrolled hypertension among participants, controlling for other covariates, a multivariate analysis was performed using a logistic regression model.

Covariates were included in the model, in the following order; first, those variables that had a statistical significant relationship with the dependent variable in the bivariate analysis: age, number of comorbidities, and the presence of diabetes mellitus. Second, the variables gender and type of attending physician were forced to be in the model, based in the association showed in previous studies (CDC, 2012a; Egan, Zhao, Axon, Brzezinski, & Ferdinand, 2011; Basu & Millett, 2013; Kim et al., 2007; Amar et al., 2003). Third, those variables considered to be potential confounding variables were included in the model; being those that provoked a change in the measure of association (odds ratio, OR) between the dependent and independent variable in more than 10% (ΔOR>10%).

To determine the presence of effect modification, interactions were tested between the main effect variable and the covariates included in the model. If an interaction was observed, stratified models based on the levels of the potential modifier would be developed, to unveil the association by each stratum.

Finally, to test whether or not our final model provides a good fit to the data, a Goodness-of-Fit Test was performed.
CHAPTER FOUR: RESULTS

Univariate Analysis – Patients Characteristics

Demographic Variables. Table 4.1 shows the study sample baseline characteristics. The participant’s mean age was 56.7 years (±13.6). From the total of participants, 58.1% (n=68) were females and 41.9% (n=49) were males.

Clinical Variables. For body mass index (BMI), 40.6% (n=41) were obese, 30.7% (n=31) were overweight, 26.7% (n=27) were at healthy weight, and 2.0% (n=2) were underweight. There were 16 observations with missing values to calculate the BMI. For hypertension classification, 53.0% (n=62) of participants were at Stage 2, 43.6% (n=51) were at Stage 1 and 3.4% (n=4) were Prehypertensive. During the first appointment, the mean systolic blood pressure (SBP) was 150.0 mmHg (±14.7), while the mean diastolic blood pressure (DBP) was 92.3 mmHg (±9.4). In the second appointment, the mean SBP was 135.6 mmHg (±18.6) and the mean DBP was 84.7 mmHg (±10.7). Systolic and diastolic blood pressure significantly decreased between the treatment and follow-up appointments (14.44 mmHg ±19.3 and 7.60 mmHg ±12.51, respectively; \( p<0.0001 \) for both). For the number of comorbidities, 17.1% (n=20) had zero comorbidities, 47.0% (n=55) had one comorbidity, 27.4% (n=32) had two comorbidities, 7.7% (n=9) had three and 0.8% (n=1) had one comorbidity. In this study sample, 28.2% (n=33) had diabetes mellitus, while 71.8% did not. General practitioners attended 62.4% (n=73) of participants, while 37.6% (n=44) were attended by a specialized medical
Table 4.1

Baseline Characteristics of Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years; Mean (±SD)</td>
<td>56.7 (±13.6)</td>
</tr>
<tr>
<td>Gender; n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>68 (58.1)</td>
</tr>
<tr>
<td>Male</td>
<td>49 (41.9)</td>
</tr>
<tr>
<td>Body Mass Index; n (%)</td>
<td></td>
</tr>
<tr>
<td>Underweight (&lt;18.5 kg/m²)</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>Healthy Weight (18.5 - &lt;25.0 kg/m²)</td>
<td>27 (26.7)</td>
</tr>
<tr>
<td>Overweight (25.0 – 30.0 kg/m²)</td>
<td>31 (30.7)</td>
</tr>
<tr>
<td>Obese (≥30.0 kg/m²)</td>
<td>41 (40.6)</td>
</tr>
<tr>
<td>Hypertension Classification, JNC 7 Stage; n (%)</td>
<td></td>
</tr>
<tr>
<td>Pre Hypertension</td>
<td>4 (3.4)</td>
</tr>
<tr>
<td>Stage 1</td>
<td>51 (43.6)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>62 (53.0)</td>
</tr>
<tr>
<td>Treatment App SBP, mmHg; Mean (SD)</td>
<td>150.0 (±14.7)</td>
</tr>
<tr>
<td>Treatment App DBP, mmHg; Mean (SD)</td>
<td>92.3 (±9.4)</td>
</tr>
<tr>
<td>Follow-up App SBP, mmHg; Mean (SD)</td>
<td>135.6 (±18.6)</td>
</tr>
<tr>
<td>Follow-up App DBP, mmHg; Mean (SD)</td>
<td>84.7 (±10.7)</td>
</tr>
<tr>
<td>SBP Mean Change, mmHg; Change (SD)*</td>
<td>14.4 (±19.3)</td>
</tr>
<tr>
<td>DBP Mean Change, mmHg; Change (SD)*</td>
<td>7.6 (±12.5)</td>
</tr>
<tr>
<td>Number of Comorbidities; n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (17.1)</td>
</tr>
<tr>
<td>1</td>
<td>55 (47.0)</td>
</tr>
<tr>
<td>2</td>
<td>32 (27.4)</td>
</tr>
<tr>
<td>3</td>
<td>9 (7.7)</td>
</tr>
<tr>
<td>4</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Diabetes Mellitus among comorbidities; n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>33 (28.2)</td>
</tr>
<tr>
<td>No</td>
<td>84 (71.8)</td>
</tr>
<tr>
<td>Attending physician; n (%)</td>
<td></td>
</tr>
<tr>
<td>General Practitioner</td>
<td>73 (62.4)</td>
</tr>
<tr>
<td>Specialist</td>
<td>44 (37.6)</td>
</tr>
<tr>
<td>Blood Pressure Status; n (%)</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled</td>
<td>78 (66.7)</td>
</tr>
<tr>
<td>Controlled</td>
<td>39 (33.3)</td>
</tr>
</tbody>
</table>

Note. SD = standard deviation; n = number of subjects; JNC = Joint National Committee; App, appointment; SBP, systolic blood pressure; DBP, diastolic blood pressure. For continuous and normally distributed variables the mean was used as central tendency measure. *A pair t-test was used to assess the change in systolic and diastolic blood pressure change; in both cases p<0.0001. As defined in “The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC Report,” by A. V. Chobanian et al, 2003, The Journal of the American Medical Association, 289(19), 2560-2572.
The majority, 66.7% (n=78), had uncontrolled high blood pressure, while 33.3% (n=39) had their blood pressure below goal levels.

Table 4.2 presents the treatment characteristics of the participants. Regarding the number of antihypertensive medication, 76.1% (n=89) of cases were prescribed with one medication, 23.1% (n=27) of cases were prescribed two antihypertensive medications and 0.8% (n=1) was prescribed with three medications. Lifestyle modification recommendations were given to 43.6% (n=51) of participants, while they weren’t given to 56.4% (n=66). The majority of physicians adhered to the pharmacological antihypertensive treatment protocols (98.3%; n=115), while in just 1.7% (n=2) the protocols were not followed. Combining the lifestyle modification recommendations and pharmacological antihypertensive treatment to assess compliance with the antihypertensive protocols, 43.6% (n=51) of participants received treatment following the PAHO Guidelines, while 56.4% (n=66) did not. The median of treatment days was 31 (IQR=10.50-69.50) in the study sample.

Table 4.2

<table>
<thead>
<tr>
<th>Treatment Characteristics of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Number of Antihypertensive medication(s) prescribed; n (%)</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>Treatment days; Median (IQR)</td>
</tr>
<tr>
<td>Lifestyle Modifications recommended; n (%)</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Antihypertensive medication(s) following protocols; n (%)</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Treatment compliance with antihypertensive protocols; n (%)</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

Note. n = number of subjects; IQR, interquartile range. For continuous and non-normally distributed variables the median was used as central tendency measure.
Bivariate Analysis

**Demographic Variables.** Table 4.3 presents the results of the bivariate analyses between the demographic and clinical characteristics, and blood pressure control status. Those with uncontrolled hypertension were older (58.6 years, ±14.2) than those with uncontrolled hypertension (53.1 years, ±11.7; \( p<0.0396 \)). Among those with uncontrolled hypertension 53.9% were females, compared to those who were controlled (66.7%). However, this difference was not statistically significant \( (p=0.1852) \).

There was a higher proportion of overweight participants in the uncontrolled group (34.8%) compared to the controlled group (22.8%). However, a higher proportion of the controlled group (48.6%) than the uncontrolled group (36.4%) were classified as obese. Nevertheless, the difference between groups was not statistically significant \( (p=0.3845) \).

**Clinical Variables.** In the uncontrolled group a higher proportion of participants were at stage 2 hypertension (56.4%) than in the controlled group (46.2%). However, it was the opposite for stage 1 hypertension, which was less prevalent in the uncontrolled group (41.0%) than in the controlled group (48.7%). But, the differences found between these groups were not significant \( (p=0.5202) \).

During the first appointment, the mean systolic blood pressure for the uncontrolled group was 151.2 mmHg (±15.7) and for the controlled group was 147.7 mmHg (±12.3), with no statistical relationship with the dependent variable \( (p=0.2234) \). At the same appointment, the mean diastolic blood pressure for the uncontrolled group was 92.4 mmHg (±9.7) and for the controlled group was 92.1 mmHg (±8.8), with no
### Table 4.3

**Patients Characteristics by Blood Pressure Control Status**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Uncontrolled</th>
<th>Controlled</th>
<th>(p)-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure Status; n (%)</td>
<td>78 (66.7)</td>
<td>39 (33.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Age, years; Mean (SD)</td>
<td>58.6 (14.2)</td>
<td>53.1 (11.7)</td>
<td>0.0396</td>
</tr>
<tr>
<td>Gender; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male(^a)</td>
<td>36 (46.1)</td>
<td>13 (33.3)</td>
<td>0.1852</td>
</tr>
<tr>
<td>Female</td>
<td>42 (53.9)</td>
<td>26 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Body Mass Index(^b); n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy Weight (25.0 - &lt;30.0 kg/m(^2))</td>
<td>19 (28.8)</td>
<td>10 (28.6)</td>
<td>0.3845(^c)</td>
</tr>
<tr>
<td>Overweight (30.0 - &lt;50.0 kg/m(^2))</td>
<td>23 (34.8)</td>
<td>8 (22.8)</td>
<td></td>
</tr>
<tr>
<td>Obese ((\geq)50.0 kg/m(^2))</td>
<td>24 (36.4)</td>
<td>17 (48.6)</td>
<td></td>
</tr>
<tr>
<td>JNC 7 Stage(^d); n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre Hypertension(^a)</td>
<td>2 (2.6)</td>
<td>2 (5.1)</td>
<td>0.5202</td>
</tr>
<tr>
<td>Stage 1</td>
<td>32 (41.0)</td>
<td>19 (48.7)</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>44 (56.4)</td>
<td>18 (46.2)</td>
<td></td>
</tr>
<tr>
<td>Tx App SBP, mmHg; Mean (SD)</td>
<td>151.2 (15.7)</td>
<td>147.7 (12.3)</td>
<td>0.2234</td>
</tr>
<tr>
<td>Tx App DBP, mmHg; Mean (SD)</td>
<td>92.4 (9.7)</td>
<td>92.1 (8.8)</td>
<td>0.8685</td>
</tr>
<tr>
<td>SBP Change(^e), mmHg; Change (SD)</td>
<td>8.5 (+18.4)</td>
<td>26.4 (+16.4)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>DBP Change(^e), mmHg; Change (SD)</td>
<td>3.6 (+10.5)</td>
<td>15.5 (+6.7)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Number of Comorbidities; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0(^a)</td>
<td>12 (15.4)</td>
<td>8 (20.5)</td>
<td>0.0488</td>
</tr>
<tr>
<td>1</td>
<td>32 (41.0)</td>
<td>23 (59.0)</td>
<td></td>
</tr>
<tr>
<td>(\geq)2</td>
<td>34 (43.6)</td>
<td>8 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus among comorbidities; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No(^a)</td>
<td>50 (64.1)</td>
<td>34 (87.2)</td>
<td>0.0089</td>
</tr>
<tr>
<td>Yes</td>
<td>28 (35.9)</td>
<td>5 (12.8)</td>
<td></td>
</tr>
<tr>
<td>First App Antihypertensive medication(s) prescribed(^d); n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1(^a)</td>
<td>58 (74.4)</td>
<td>31 (79.5)</td>
<td>0.5400</td>
</tr>
<tr>
<td>(\geq)2</td>
<td>20 (25.6)</td>
<td>8 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Attending physician; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist(^a)</td>
<td>31 (39.7)</td>
<td>13 (33.3)</td>
<td>0.4998</td>
</tr>
<tr>
<td>General Practitioner</td>
<td>47 (60.3)</td>
<td>26 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Treatment compliance with antihypertensive protocols; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No(^a)</td>
<td>43 (55.1)</td>
<td>23 (59.0)</td>
<td>0.6925</td>
</tr>
<tr>
<td>Yes</td>
<td>35 (44.9)</td>
<td>16 (41.0)</td>
<td></td>
</tr>
<tr>
<td>Treatment days; Median (IQR)</td>
<td>30.5 (10.0-56.3)</td>
<td>33 (14.0-90.0)</td>
<td>0.4250</td>
</tr>
</tbody>
</table>

*Note. n = number of subjects; NA = do not apply; SD = standard deviation; Ref = reference group; JNC = Joint National Committee; Tx = Treatment; App = appointment; SBP = systolic blood pressure; DBP = diastolic blood pressure; IQR = interquartile range. P-values were obtained by using the t-test for continuous variables, the chi-square test for categorical variables and pair t-test for pair data. \(^*\)p<.05. \(^a\)Reference group. \(^b\)The body mass index categories Healthy Weight (n=27) and Underweight (n=2) were collapsed in the category Healthy Weight. \(^c\)Missing data not included in the analysis (n=16). \(^d\)As defined in “The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC Report,” by A. V. Chobanian et al, 2003, *The Journal of the American Medical Association*, 289(19), 2560-2572. \(^e\)Mean change. \(^a\)The antihypertensive medication categories “2” (n=27) and “3” (n=1) were collapsed in category “2”.

21
statistical relationship with the dependent variable \((p=0.8685)\). The reductions in systolic and diastolic blood pressure were significantly higher in the control group than in the uncontrolled group (in both cases \(p<0.0001\)).

A larger percentage of participants in the uncontrolled group (43.6%) had two or more comorbidities, compared to those in the controlled group (20.5%). The differences found between groups in the number of comorbidities were statistically significant \((p=0.0488)\). The categories “two comorbidities”, “three comorbidities” and “four comorbidities” were merged due to low frequencies (n=9 and n=1, respectively).

Diabetes mellitus, as a comorbidity, was observed more frequently in the uncontrolled group (35.9%) than in the control group (12.8%, \(p=0.0089\)). There was no difference in the proportions prescribed with two or more antihypertensive medication in the uncontrolled group (25.6%) compared to those in the controlled group (20.5%, \(p=0.5400\)). The percentage of participants attended by a general practitioner in the uncontrolled group (60.3%) was not different compared to the controlled group (66.7%, \(p=0.4998\)).

The percentage of medical doctors that followed the recommendations of the antihypertensive protocols was 44.9% for the uncontrolled group, compared to the controlled group (41.0%). However, the differences were not significant \((p=0.4998)\).

Finally, the number of antihypertensive treatment days did not differ for the uncontrolled group (30.5 days, Interquartile range [IQR]: 10.0-56.3), compared to the controlled group (33.0 days, IQR=14.0-90.0; \(p=0.4250\)).
Multivariate Analysis

Table 4.4 presents the crude and adjusted odds ratio estimates for physician adherence to antihypertensive protocols and the demographic and clinical characteristics of the subjects. Physician adherence to antihypertensive protocols was not significantly associated with blood pressure control status in either the crude or adjusted models.

Table 4.4

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude Model OR (95% CI)</th>
<th>Adjusted Model OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Adherence Ref = No</td>
<td>1.17 (0.54-2.55)</td>
<td>1.31 (0.48-3.564)</td>
</tr>
<tr>
<td>Age</td>
<td>1.03 (1.00-1.06)</td>
<td>1.05 (0.99-1.10)</td>
</tr>
<tr>
<td>Diabetes Mellitus Ref = No</td>
<td>3.81 (1.34-10.84)</td>
<td>2.90 (0.58-14.46)</td>
</tr>
<tr>
<td>Gender Ref = Male</td>
<td>0.58 (0.26-1.30)</td>
<td>0.649 (0.25-1.70)</td>
</tr>
<tr>
<td>Attending Physician Ref = No</td>
<td>0.76 (0.34-1.70)</td>
<td>1.89 (0.54-6.62)</td>
</tr>
<tr>
<td>Number of Comorbidities 1 vs 0 Ref = Zero</td>
<td>0.93 (0.34-2.63)</td>
<td>0.76 (0.17-3.50)</td>
</tr>
<tr>
<td>Number of Comorbidities 2 vs 0 Ref = Zero</td>
<td>2.83 (0.87-9.23)</td>
<td>1.20 (0.16-8.93)</td>
</tr>
<tr>
<td>Body mass index Obese vs Healthy Weight</td>
<td>0.74 (0.28-2.00)</td>
<td>1.46 (0.31-6.87)</td>
</tr>
<tr>
<td>Body mass index Overweight vs Healthy Weight</td>
<td>1.51 (0.50-4.60)</td>
<td>2.03 (0.56-7.37)</td>
</tr>
</tbody>
</table>

Note. OR = odds ratio; CI = confidence interval; Ref = reference group.

To determine the presence of effect modification, interactions were tested between the main effect variable (physician adherence to antihypertensive protocols by medical doctors) and the covariates included in the model. Table 4.5 presents the p-values for the interaction terms. A significant interaction was found with age ($p=0.0454$).
There were no significant differences by levels of the number of comorbidities ($p=0.6539$), diabetes mellitus ($p=0.7194$), gender ($p=0.3941$), and type of attending physician ($p=0.7286$). For body mass index, the interaction was dropped from the final model, because the point estimate was not estimable for the main effect variable due to low numbers in the healthy weight category.

Stratified models were run for the potential effect modifier “age”, using a cut point at the mean age (56.7 years); one model for those below or equal to the mean, and

<table>
<thead>
<tr>
<th>Variable</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.0454</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>0.7194</td>
</tr>
<tr>
<td>Gender</td>
<td>0.3941</td>
</tr>
<tr>
<td>Attending Physician</td>
<td>0.7286</td>
</tr>
<tr>
<td>Number of Comorbidities</td>
<td>0.7883</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.0311</td>
</tr>
</tbody>
</table>

* $p<.05.$

### Table 4.6

**Stratified Models by Age as a Potential Modifier**

<table>
<thead>
<tr>
<th>Age ≤ 56.7 years</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Adherence</td>
<td>0.85 (0.22-3.22)</td>
</tr>
<tr>
<td>Ref = No</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>0.85 (0.29-2.51)</td>
</tr>
<tr>
<td>Ref = Male</td>
<td></td>
</tr>
<tr>
<td>Attending Physician</td>
<td>0.73 (0.18-2.97)</td>
</tr>
<tr>
<td>Ref = No</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age &gt; 56.7 years</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Adherence</td>
<td>1.61 (0.35-7.34)</td>
</tr>
<tr>
<td>Ref = No</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>0.19 (0.03-1.04)</td>
</tr>
<tr>
<td>Ref = Male</td>
<td></td>
</tr>
<tr>
<td>Attending Physician</td>
<td>1.31 (0.28-6.10)</td>
</tr>
<tr>
<td>Ref = No</td>
<td></td>
</tr>
</tbody>
</table>

*Note. OR = odds ratio; CI = confidence interval; Ref = reference group.*
one model for those above the mean. Inestimable parameters were found for the variables
number of comorbidities, the presence of diabetes mellitus and BMI; therefore, these
variables were dropped from the models; and the models were run again.

In Table 4.6 are shown the results for the models stratified by age. From these
models it can be observed that the estimates were different for the levels of age. These
findings suggest that age is a potential effect modifier for the association between
uncontrolled hypertension and the physician’s adherence to antihypertensive protocols.

The Hosmer-Lemeshow Goodness-of-Fit test indicated a good model fit
\((p=0.5717)\).
CHAPTER FIVE: DISCUSSION

Key Findings

The aim of this study was to describe the characteristics of uncontrolled hypertension in a primary healthcare center and the factors associated with this condition.

This study was designed as a feasibility study to assess the current treatment practices for hypertensive adults. One of the critical findings of this study is that 66.7% of the study sample had uncontrolled hypertension, a result that differs from another study in Panama in which the prevalence of uncontrolled hypertension was 47.2% (McDonald et al., 2012). However, this results was not unexpected considering that our study was clinically based at a primary healthcare center serving a single county of the Panama province, the target population was the hypertensive adult population visiting the clinic, and, finally, the study used a more conservative blood pressure cut point to define uncontrolled hypertension (>130/80 mmHg, or >140/90 mmHg, depending on the type of comorbidities). The Gorgas study was population based, with a target population of the general adult population (hypertensive and non-hypertensive adults) in the two main Panama provinces (in which the 57.4% of the total Panamanian population reside), and defined uncontrolled hypertension using a more liberal cut point (>140/90 mmHg for all hypertensive population, regardless the type of comorbidities).

A logistic regression model was used to investigate the relationship between physician adherence to antihypertensive protocols and the presence of uncontrolled
hypertension. A significant interaction term was found between physician adherence to protocols and age. In the stratified models, the odds ratios for physician adherence to protocols were in opposite directions, although the estimates were not significantly different from one. These results suggest that age could be a potential effect modifier for the association between physician adherence to antihypertensive protocols and the presence of uncontrolled hypertension. However, due to the small sample size, the possible role of age as an effect modifier for the mentioned the relationship needs further examination.

There is a potential biologic explanation for these findings. A study derived from the Framingham cohort, showed that systolic blood pressure increased linearly with age during lifetime; however, diastolic blood pressure increased linearly until the age of 50 to 60 years, and after this tended to level off over a decade, and later on may stay the same or decrease (Franklin et al., 1997). This phenomenon produces a steep increase, after 50 to 60 years, in pulse pressure (systolic minus diastolic blood pressure); and became, along with systolic blood pressure, potent cardiovascular risk factors in this age group (Chobanian et al., 2003; Mancia et al., 2007). However, for those aged <50 years, diastolic blood pressure is more important cardiovascular risk factor than systolic blood pressure or pulse pressure (Franklin et al, 2001; Chobanian et al., 2003). The joint increase of systolic and diastolic blood pressure until the age of 50 years, makes the pharmacological titration process easier for physicians since both systolic and diastolic blood pressure will be relatively high; however for those above 50 years old, isolated systolic hypertension is more expected, and therefore it will be difficult to induce a decrease in systolic blood pressure without a decrease in diastolic blood pressure, that
could lead to hypotension symptoms; which makes hypertension control in this age group more difficult. This is supported by several studies in primary care settings that demonstrated that 75% of physicians failed to initiate hypertension treatment in older individuals with systolic blood pressure 140 – 159 mmHg and most of them did not chase control rates (systolic blood pressure <140 mmHg; Hyman, Pavlik, & Vallbona, 2000; Berlowitz et al., 1998).

In the bivariate analyses the following variables were associated with having uncontrolled hypertension: age, number of comorbidities and the presence of diabetes mellitus. However, in the adjusted models these variables were no longer significant.

Other studies have reported an association between increasing age and uncontrolled hypertension (CDC, 2012a; Mejía-Rodríguez et al., 2009); while a recent study by Basu and Millett (2013) reported that age was not associated with uncontrolled hypertension in middle-income countries. However, the statistically significant interaction found in our study (between age and the physician adherence to antihypertensive protocols), was not considered in these studies.

The association found between the number of comorbidities and having uncontrolled hypertension is consistent with a previous study that demonstrated similar findings (Amar et al, 2003); however, in the previously mentioned study, the risk factors considered as comorbidities were not exactly the same than the comorbidities defined in the current study. We used the Panamanian Guidelines for the Hypertensive Population Treatment (Organización Panamericana de la Salud, 2009) to define these comorbidities, so the role of specific comorbidities in the development of uncontrolled hypertension is a topic that will prompt more research.
For diabetes mellitus, we found that 28.2% of study sample had this condition as a comorbidity, in contrast with the 55% reported by a previous study in Panama (McDonald, 2012). Diabetes mellitus, as a comorbidity, was associated with having uncontrolled hypertension; this finding is consistent with the literature that has demonstrated a similar relationship (Amar et al, 2003; Egan et al., 2011; Mejia-Rodriguez et al., 2009).

In the bivariate analysis, no associations were found for gender, body mass index, hypertension stage (according to the classification of the JNC 7 Report; Chobanian et al, 2003), systolic and diastolic blood pressure during the treatment appointment, number of antihypertensive medications prescribed, type of attending physician, time since treatment started, and treatment following protocols recommendations. However, several studies had shown the relationship between these independent variables and having uncontrolled hypertension (Egan et al, 2011; CDC, 2012a; Basu & Millett, 2013; Mejia-Rodriguez, 2009; Kim et al, 2009; Mounier-Vehier, Sanchez-Ponton, Delsart, & Miljkovic, 2010; Hyman & Pavlik, 2002). These results could be a reflection of one of the main limitations of this study, the sample size.

**Limitations and Strengths**

This study was designed as a feasibility study and it provides some insight on how future studies need to be designed; however some important limitations should be mentioned.

The main limitation is the sample size, which was a third of the required number (117 out of 383 participants), resulting in a lack of power to detect statistically significant
differences. This means that even when there was a difference between those patients that were treated following the protocols and those that were not, our study was not able to detect a statistically significant difference between these groups.

These results may not be generalizable to the general population because the study center was not chosen by randomization; instead it was selected based on accessibility and available permission to perform the study. As the study was based on clinical chart review, the diagnosis of hypertension was not independently confirmed.

Also, data were not collected for some important covariates that have previously been shown to have an association with uncontrolled hypertension, such as smoking history (Amar et al., 2003; Chmiel et al., 2012), cholesterol levels (Amar et al., 2003), renal function (Mounier-Vehier et al., 2010), therapeutic inertia (Egan et al., 2011), income (CDC, 2012a; Basu & Millett, 2013), education (Mounier-Vehier et al., 2010) and alcohol intake (Mounier-Vehier et al., 2010). Race/ethnicity was not recorded in the clinical chart, and therefore could not be considered in the analysis. Approximately 14% of observations were missing height, weight or both to calculate body mass index, and were not included in the multivariate analysis. Another limitation was that patient compliance with antihypertensive treatment and lifestyle modifications recommendations were not assessed. From the mentioned above and the fact that our design does not let us to establish temporality, no statements on causality or prevalence of uncontrolled hypertension in the general population can be derived.

The strengths of this study include that it was designed to minimize sources of systematic error. Multivariate logistic regression models were developed to test association between physician adherence to protocols and uncontrolled hypertension.
Another strength of this study is that a more conservative blood pressure cut point (>130/80 mmHg) was used for those with diabetes mellitus or any kind of nephropathy to establish the presence of uncontrolled hypertension. Other studies have used a set blood pressure cut point of >140/90 mmHg for all subjects.

**Conclusions**

Uncontrolled hypertension is a public health problem worldwide, and the population prevalence estimates for Panama is 47.2%. Among this study population the prevalence of uncontrolled hypertension was 66.7%, which is reflective of a clinic-based population but it cannot be generalized to the general population.

Nearly half of the attending physicians did not follow the recommendations given by current antihypertensive protocols, primarily due to a lack of recommending lifestyle modifications. Physician adherence to pharmacological treatment recommendations was high (98.3%). However, it was not possible to demonstrate an association between physician adherence to antihypertensive protocols and the presence of uncontrolled hypertension, in the multivariate analysis.

Further research is necessary to fully assess the association between age, number of comorbidities and presence of diabetes mellitus with uncontrolled hypertension; specifically to assess the role of age as a potential modifier for the association between uncontrolled hypertension and the physician adherence to antihypertensive protocols recommendations. Is imperative to know which antihypertensive protocols recommendations work for what specific age groups, because specific recommendations can be restated to benefit the hypertensive population with poor blood pressure control.
As a feasibility study, this research provides valuable insight in the design and direction of future studies. For example, future studies should comprehensively examine the role of age in uncontrolled hypertension and as a potential effect modifier of physician adherence to protocols. In addition, future studies should adequately control for all potential confounders, should be appropriately sized, and should include a measure of patient compliance to antihypertensive protocols.

Recommendations

Further research needs to be conducted using an adequate sample size to confirm the results of this study. In addition, further exploration of the roles of age in uncontrolled hypertension is warranted.

In Panama, further research in hypertension is necessary to determine the population prevalence of uncontrolled hypertension using a blood pressure cut point specific for individual comorbidities; as well as, to establish the risk factors associated with uncontrolled hypertension.
CHAPTER SIX: LIST OF REFERENCES


APPENDICES
Appendix A: Electronic Data Entry Form

Study Identification Number: _______________________

Age: _______ Gender: □ Male □ Female □ Indigenous □ African American
Race/Ethnicity: □ Indigenous □ African American

Height: _____ Weight: _________ □ Other:

Comorbidities:

1. ______________________ 4. ______________________
2. ______________________ 5. ______________________
3. ______________________ 6. ______________________

Treatment Appointment

Blood Pressure: Date:

Lifestyle Modifications? Yes
No

Antihypertensive Dosage Frequency
1. ______________________ ______________________
2. ______________________ ______________________

Follow-Up Appointment

Blood Pressure: Date:

Antihypertensive Dosage Frequency
1. ______________________ ______________________
2. ______________________ ______________________
Appendix A: (Continued)

According to the antihypertensive medication given in the first appointment and according to the treatment category, was the patient treated according to protocols?
☐ Yes         ☐ No

According to the blood pressure in the second appointment, was the expected blood pressure level reached?
☐ Yes         ☐ No

Type of Attending Physician
☐ General Practitioner         ☐ Specialist
Appendix B: Classification in Appropriately and Inappropriately Treated Hypertension According to the Guidelines of the Pan American Health Organization – Republic of Panama

Table B.1

*Treatment Classification According to the Guidelines of the Pan American Health Organization*

<table>
<thead>
<tr>
<th>Category</th>
<th>Appropriately Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT alone, Stage 1 or 2&lt;sup&gt;b&lt;/sup&gt;</td>
<td><em>Treated</em> with a diuretic, β-blocker, ACEI, ARB or CCB either alone or in combination (up to 2 agents)</td>
</tr>
<tr>
<td>HT + Late adulthood (&gt;55 years old)</td>
<td><em>Treated</em> with a diuretic, β-blocker, ACEI, ARB, α-blockers, either alone or in combination</td>
</tr>
<tr>
<td>HT + African American</td>
<td><em>Treated</em> with a diuretic, ACEI, CCB, ARB, α-blockers, either alone or in combination</td>
</tr>
<tr>
<td>HT + Diabetes Mellitus (DM)</td>
<td><em>Treated</em> with a ACEI, ARB, diuretic, CCB, α-blocker, β-blocker either alone or in combination</td>
</tr>
<tr>
<td>HT + Chronic Kidney Disease</td>
<td><em>Treated</em> with a loop diuretic alone or in combination with CCB, ACEI or ARB</td>
</tr>
<tr>
<td>HT + DM + Nephropathy</td>
<td><em>Treated</em> with either a ACEI or a ARB alone or in combination with CCB’s, diuretics, α-blockers or β-blockers</td>
</tr>
<tr>
<td>HT + Coronary Heart Disease</td>
<td><em>Treated</em> with a β-blocker, ACEI, ARB, CCB either alone or in combination</td>
</tr>
<tr>
<td>HT + Heart Failure</td>
<td><em>Treated</em> with a ACEI, ARB, β-blocker, diuretics, Aldosterone Antagonist, either alone or in combination</td>
</tr>
<tr>
<td>HT + Left Ventricular Hypertrophy</td>
<td><em>Treated</em> with ACEI, ARB, diuretics, β-blocker, or CCB, either alone or in combination</td>
</tr>
<tr>
<td>HT + Obesity</td>
<td><em>Treated</em> with a ACEI, ARB, diuretics, β-blocker, or CCB, either alone or in combination</td>
</tr>
<tr>
<td>HT + Dyslipidemia</td>
<td><em>Treated</em> with a ACEI, ARB, CCB, thiazide diuretic, or β-blocker, either alone or in combination</td>
</tr>
<tr>
<td>HT + Asthma</td>
<td><em>Treated</em> with any antihypertensive medication, either alone or in combination, excluding any β-blocker (is totally contraindicated)</td>
</tr>
</tbody>
</table>

Appendix C: University of South Florida’s Institutional Review Board Letter of Approval

January 14, 2013

Roderick Chen-Camano, MD
Epidemiology and Biostatistics
13201 Bruce B Downs, MDC56
Tampa, FL 33612

RE: Expedited Approval for Initial Review
IRB#: Pro00010571
Title: Uncontrolled Hypertension Among The Hypertensive Population Seen In a Primary Healthcare Center of the Panama Province, Republic of Panama: A Feasibility Study

Dear Dr. Chen-Camano:

On 1/11/2013 the Institutional Review Board (IRB) reviewed and APPROVED the above referenced protocol. Please note that your approval for this study will expire on 1/11/2014.

Approved Item(s):
Protocol Document(s):
RRCC - Hypertension Protocol v1.3.pdf

Please note that this study is approved, but access to medical records and data collection may not begin until the Panamanian National Bioethics Committee letter of approval is submitted and reviewed by the USF IRB via the submission of an amendment.

It was the determination of the IRB that your study qualified for expedited review which includes activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories outlined below. The IRB may review research through the expedited review procedure authorized by 45CFR46.110 and 21 CFR 56.110. The research proposed in this study is categorized under the following expedited review category:

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

Your study qualifies for a waiver of the informed consent process as outlined in the federal regulations at 45CFR46.116 (d) which states that an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent provided the IRB finds and documents that
Appendix C: (Continued)

(1) the research involves no more than minimal risk to the subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver or alteration; and (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

As the principal investigator of this study, it is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB. Any changes to the approved research must be submitted to the IRB for review and approval by an amendment.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

Janelle Perkins, PharmD, Chairperson
USF Institutional Review Board
Appendix D: University of South Florida’s Institutional Review Board Letter of Approval of Amendment 1

3/6/2013

Roderick Chen-Camano, M.D.
Epidemiology and Biostatistics
13201 Bruce B. Downs, MDC56
Tampa, FL 33612

RE: Expedited Approval for Amendment
IRB#: Amel  Pro00010571
Title: Uncontrolled Hypertension and Associated Factors in Hypertensive Patients at the Primary Healthcare Center Luis H. Moreno, Panama: A Feasibility Study

Dear Dr. Chen-Camano:

On 3/6/2013, the Institutional Review Board (IRB) reviewed and APPROVED your Amendment. The submitted request has been approved for the following:

1. As was requested in the approval letter for this study, the study team has attached the APPROVAL LETTER from the Research Ethics Institutional Committee of the Punta Pacifica Hospital (Bioethics Committee authorized by the Panamanian National Bioethics Committee to review clinical studies), including the original Spanish version and the translated version
2. Changes to Study Title: "Uncontrolled Hypertension and Associated Factors in Hypertensive Patients at the Primary Healthcare Center Luis H. Moreno, Panama: A Feasibility Study"

Approved Item(s):
Protocol Document(s):
RRCC - Hypertension Protocol v1.3 - CLEAN VERSION.pdf
RRCC - Hypertension Protocol v1.3.pdf

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

Janelle Perkins, Pharm.D.
Chairperson
USF Institutional Review Board
Appendix E: Panama’s Institutional Review Board Letter of Approval (Spanish)

<table>
<thead>
<tr>
<th>Fecha de recepción de la solicitud</th>
<th>4 de Enero del 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Título del estudio propuesto</td>
<td>“Hipertensión No Controlada y factores asociados en pacientes hipertensos en el Polifacén de Salud Luis H. Moreno, Panamá: un estudio de factibilidad”</td>
</tr>
<tr>
<td>Nombre del investigador principal</td>
<td>Dr. Roderick Ramón Chen Camaño</td>
</tr>
</tbody>
</table>

La firma del secretario/administrador y del presidente de la CIEI que aparece a continuación da fe de la decisión acerca de la solicitud, tal como lo votó el comité:

- **Aprobada**: Opinión favorable a la continuación del proyecto.
  - Aprobación condicional: Cuando se requieren aclaraciones y/o modificaciones, según lo descrito a continuación, para su aprobación.
    - □
    - □
  - Denegación: Cuando los proyectos no cumplen con las condiciones requeridas para continuar.
    Comentarios:
    - □
  - Suspensión: Cuando se produce una violación grave en la manera en que se lleva a cabo la investigación.
    Comentarios:

La IRB tendrá que revisar este protocolo: este protocolo ha sido aprobado y será revisado una vez al año

Dra. Giselle Fernández  
Coordinadora del CIEI del HPP

Dr. Edwin Villalobos  
Presidente del CIEI del HPP

19/2/2013  
Fecha

PARA USO CONFIDENCIAL DE LA EMPRESA
Página 1 de 1
Appendix F: Panama’s Institutional Review Board Letter of Approval (Translation)

[Image of the document]

I hereby certify this a true translation from its original document in the Spanish language.

By Carlos Olmos on February 28th, 2013 Resolution 473 of 10-6-2004