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# Exploring Factors Impacting Veterans' Hypertension Control

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UNIVERSITY OF SAN DIEGO

Hahn School of Nursing and Health Science

DOCTOR OF PHILOSOPHY IN NURSING

EXPLORING FACTORS IMPACTING VETERANS' HYPERTENSION CONTROL

by

Jian Hua Liu

A dissertation presented to the

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UNIVERSITY OF SAN DIEGO

In partial fulfillment of the

Requirements for the degree

DOCTOR OF PHILOSOPHY IN NURSING

April 10, 2017

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Dr. Jian Hua Liu, PhD, FNP

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## Abstract

Exploring factors impacting veterans' hypertension (HTN) control is essential in reducing the common cardiovascular disease event of stroke, heart attack, chronic kidney disease and mortality. The purpose of this study was to describe multidimensional factors impacting veterans' HTN control. Utilizing a descriptive, exploratory, cross-sectional, retrospective, convenience sampling research design, 331 electronic medical records in a VA dashboard data set were reviewed for men and women veterans between the age 24 and 98 years ( $M=62$ ,  $SD=13$ ) in a Southern California Veterans Affairs primary care clinic from October 17, 2014 through October 17, 2016. Data were analyzed by univariate, bivariate and multivariate statistics. The study found that self-reported medication adherence to antihypertensive drugs ( $p < .001$ ) was an independent predictor to veterans' final systolic blood pressure. Future HTN control research may focus on some theory-guided multidimensional determinants of patients' adherence to HTN treatments and HTN control outcomes fully, utilizing a consistent HTN definition defined by JNC-7.

*Keywords:* factors impacting hypertension control, self-reported medication adherence, veteran, systolic blood pressure



## Dedication

The completion of this dissertation has been a laborious self-learning journey for five years. I would like to dedicate my work to GOD, my husband, my brothers, sisters, daughter, niece and nephews who offered great inspiration and support. Without their love and encouragement, I would never have been able to complete the work.

Dear God of love, help me to become the spiritual being you created me to be, that I can always draw strength from the foundation of my faith that I had on the journey of earning my PhD degree. Thanks to the Lord for reaching out to me when I needed it the most. Help me do the same for others.

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## Chapter 1: Overview

### Background and Rational

Exploring factors impacting veterans' hypertension (HTN) control is important in reducing common cardiovascular disease events of stroke, heart attack, chronic kidney disease and mortality. Despite decades of efforts by government agencies, researchers, healthcare providers and patients to improve the rate of HTN control, it remains a major public health challenge in the United States. Compared with a target HTN control goal of 61.2% set by Healthy People 2020 (Gillespie & Hurvitz, 2013), the overall HTN control rate remains suboptimal at 51.8% (Nwankwo, Yoon, Burt, & Gu, 2013). Reasons for the suboptimal HTN control rate are multifactorial and likely associated with the insufficient and or inaccurate description of predictive factors impacting HTN control. Guided by *the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure* (JNC-7, Chobanian et al., 2003), the purpose of this study was to describe multidimensional factors impacting veterans' HTN control.

### Significance

This study was significant for the nursing profession for a couple of reasons. First, the study added comprehensive new knowledge concerning the characteristics of hypertensive veterans in the Southern California region to the scholarly nursing research database. Second, the finding of self-reported medication adherence as a predictor ( $p < 0.001$ ) may stimulate further nursing research toward exploring some theory-guided multidimensional determinants of patients' adherence to HTN treatments and HTN

control outcomes fully, utilizing a consistent HTN definition defined by JNC-7 which may in turn, lead to an improved data collection, quality healthcare outcome and cost saving. Third, the study offered many insights into conducting a retrospective analysis with a Veterans' Affairs (VA) dashboard data set in an EMR system that may help novice researchers with this approach in the future.

### **Hypertension (HTN) Control Conceptual Framework**

The conceptual framework guiding the study design was based upon the JNC-7 HTN management guideline (Chobanian et al., 2003). Although this guideline approached the HTN-control challenge from four-domains (Domains 1 to 4, see *Figure 1*), an additional domain was added to illustrate the conceptualization of the HTN-control issue within Domain 5 (see *Figure 2*). As such, the HTN control conceptual framework consisted of five domains: prevention, detection, evaluation, treatment, and outcome. This study focused on the relationship between seven dimensional independent variables (IVs) and one dependent variable (DV) at a final point of EMR review within Domain 5. The seven dimensions were (a) socio-demographic (e.g., age, sex, race, religion, branch of military service, time of military service, education, disability rating, insurance/copay), (b) lifestyle (e.g., tobacco, alcohol, DASH, exercise, caffeine, stress), (c) secondary HTN (e.g., obstructive sleep apnea [OSA]), (d) comorbidity (e.g., diabetes mellitus [DM], dyslipidemia, obesity [BMI]), (e) mental health disorder (e.g., major depressive disorder [MDD], generalized anxiety disorder [GAD], post-traumatic stress disorder [PTSD]), (f) medication (e.g., effectiveness, adherence, number of primary and cardiology clinic visits, antihypertensive medication names and quantities based on BP drug class, number

of all medication), (g) uncontrolled HTN-associated end organ damage (e.g., cerebral vascular accident [CVA], transient ischemic attack [TIA], congestive heart failure [CHF], coronary artery disease [CAD], myocardial infarction [MI], coronary artery bypass graft [CABG], chronic kidney disease [CKD]). This framework was used primarily for identifying key study variables and developing a standardized data collection instrument (see Appendix A).



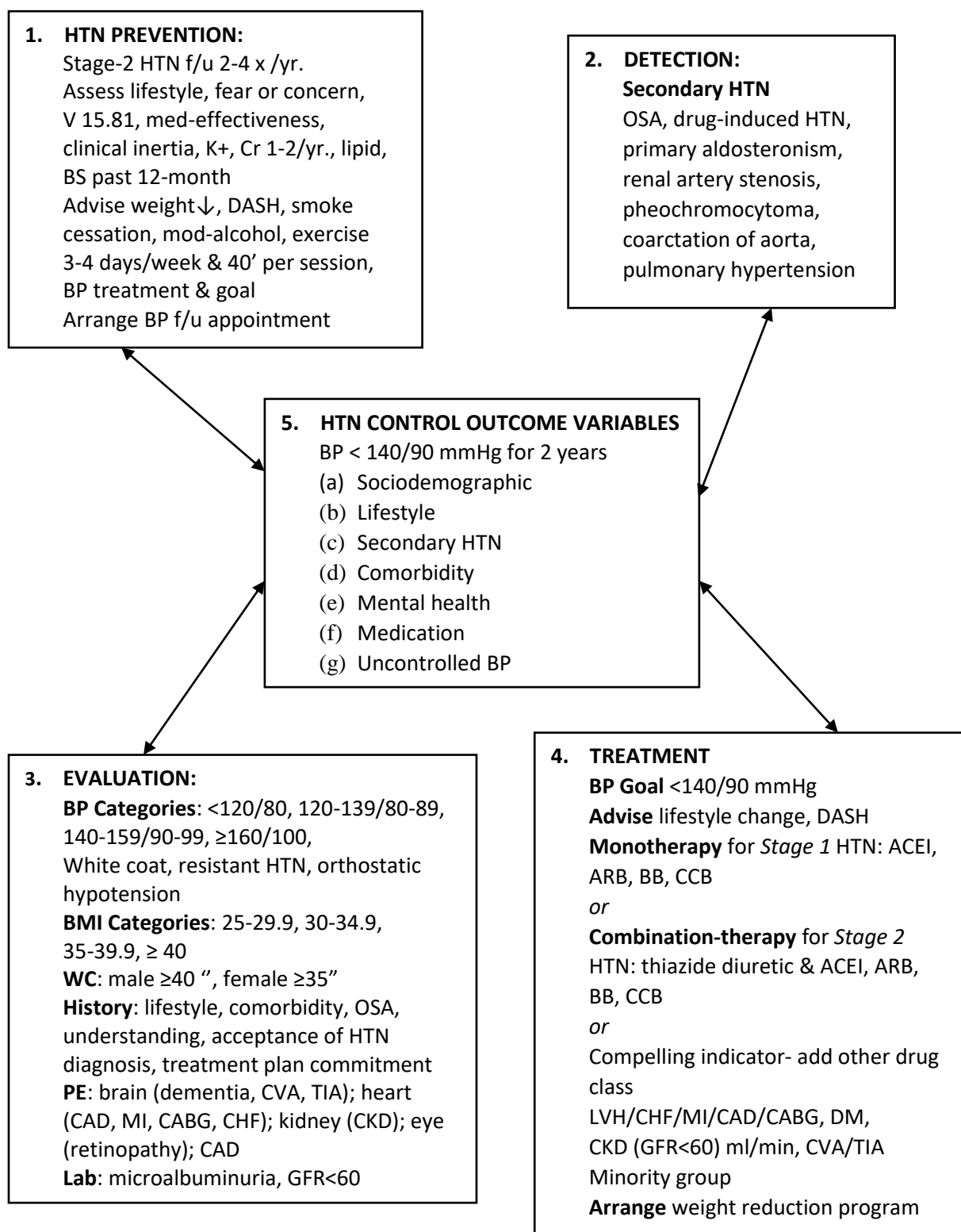


Figure 1. Hypertension (HTN) Control Conceptual Framework (5-domaine)

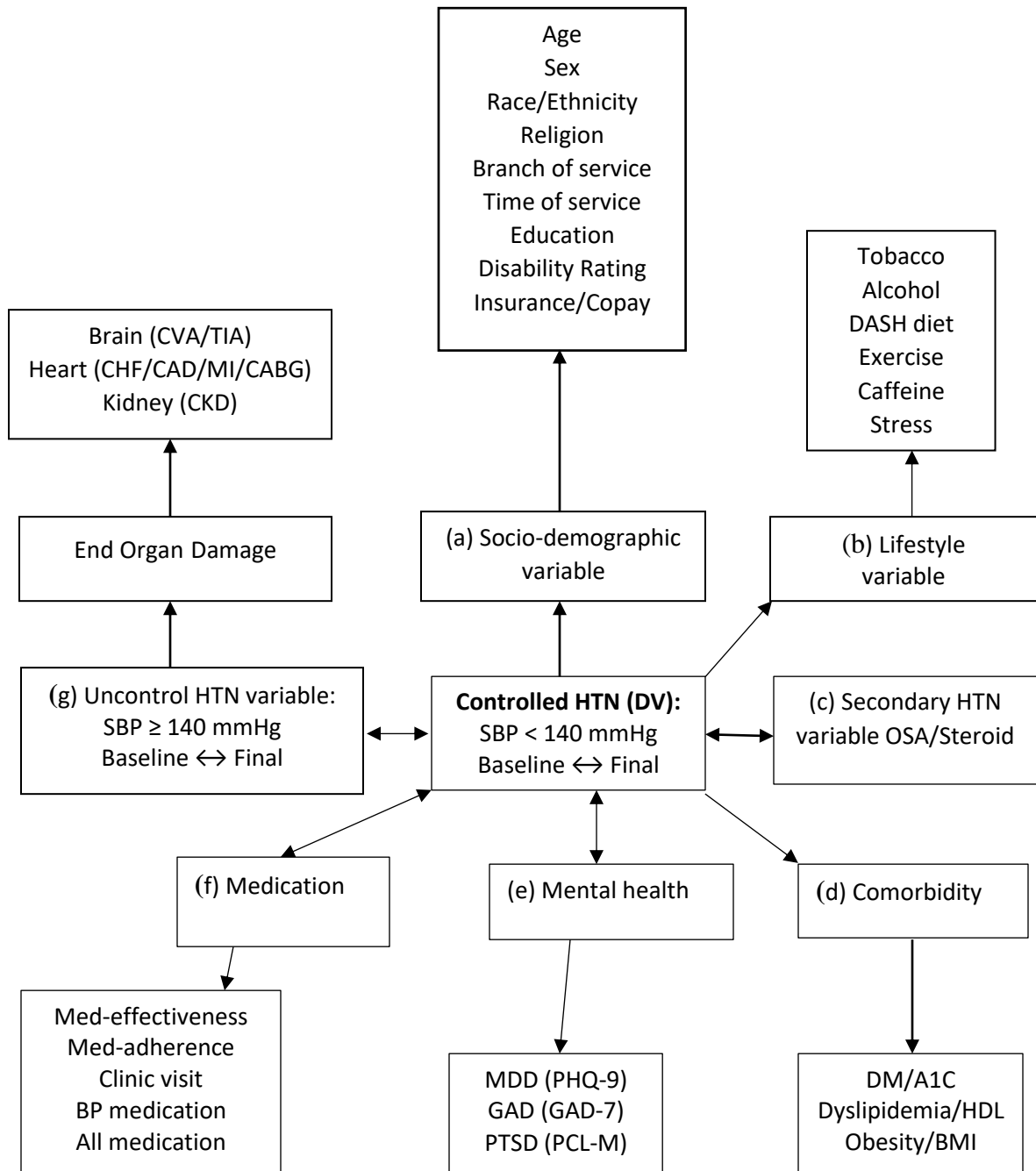


Figure 2. Hypertension (HTN) Control Conceptual Framework (5<sup>th</sup>-domaine)

### Purpose Statement

The purpose of this study was to describe multidimensional factors impacting veterans' HTN control. In this descriptive, exploratory, cross-sectional, retrospective,

convenient sampling of primary data, 331 EMRs in a VA dashboard data set were reviewed for men and women veterans aged 24 and older with essential HTN in one Southern California VA primary care clinic from October 17, 2014 through October 17, 2016. Data was analyzed utilizing univariate, bivariate, and multivariate statistics.

### **Research Aims and Questions**

#### Aim # 1.

Describe the characteristics of hypertensive veterans in one Southern California VA clinic from data collected during a period of October 17, 2014 through October 17, 2016.

#### Question # 1.

What were characteristics of hypertensive veterans in one Southern California VA clinic for the seven dimensions of IVs from data collected during a period of October 17, 2014 through October 17, 2016?

#### Aim # 2.

Examine the relationships among the predictor variables of blood glucose level (A1C), high-density lipoprotein (HDL), body mass index (BMI), total number of BP medications prescribed, total number of clinic visits, baseline SBP and the outcome variable of the final point SBP.

#### Question # 2a.

Which of the possible six predictor variables were included in an equation for predicting veterans' final point SBP?

Question # 2b.

Does the obtained regression equation resulting from a subset of the six predictor variables allow us to reliably predict veterans' final point SBP?

Aim # 3.

Describe any significant association between and among non-normally distributed IVs and the final SBP.

Question # 3.

Can status of veterans' final SBP be correctly predicted from knowledge of A1C, HDL, BMI, Baseline SBP?

Aim # 4.

Describe any relationships between categorical predictor variables (Yes/No) and an outcome variable of final controlled ( $SBP < 140$ ) or uncontrolled ( $SBP \geq 140$ ).

Question # 4.

What were the significant relationships between age ( $\geq 60 / < 60$ ), race (Black/non-Black), religion (yes/no), tobacco use (yes/no), alcohol use (yes/no), OSA (yes/no), DM (yes/no), dyslipidemia (yes/no), BMI ( $\geq 30 / < 30$ ), MDD (yes/no), GAD (yes/no), PTSD (yes/no), medication adherence (yes/no), brain damage (yes/no), heart damage (yes/no), CKD (yes/no) and final SBP ( $\geq 140 / < 140$ )?

## Chapter 2: Review of the Relevant Literature

The purpose of this chapter is to conduct a comprehensive review of the research literature relevant to key concepts of HTN control. The chapter begins with a critical review of a JNC-7 guided study, an historic overview of JNC BP treatment goals, and HTN prevalence and risk factors. Ultimately, a systematic review of the most up-to-date research studies is presented in domains of HTN prevention, detection, evaluation, treatment, and control outcomes. The chapter will conclude with a summary of major themes based on the literature reviewed and will suggest how this study might further add to the scholarly nursing literature.

### **JNC-7 as a Study Conceptual Framework**

A search of the literature using the key terms *conceptual framework and JNC-7 and hypertension and veteran* was conducted in Academia Premier, CINAHL, Health Source (Nursing/Academic Edition), and PsychInfo within the past 5 years to identify peer-reviewed journal articles pertaining to articles that utilizes the JNC-7 as a conceptual framework. This approach yielded 16 articles with non-veteran populations. After screening the abstracts, only one article was found to be relevant to the focus of this study and was reviewed with attention to its study design.

Koti and colleagues (2015) conducted a retrospective chart review to compare the documented provision of HTN care against JNC-7 HTN treatment guidelines (Chobanian et al., 2003). In this study, the JNC-7 was utilized to develop a 15-item instrument used for EMR chart audits (Koti & Roetzbeim, 2015). The provision of HTN care was scored per the instrument and included:

1. Cardiovascular risk factor
2. Identification of BP goal
3. Communicating BP goal to patients verbally or in writing
4. Monotherapy for Stage I HTN
5. Combination therapy for Stage II HTN or Stage I HTN with comorbidity
6. Notation of uncontrolled HTN by healthcare providers (BP  $\geq$ 140/90 mmHg)
7. Discussing lifestyle modification for  $\geq$  50% of encounter by providers

Within the past 12 months:

8. Fasting lipid panel
9. DM, CKD, albuminuria
10. Serum creatinine
11. Blood glucose
12. Hematocrit
13. Serum potassium
14. Serum calcium
15. Electrocardiogram (EKG) measured at any point in the past

The study sample of 150 cases included 83 women and 67 men ( $M_{age} = 64.7$  years;  $SD = 12.7$  years) and clinic visits ( $M = 4.5$ ;  $SD = 2$ ). The study reported HTN-detection rate (96.7%), drug treatment rate (97.7%), healthcare provider's explicit identification of BP goals (18.7%), communicating BP goal to patients (10.7%), discussion about lifestyle modifications at  $> 50\%$  of their visits (22.0%), and HTN-laboratory evaluation for CKD (68.8% - 96.7%), including serum creatinine, blood

glucose, and potassium. The study also found that married patients received more guideline-recommended care than unmarried patients (80.4% vs 74.4%,  $p < 0.05$ ) and men received more guideline-recommended care than did women (80.7% vs 76.4%,  $p < 0.05$ ).

#### Strengths of the study.

The study design was conceptualized by JNC-7 and capable of addressing four domains of HTN control issues. Koti and Roetzbeim (2015) provided innovation as evidenced by the creation of JNC-7 blueprint instrument for systematic chart auditing. The study incorporated clearly-defined inclusion and exclusion criteria. The broad age spectrum of the study subjects ( $M_{age} = 64.7$  years,  $SD = 12.7$  years) was representative of hypertensive populations.

#### Weaknesses of the study.

The developed scoring instrument was not psychometrically validated prior to its application. Additionally, the instrument scores were altered multiple times creating a threat to the instrument's internal validity (Waltz, Strickland, & Lenz, 2010). The practice of oversampling non-Hispanic Black and Hispanic patients to maximize statistical power for the study created a risk for selection bias, another threat to internal validity. With multiple concerns for validity, these study results should be viewed as less credible.

Knowledge gaps.

JNC guidelines are not mandatory for providers; few studies have utilized JNC as a conceptual framework. Healthcare providers must exercise their own clinical judgement when referring to this guideline (Chobanian et al., 2003).

### **Historic Overview of Joint National Committee (JNC) BP Treatment Goals**

Understanding the rationale of recent changes in BP treatment goals necessitated an historical perspective. Studies by Ogihara et al. (2010) and the JATOS Study Group (2008) cited by JNC-8 (James et al., 2013), supporting these changes. In 2014, the BP treatment goal for the general population was changed for people age 60 years or older (< 150/90 mmHg; James et al., 2013), up from the previous goal (140/90 mmHg) found in the guidelines of JNC-4 through JNC-7 (Chobanian et al., 2003; "JNC 4," 1988; Pogue, Ellis, Michel, & Francis, 1996; Sheps, 1997). Although the increase in this threshold was recommended based on Grade A, strong scientific evidence by JNC-8 (James et al., 2013), it has not been without controversy among experts in the field. First, the use of a various BP treatment goals has resulted in a variation of reported HTN prevalence and control, even when evaluating the same dataset (Crim et al., 2012). Second, the increase in the threshold for this new BP goal precluded previously-eligible hypertensive patients from being eligible for care, potentially leading to negative health outcomes. Third, JNC 1 through JNC-7 guidelines were traditionally produced by the National Heart, Lung, and Blood Institute every 4 to 6 years, but JNC-8 was authored by the American Medical Association, whose guideline quality might be different (James et al., 2013). Therefore, it was important to look at the evidence presented by JNC-8 to understand the rationale



behind this change in BP treatment goal. A title search in the Google Scholar database aided in locating two original research articles cited by JNC-8.

### **Should SBP be decreased in hypertensive elders?**

Oibara and colleagues (2010) conducted a prospective randomized clinical trial (RCT) comparing the incidence of cardiovascular events between two groups of Japanese patients. The *strict* group had a target SBP goal of less than 140 mmHg, while the *moderate* group had a target SBP goal between 140 mmHg and 150 mmHg. The study sample comprised outpatients, ages 70 to 85, either gender, with seated SBP at or above 160mmHg and DBP less than 90 mmHg at two-visits within 2 to 4 weeks, and on antihypertensive drug therapy that could be converted to valsartan. Excluded from the study were patients with secondary HTN, malignant HTN, seated SBP at or greater than 200 mmHg or DBP at or greater than 90 mmHg, history of CVA, MI in past 6-months, planned or previous arterio-plastic surgery within 6 months of study, Stage-3 CHF or per New York Heart Association (NYHA) criteria, severe aortic stenosis or valve disease, atrial fibrillation (a-fib), atrial flutter, arrhythmia, renal dysfunction with serum creatinine at or greater than 2 mg/dl, severe liver dysfunction, hypersensitivity to valsartan, or subjects deemed inappropriate for study per the investigators' discretion (Ogihara et al., 2004). Utilizing a log-rank test, Kaplan-Meier, and Cox proportional hazard statistical analysis model, this study found that rates of adverse events were 18.2% in strict group vs. 17.9% in moderate group ( $p = .851$ ), concluding that strict BP control with SBP greater than 140 mmHg might not be associated to the prevention of cardiovascular disease (CVD) as compared with moderate BP control (SBP  $\geq$  140 but  $<$  150 mmHg).

#### Strengths of the study.

This study addressed a clinically significant question (Figure 1). The study profile was helpful with understanding participants' flow. Sample size calculations were present. Valsartan intervention, as well as primary and secondary end-point measures were described sufficiently.

#### Weaknesses of the study.

The age of the research subjects ( $M = 76.1$ ,  $SD = 4.1$ ) was too homogenous reducing its external validity, thereby making the results non-generalizable to populations younger than 72 years of age. The major confounders of BMI and alcohol use were not statistically controlled. Using this evidence as a rationale to increase the threshold of the SBP treatment goal for people over 50 years of age was not scientifically sound because the study did not cover groups aged 50 years - 72 years, major confounders were not considered and controlled for, and major differences exist between Japanese and American cultures.

#### Knowledge gap.

An optimal SBP goal for people over age 50 remained unknown.

#### **Assessing the optimal SBP treatment goal.**

The Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS) Study Group conducted a RCT to assess optimal SBP in Japan (JATOS Study Group, 2008). The study had two intervention groups with a target treatment goal of SBP less than 140 mmHg in the strict treatment group and SBP at 140 mmHg - 160 mmHg in mild treatment group. Two randomly assigned study samples

comprised of Japanese patients with essential HTN had a total of 2,212 subjects in strict treatment group (40% men, 60% women) and 2,206 in mild treatment group (38% men, 62% women). Subjects were aged 65 to 85 years with persistent SBP at or above 160 mmHg, received either no drugs or the same drugs for 4 weeks, and efonidipine could either be given additionally or substituted for one of the drugs received before study entry. Exclusion criteria were participants with DBP at or greater than 120 mmHg, secondary HTN, stroke, MI, angioplasty within past 6-month, angina requiring hospitalization, CHF at or greater than Class 2 per NYHA, a-fib, dissecting aneurysm of the aorta, occlusive arterial disease, hypertensive retinopathy, liver enzymes more than double the respective upper limits, fasting blood sugar at or greater than 200 mg/dl or A1C at or greater than 8 mg/dl, serum creatinine at or greater than 1.5 mg/dl, malignancy or collagen disease, and those deemed unsuitable for study (JATOS Study Group, 2008).

The study found (a) the primary endpoint events (e.g., brain, heart, kidney) occurred among 86 patients in both treatment groups; (b) the secondary endpoint events (e.g., discontinuation of treatment due to adverse events) indicated that 54 patients died in the strict-treatment group, compared with 42 patients in the mild treatment group; and (c) rates of morbidity and mortality from the primary end-point and its components did not differ significantly between the two treatment groups. Therefore, the study concluded that there was no significant difference in outcomes between the strict treatment group and mild treatment group (JATOS Study Group, 2008).

#### Strengths of the study.

This study addressed a clinically significant question. As shown in Figure 1, the flowchart depicting the allocation of subjects was well-defined. Sample size calculations were present and clear. The efonidipine intervention as well as the primary and secondary end-point measures were described sufficiently.

#### Weaknesses of the study.

The study was fundamentally flawed for the following reasons:

1. While the study has a strict and mild treatment groups, the RCT lacked a true control arm, one without any drug intervention; therefore, an objective comparison of the primary and secondary end events could not be. Comparisons between the two intervention groups were made relative to each other by manipulating the interventional efonidipine or additional drugs and the baseline medication used in each group was not equivalent.

The RCT design lacked detailed description about (a) the randomization allocation sequence (RAS) method in how RAS was generated, what mechanisms were used to implement RAS, and the party generating the RAS; (b) the person(s) enrolling participants; (c) the person(s) assigning participants to the intervention groups, (d) single blinded as only investigators were blinded and no detail about how they were blinded, what they were told about the study; (e) the exclusion criterion, “patients considered unsuitable as subjects were also excluded” (JATOS Study Group, 2008, p. 2117) increased the potential for selection bias, a threat to internal validity.

2. There was absence of information about inter-rater reliability among all end-point evaluators.
3. The sample characteristics did not include a mean and standard deviation for age in the strict and mild treatment groups.
4. BMI for strict treatment group ( $M = 23.6, SD = 3.4$ ) and mild treatment group ( $M = 23.6, SD = 3.5$ ) were non-generalizable to the population of the United States where most  $M \pm SD \geq 30 \pm 4$  is common based on 50 relevant articles reviewed.
5. Table 3 was missing evidence of significant p-values, making the results invalid.

In summary, this study had multiple internal and external validity concerns that suggest the results might be untrustworthy. Changing national HTN-management guidelines without strong evidence or rationale could present a disservice to the medical and research community, potentially misleading stakeholders in the HTN-management process.

Knowledge gap.

Optimal SBP as well as primary and secondary end-point events described by the study could also be assessed through a systematic review of RCTs, nonrandomized trials, and/or meta-analysis of studies on patient populations within the United States.

### **HTN Prevalence Rates and Risk Factors**

HTN is known as a disease of industrial society; its prevalence is low among hunters, herders, and traditional agricultural communities (Landsbergis, Dobson, Koutsouras, & Schnall, 2013). Prevalence rates for HTN are essential in measuring the benefits of prevention, detection, evaluation, and treatment. In 2010, the prevalence of

HTN among the world's adults aged 21-year or older (31.1%; 95% CI [30.0%, 32.2%]), with high-income countries (28.5%; 95% CI [27.3%, 29.7%]) compared to low-or-middle income countries (31.5%; 95% CI [30.2%, 32.9%]; Mills et al., 2016). From 2011 to 2014, an overall prevalence of HTN among United States adults aged 18-year or older was 29.0%, was similar among men (30.0%) and women (28.1%), increased with age (7.3% for 18-39-year-olds, 32.2% for 40-59-year-olds, 64.9% for 60 years or older), and the controlled HTN rate was only 53% among adults aged 18-39 (Yoon, Fryar, & Carroll, 2015). From 2009 to 2012, an age-adjusted HTN prevalence among U.S. veteran men was 34.4% (95% CI [29.9%, 39.2%]); 2.2% higher than civilian population (Fryar, Herrick, Afoul, & Ogden, 2016). In fiscal year 2010, HTN prevalence among U.S. veteran women aged 35-44-year-olds was 13%, 45-54-year-olds was 28%, and 55-64-year-olds was 42% (Vimalananda et al., 2013). A systematic review and meta-analysis found the prevalence of HTN among homeless adults in America was like the general population (Bernstein, Meurer, Plumb, & Jackson, 2015).

A comparison of male veterans to male non-veterans in the United States from 2009 to 2012 revealed that the prevalence of obesity was higher among male veterans (43% vs. 34%), yet similar in dyslipidemia (49%, 48%), diabetes (10% vs. 9%) and smoking (33% vs. 30%; Fryar et al., 2016). In one study of almost 2 million veterans aged 65 years or older, risk factors for CV multimorbidities of HTN, CAD, and dyslipidemia were higher in men (37.4% vs. 22.0%); also reported were the prevalence of HTN (85% men, 82% women), dyslipidemia (78% men, 72% women), and CAD (46% men, 28% women; Steinman et al., 2012).

A study by Fletcher et al. (2012) reported HTN control rates for veterans had improved 3% per year, to 76.3% over the 10-year period from 2000 to 2010. However, this study had major systematic biases. First, the definition of HTN (BP > 140/90 mmHg vs. BP  $\geq$  140/90 mmHg) was biased toward a higher HTN control rate based on JNC-7 guideline (Chobanian et al., 2003). Second, the definition of hypertensive as 3 or more days of elevated BP, rather than 2 or more days or 2 occasions, was biased toward a higher HTN control rate based on JNC-7 guideline. Third, the exclusion criterion of missing readings without reporting the percent of missing data was a potential risk for bias toward a higher HTN control rate. These risks for bias could have resulted in an inflated HTN control rate (76%) and was likely spurious considering the sample size included 582,881 veterans with HTN and 260,924 without HTN. Therefore, the study conclusion was invalid.

### **HTN Prevention Domain**

A search of the literature using key terms hypertension, prevention, qualitative, observational, longitudinal, cohort, quantitative, RCT, interventional, systematic review, meta-analysis and veteran in the databases of Academia Premier, CINAHL plus with text, Health Source: Nursing/ Academic Edition, Military, Google Scholar, and PsychInfo within past 5 years was performed to identify peer-reviewed journal articles pertaining to the HTN prevention domains within the framework. The search yielded 47 articles. After reading through the abstracts, only two articles were relevant to the focus of this study and they were selected for review. Additional articles were found from the

reference list in the selected articles. The addition was older than 5 years, but deemed relevant and are therefore included in this review.

### **HTN prevention strategy.**

Schmid and colleagues (2009) conducted a qualitative study to extract themes of the HTN prevention strategy among 28 hypertensive veterans with a history of stroke or transient ischemic attack. Utilizing a mixed method design and a focus group interview approach, this study identified themes of external support, medication adherence, routine development, BP monitoring, and HTN risk factor management (e.g., heart healthy diet, exercise, stress reduction), and take advantage of teachable moments.

#### Strength of the study.

(a) The study addressed an important issue with HTN prevention. (b)

Interviewing bias was decreased by utilizing three independent stroke researchers apart from the moderator to review and transcribe interview data. This also increased the validity of the study result.

#### Weakness of the study.

Risk for self-selection sampling bias might have existed. The small sample size within one region might be a risk to external validity of the study results.

#### Knowledge gap.

Despite protentional methodological weaknesses, the results were consistent with much of the evidence-based research on the JNC-7 (Chobanian et al., 2003).



### **Barriers of adherence to antihypertensive drug therapy.**

AlGhurair and colleagues (2012) reviewed 74 articles of patient's self-reported barriers to the adherence of antihypertensive medications based on survey instruments with attention to their psychometric properties. Adherence was defined as "the extent to which a person's behavior correspond with agreed recommendations from a healthcare provider" (Sabate, 2003, p. 3). The review found that most surveys addressed patient-related adherence (76%). Other barriers included therapy (29%), healthcare system or team (27%), socioeconomic (22%), and condition-related (8%) The review stated that the Morisky Medication Adherence scale (Morisky, Ang, Kardrousel-Wood, & Ward, 2008) was the most commonly used instrument (69% of survey studies), but only 20 out of 70 (39%) had established reliability and validity evidence.

#### Strengths of the study.

(a) The review addressed self-reported barriers of adherence to antihypertensive medication issue. (b) Both observational and experimental studies were included in the study design. (c) Five major bibliographic databases were used to identify relevant studies to be reviewed, likely encompassing all important studies. (d) Inclusion and exclusion criteria were stated clearly. (e) The World Health Organization Multidimensional Adherence Model was utilized to guide the study. (f) The tables were clear and well organized. (g) The conclusions offered direction for future research.

#### Weakness of the study.

Adherence lacks a theory-based operational definition and linkage to healthcare outcomes, including SBP/DBP.

Knowledge gap.

Future research should examine multidimensional adherence models to guide the measurement of barriers to adherence of HTN treatment to help stakeholders appreciate how to optimize treatments and reduce the burden of uncontrolled HTN. Most studies were poor in quality as only 39% out of 20 surveyed had evidence of validity testing (AlGhurair, Hughes, Simpson, & Guirguis, 2012).

### **Self-measured BP monitoring and BP control.**

Uhlig and colleagues (2013) conducted a systematic review and meta-analysis to summarize evidence of the effectiveness of self-measured BP monitoring (SMBP) in adults with HTN. The review included 52 prospective comparative SMBP studies versus usual care or an alternative SMBP intervention in persons with HTN and found that SMBP, with or without additional support, lowered BP compared with usual care, but the BP lowering benefits beyond 1 year was uncertain (Uhlig, Patel, Lp, Kitsios, & Balk, 2013).

Strengths of the study.

(a) The review addressed a clearly focused issue on the effectiveness of SMBP. (b) Inclusion and exclusion criterion were clearly stated. (c) The databases searched were broad enough to have included all important, relevant articles. (d) All articles included in the review were evaluated for quality. (e) The numerical BP results were reported appropriately with confidence intervals in two standalone tables.

Weaknesses of the study.

Although JNC-7 recommended SMBP with validated BP devices, this practice has not been popular for two reasons. First, most hypertensive individuals did not need SMBP, except for patients with white coat syndrome, persistent HTN, or orthostatic hypotension. Second, the accuracy of SMBP could not be guaranteed as most healthcare providers were reluctant to document the results of SMBP as a part of the patient's medical record).

Knowledge gap.

The validity of SMBP has been uncertain and should be used only if clinically indicated and at the clinician's discretion.

### **HTN Detection Domain**

A search of the literature using the key terms hypertension, detection, qualitative, quantitative, RCT, cohort, systematic review, meta-analysis, secondary HTN, drug induced, primary aldosteronism, renal artery stenosis, pheochromocytoma, coarctation of aorta, thyroid and parathyroid disease in the databases of Academia Premier, CINAHL plus with text, Health Source: Nursing/Academic Edition, Military, and PsychInfo within the past 5 years was performed to identify peer-reviewed journal articles pertaining to the HTN detection domain within the framework. The search yielded 138 articles. After reading through the abstracts, only one article was relevant to the focus of this study. The article was older than 5 years with smart-text search, but was deemed relevant and therefore included in this review.

### **Drug-Induced Hypertension**

Handler (2003) provided an in-depth discussion on secondary HTN specific to drug-induced HTN through a case study methodology. The case began with a history of present illness (HPI); the patient was a 59-year-old female who presented in a HTN clinic for persistent HTN (e.g., BP 180-200/80-110 mmHg between home and clinic for 6 months) in December 2001. Her past medical history (PMH) included 12 years of controlled HTN on HCTZ monotherapy, clonidine, and/or Felodipine for 6 months with no effect and Tylenol® for osteoarthritic knee pain. Her brother, a physician, prescribed Celebrex® 200 mg QD for her knee pain; she also reported taking various herbal medicines to enhance well-being. On physical exam (PE), she was an overweight female with BP 182/94 mmHg, HR 100 beats/min., heart and lungs sound normal, and 1-2+ ankle edema were noted. Laboratory included a urine analysis negative for proteinuria and a serum creatinine that was 1.2 mg/dl. The extent of polypharmacy was not appreciated until she was asked to bring in her pill bottles, including all prescription and over-the-counter medications. That is when it was discovered that she was taking Celebrex® and an herbal supplement containing ginger root. Once she stopped taking the Celebrex, her BP dropped to 138/86 at the 3-week follow-up appointment. Removal of Felodipine led to a resolution of her ankle edema and palpitation. Clonidine was tapered off subsequently.

Upon analysis, Handler (2003) linked two results from a meta-analysis that explored the association between nonsteroidal anti-inflammatory drugs (NSAIDs) and HTN among persons already on antihypertensive medications. One finding suggested

NSAID-induced BP increased from “6.10 mm for Naproxen, 4.77 mm for Indomethacin, 2.86 for Piroxicam compared to 2.20 for Sulindac and -0.30 mm for Ibuprofen” (Pope, Anderson, & Felson, 1993, p. 83). Another study reported an NSAID-induced BP increase of 6.2 mm and that Sulindac affected BP the least amount (Johnson, Nguyen, & Day, 1994). A greater risk for increased BP existed when patients took both NSAIDs and prescribed  $\beta$ -blocker concomitantly (Handler, 2003). Mechanism of NSAID induced HTN was associated with an “inhibition of synthesis of vasodilatory and natriuretic prostaglandins” (p. 83). Ginger root was thought to have some anti-inflammatory effect. The study concluded that high BP might occur with discontinuation of clonidine and/or methyldopa. In addition, surveying patients about their store-bought supplements was essential to ensure that patients were not inadvertently causing any secondary HTN.

#### Strengths of the study.

The study design was appropriate for addressing the NSAID-induced HTN issue. In both studies, the setting and subjects were representative of hypertensive veterans. The researcher clearly articulated his perspective, which was backed up by the data collection methodology (e.g., PHI, PMH, PE). The method of data analysis was valid when referring to findings from two previous meta-analyses. The result was relevant to patients and providers in healthcare settings and was transferable.

#### Weaknesses of the study.

The study lacked a clearly stated research question (e.g., Could Celebrex and ginger root induce HTN?).

Knowledge gap.

Many drugs were listed as potential for drug induced HTN, only a few have established case studies in the literature. More case studies are needed to establish solid scientific background for other drugs listed in the literature.

### **HTN Evaluation Domain**

A search of the literature using key terms hypertension, evaluation, qualitative, observational, longitudinal, cohort, quantitative, RCT, interventional, systematic review, meta-analysis and veteran in the databases of Academia Premier, CINAHL plus with text, Health Source: Nursing/ Academic Edition, Military, Google Scholar, and PsychInfo within past 5 years was performed to identify peer-reviewed journal articles pertaining to the HTN evaluation domains within the framework. The search yielded 38 articles. After reading through the abstracts, only a handful articles were relevant to the focus of this study and they were selected for review. Additional articles were found from the reference list in the selected articles. These additions were older than 5 years, but deemed relevant and are therefore included in this review.

#### **Longitudinal predictors of masked HTN.**

Skårn and colleagues (2015) conducted a longitudinal study with 10-20 years' follow-up to identify longitudinal predictors of masked HTN defined as normal clinic BP and hypertensive out-of-office. The study was relevant because masked HTN could not be revealed by routine office BP measurements but could still be associated with CVD events. HTN was defined as an average office BP at or above 140/90 mmHg; ambulatory HTN was defined as day time (06:00-22:00) SBP/DBP at or above 135/85 mmHg and at

night (22:00-06:00 hour) SBP/DBP at or above 120/70 mmHg; white-coat HTN was defined as BP at or above 140/90 mmHg in the office but normal out-of-office; sustained HTN was defined as BP at or above 140 mmHg both in the office and out-of-office settings. The study design included 100 Scandinavian men ( $M_{age} = 22, SD = 1$ ), healthy, and not on any medications. Subjects were recruited while attending compulsory medical screening at a military draft laboratory in Norway from 1991 to 2002; these readings served as the baseline. From January 2012 through November 2013, 17 years later, follow-up measurements were taken on subjects ( $M_{age} = 39, SD = 4$ ). Predictor variables included age, fasting blood sugar (FBS), total cholesterol, triglycerides, BMI, waist circumference (WC), daily smokers, office SBP/DBP, ambulatory SBP/DBP, white coat BP, persistent BP, HR, adrenaline at rest and during activity; data were collected by two people at baseline. A physician performed follow-up data collection. The study found that participants with high screening BP at baseline had a much higher likelihood of having masked HTN at follow-up (40%) compared to men with low screening BP ( $OR = 4.8, 95\% CI [1.7, 13.5], p < .05$ ).

#### Strengths of the study.

- (a) The abstract provided a concise summary of the main features of the report.
- (b) The introduction provided the rationale and aims for the study.
- (c) All tables and figures were clear, simple, and independent.
- (d) Key study variables were clearly operationally defined.
- (e) An effort of more than 17 years for this longitudinal study has been recognized and appreciated.

### Weaknesses of the study.

The cross-sectional study result was not transferable to patients in the United States for several reasons. (a) Operational definitions of ambulatory and masked HTN were inconsistent with JNC-7 HTN management guideline. (b) The study design lacked a detailed description of follow-up method, the study mentioned that subjects were not on any medications at baseline, yet omitted participants' medication status at follow-up, and the inter-rater reliability statistic was not addressed; however, two people were involved in the data collection process at baseline posing threats to internal and external validity. (c) There was only one follow-up measurement point in the rare longitudinal study; results could have been different with two or more measurements. (d) There was no power analysis for the statistical analyses used by the study. (e) Reliability and validity of the Smart Diet instrument in the original study and within the study sample were omitted, another threat to internal validity and ultimately could affect external validity. (f) There was no table or description of how the researchers controlled for major confounders (e.g., alcohol consumption, physical activity, diet, weight, BMI, medication) at baseline and at the final point of data collection. Nevertheless, one could view the introduction of masked BP as either a new challenge within the complex HTN control research arena or an unremarkable phenomenon considering that HTN research has yet to identify an optimal SBP for individuals with HTN.

### Knowledge gap.

The associations between adolescent and adult BP in longitudinal studies is needed as the literature on the topic is limited.



**Deep breathing: A test of the white coat effect.**

Tomičić and colleagues (2015) conducted a controlled clinical trial to evaluate the reliability of a deep breathing test to detect the white coat HTN phenomenon. The study sample consisted of hypertensive men and women who were age and gender stratified; 106 subjects from 53-72 years old in the intervention group and 108 subjects from 59-72 years old in the control group. Data were collected during outpatient visits. The control group had standard BP measurements and the intervention group had BP readings done after 30 seconds of slow, deep breathing for three or four cycles. Utilizing a receiver operating characteristic (ROC) curve methodology, the study found slow, deep breathing of 30 seconds for three or four cycles (DBT) was the best detection for white coat HTN. DBT was associated with a 15% or more reduction in SBP with a sensitivity of 94% (95% CI [72, 100]). A BP reduction of 8% or less could rule out white coat HTN with a specificity 78.4% (95% CI [64%, 85.9%]).

**Strengths of the study.**

(a) The abstract precisely captured the features of the main study. (b) The study design was helpful in advancing science on the topic.

**Weaknesses of the study.**

(a) The conclusions drawn were misleading as 78.4% specificity of the deep breathing test does not meet a reliability standard of 90% for a clinical test (Rice, 2013). (b) Deep breathing may cause hyperventilation-associated numbness and tingling, dizziness sensations.

Knowledge gap.

More innovative studies are needed to find a reliable clinical test to help differentiate white coat HTN from resistant HTN in primary care settings.

### **Diagnosis and treatment of resistant HTN.**

Waeber and colleagues (2014) published an article to discuss the issue of diagnosing and treating resistant HTN. The authors cited multiple studies in forming their conclusion that a systematic out of office BP recording by either 24-hour ambulatory BP monitoring or self-measurement at home were necessary to properly diagnose patient with resistant HTN (Waeber et al., 2014). For treating resistant HTN, these authors recommended a triple-drug regimen to include diuretic, blocker of the renin-angiotensin system, and calcium channel blocker to not only normalize BP, but to regress target organ damage and delay cardiorenal complications. Several definitions of terminology made by the author group were useful for HTN research. For example, uncontrolled and resistant HTN were similar in the definition of BP ( $\geq 140/90$  mmHg), but differed by the number of antihypertensive drugs patients took to lower their BP. In uncontrolled HTN, patients' BP remained above 140/90 mmHg regardless of the type and the number of antihypertensive agents taken, whereas in resistant HTN, patients' BP remained above 140/90 mmHg regardless of lifestyle measures and the concurrent use of three antihypertensive agents belonging to different classes with all drugs being prescribed at full dosage, including one diuretic (Waeber et al., 2014). Patients with white coat HTN were resistant to antihypertensive treatment (BP  $\geq 140/90$  mmHg) in the clinical setting, but normal when out of the office (Waeber et al., 2014).

#### Strengths of the study.

The authors, consisted experts in the field, provided a candid discussion from their review of the empirical literature.

#### Weaknesses of the study.

(a) This article was based on a literature review of original publications rather than being an empirical study. (b) The definition of uncontrolled HTN could overlap with the definition of resistant HTN; the number of antihypertensive drugs defined were vague. (c) The concepts of uncontrolled HTN, resistant HTN, and white coat HTN were similar in the context of HTN treatment and should be further developed. (d) The measurement of 24-hour ambulatory BP is labor intensive and home BP monitoring is potentially unreliable associated with calibration and or BP taking technique variabilities and cheating, raising validity concerns.

#### Knowledge gap.

More studies are needed to evaluate any overlap in defining the concepts of uncontrolled HTN, resistant HTN, and white coat HTN. In addition, more studies are needed to evaluate a sufficient way to diagnose and treat resistant HTN utilizing a behavior modification approach.

#### **Orthostatic hypotension and orthostatic HTN.**

Wecht and colleagues (2016) conducted a cross-sectional survey to investigate rates of prevalence in orthostatic hypotension (OH) and orthostatic hypertension (OHTN) and associated factors among U.S. veterans. A convenient sample of 286 veterans was collected at an urban VA medical center. Exclusion criteria included veterans who were

unable to stand for 10 consecutive minutes, had an illness, infection, or were pregnant at the time of recruitment. Outcome measures included heart rate and BP, collected with an automated sphygmomanometer BP cuff, and orthostatic symptoms were collected by a 6-item, 10-point orthostatic hypotension symptom assessment (OHSA) scale (Wecht et al., 2016). Utilizing univariate  $X^2$ , ANOVA, binary logistic regression, and logit calculation data analysis, this study reported that: (a) 14% of veteran participants had OH, 22% had OHTN, and 64% had normal BP (control group); (b) an increased prevalence of OH and OHTN among veterans with DM (27%) and HTN (63%); (c) veterans with OH were older than the control group and were taking more antihypertensive drugs than the control and OHTN groups; (d) the prevalence of OH increased with age, the OHTN was comparable in young (20-30) and old (70+) veterans (17% vs. 19% respectively), the severity of fatigue and dizziness increased in veterans with OH and OHTN compared to the reference group.

#### Strengths of the study.

(a) The title captured the study phenomenon and population involved. (b) The abstract provided a precise summary of the main features of the report. (c) The introductory paragraph provided sufficient background information and rationale for conducting the study and the purpose statement was clear. (d) Key study variables (e.g., OH, OHTN, orthostatic symptoms) were operationally defined. (e) Findings were presented appropriately.

Weaknesses of the study.

(a) The study design lacked detailed descriptions identifying who collected the data, the data collection period, the type of clinic, the number of interviewers, and the location of the interviews. While minor, these research design issues could create risks for bias. (b) The omission of reliability and validity data about the original OHSA scale with this type of study sample could pose a threat to internal and external validity. (c) The article did not reveal the identity of the person(s) analyzing the data. (d) a power analysis should have been included estimating the minimum required sample size. The cross-sectional study results from a convenience sample ( $N = 286$ ) without power analysis at a single site presented concerns with validity and credibility.

Knowledge gap.

Tests for the reliability and validity of an OHSA scale with the study sample could have been conducted with resulting indexes being reported; therefore, replicating the study could correct this methodological weakness.

#### **Patients' evaluation of appropriateness of HTN management.**

Morecroft and colleagues (2006) conducted a semi-structured interview to evaluate the appropriateness of HTN management to extract attributes from patients' perspectives. The purposeful sample of 28 patients (12 women, 16 men), ages ranging from 20 to 78-year-olds ( $M = 59$  years), with an average of 10 years of HTN treatment in East England were selected for the study. Findings reported that all patients considered their HTN management regimen appropriate with two attributes justifying their decision: explicit and implicit. Explicit attributes were those consciously known by patients (e.g.,

*relationship* with the General Practitioner [GP], *lowering of the BP*). Implicit attributes were those not consciously known by patients, but inherently meaningful to them (e.g., *anxiety with concern* of treatment and diagnosis, *explanation of consequences* from HTN treatment, *choice* with number of antihypertensive drugs, *side effects* experienced from taking antihypertensive drugs). The study suggested that having patients evaluate the appropriateness of their HTN treatment might be unsuitable as (a) patients might not be familiar with the concept of *appropriateness* in terms of their prescribed HTN treatment, (b) patients might not be knowledgeable of medical terminology, (c) patients might prefer to rely on their GP to interpret BP readings as *okay, as before, higher/lower* rather than taking personal responsibility.

#### Strengths of the study.

(a) The title suggested a phenomenon of patients' evaluation of the appropriateness of their HTN management using qualitative methodology. (b) The abstract provided a concise summary of the main features of the report. (c) The introductory paragraph provided sufficient background information with the rationale for doing the study. (d) The research aims and questions were explicitly stated. (e) Inclusion/exclusion criteria were appropriate. (f) The sample size was adequate for saturation of the themes. (g) The data collection method and audiotaped interview time (45-60 minutes) in patients' homes were adequate. (h) The figures detailing the interview questions, mind-map, and example of a pen portrait were helpful for readers to quickly grasp key points. (i) Findings were detailed, organized, logical, and consistent; the

quantitative findings were validated by member checking and were trustworthy. (j) The discussion was thoughtful and conclusions were thought provoking.

Weaknesses of the study.

The plethora of interview questions could be burdensome for some patients, but was not mentioned as a limitation.

Knowledge gap.

Additional similar studies should be conducted among VA patients and VA healthcare providers to gain these perspectives both qualitatively and quantitatively.

#### **Twenty-four-hour blood pressure variability.**

Pengo and colleagues (2015) conducted a 24-hour observational study to analyze the changes in 24-hour BP variability (BPV) in relation to determinants (e.g., age, sex, medication, absolute BP, nocturnal fall) among patients with controlled and uncontrolled BP. The justification for this study was based on the association between BPV, CV events, and mortality without known determinants. BPV was defined as the fluctuation of BP values among various measurements over a defined time that were influenced by behavioral, environmental, and humoral factors as well as neural central reflex stimuli. The study sample comprised 446 subjects (53% male, 47% female;  $M_{\text{age}} = 57$ ,  $SD = 16$ ), with essential HTN but without secondary HTN, who were recruited at an HTN clinic in Italy between December 2010 and March 2013. Outcome measures were 24-hour ambulatory BP (AMBp), daytime SBp/DBp, night-time SBp/DBp, nocturnal fall, dippers, non-dipper, extreme dippers, and 24-hour activity diary including time of meals, bed rest or sleep, and awakening times. Utilizing  $t$ -tests,  $X^2$ , Kruskal-Wallis test, Dunn's

multiple comparison test, and multiple linear regression, this study found (a) no significant mean differences in BPV between subgroups with controlled and uncontrolled BP; (b) 24-hour BPV significantly increased in patients with uncontrolled BP, especially at night; (c) the number of antihypertensive drugs used was not a predictor for BPV in patients with uncontrolled HTN; (d) more than 40% patients were incorrectly classified as resistant HTN rather than BPV. The conclusion was that absolute BP, nocturnal BP falls, and age were predictive of one's BPV.

#### Strengths of the study.

(a) The study examined a novel phenomenon associated with HTN control. (b) Reporting was concise. (c) Tables and figures were well organized and self-explanatory. (d) The discussion included a detailed explanation of the findings and associations with previous research studies.

#### Weaknesses of the study.

Study results were less credible for the following reasons. (a) The study design lacked a detailed description in inclusion and exclusion criteria, data collection procedure identifying who measured the 24-hour ambulatory BP and counted items in the 24-hour diary, operational definitions of key study variables (e.g., controlled BP, uncontrolled BP, absolute BP, resistant BP), power analysis to support the sample size. (b) The cross-sectional study design with data collection in 24-hours, then analyzed retrospectively, could result in over- or under-estimating relationships between predictors and outcome variables.



Knowledge gap.

This topic has been extensively studied for over 30 years. A systematic review or meta-analysis investigating the association between BPV, CV events, and/or mortality should be done to evaluate the significance of topic.

### **HTN Treatment Domain**

A search of the literature using key terms hypertension, treatment, qualitative, observational, longitudinal, cohort, quantitative, RCT, interventional, systematic review, meta-analysis and veteran in the databases of Academia Premier, CINAHL plus with text, Health Source: Nursing/ Academic Edition, Military, and PsychInfo within past 5 years was performed to identify peer-reviewed journal articles pertaining to the HTN treatment domains within the framework. The search yielded more than 200 articles. After reading through the abstracts, only a handful articles were relevant to the focus of this study and they were selected for review. Additional articles were found from the reference list in the selected articles. These additions were older than 5 years, but deemed relevant and are therefore included in this review.

### **DASH diet and body weight.**

Soltani and colleagues (2016) conducted a systematic review and meta-analysis to assess the effects of a dietary approach to stop HTN (DASH) on body weight and composition among adults. The 13 reviewed articles were captured from the databases of PubMed, EMBASE, Scopus, and Google Scholar through December 2015. This study found that the DASH diet significantly reduced body weight by  $-1.42 \text{ kg/m}^2$  (95% CI [-

2.03, -0.82]), BMI by  $-0.42 \text{ kg/m}^2$  (95% CI [-0.64, -0.20]) and waist circumference (WC) by  $-1.05 \text{ cm}$  (95% CI [-1.61, -0.49]) over a period of 8 weeks to 1 year.

#### Strengths of the study.

- (a) The study addressed a clearly focused issue. (b) The search of four bibliographic databases and inclusion of 13 articles adequately included important, relevant articles assessing the effect of DASH on weight and body composition in adults.
- (c) The table presentation was helpful for reviewers to grasp the study sample characteristics quickly. (d) There was no publication bias per Begg's and Egger's tests.
- (e) The results appeared to be in line with the JNC-7 guideline (Chobanian et al., 2003).

#### Weaknesses of the study.

Although the study reported a non-publication bias by funnel plotting, referring to a figure, that figure was missing from the report.

#### Knowledge gap.

The omission of a figure illustrating funnel plots for non-publication bias was a quality gap by the study. Replication of this study is necessary to confirm the study result.

#### **Body weight and blood pressure.**

Neter and colleagues (2003) conducted a meta-analysis of RCTs to estimate the effect of weight reduction on BP. A total of 25 RCTs published between 1966 and 2002 were included in the meta-analysis. This study found a net weight reduction of  $-5.1 \text{ kg}$  (95% CI [-6.03, -4.25]) by means of energy restriction and physical activity, reduced SBP by  $-4.44 \text{ mmHg}$  (95% CI [-5.93, -2.95]), and DBP by  $-3.57 \text{ mmHg}$  (95% CI [-4.88, -

2.25]). Significantly larger BP reduction were observed in populations with an average weight loss of more than 5 kg when compared to populations with less weight loss both for SBP (-6.63 mmHg, 95% CI [-8.43, -4.82] vs. -2.70 mmHg, 95% CI [-4.59, -0.81]) and DBP (-5.12 mmHg, 95% CI [-6.48, -3.75] vs. -2.01 mmHg, 95% CI [-3.47, -0.54]). The study concluded that weight reduction was important for HTN prevention and treatment.

#### Strengths of the study.

(a) The study addressed a significant HTN prevention and control issue in a scientifically rigorous manner. (b) The data sources were all RCTs; theoretically more reliable results when compared with non-RCTs.

#### Weaknesses of the study.

A risk of bias existed due to an extreme outlier indicated on the funnel plot of SBP (p. 879) and the results of meta-analysis might have concluded otherwise without the outlier article.

#### Knowledge gap.

(a) The relationship between weight reduction and BP, particularly beyond 1 year, remained unknown. (b) HTN research needed evidence from longitudinal studies of the relationship between weight reduction and BP with three to five observational time intervals over 3 to 5 years of follow-up. (c) The meta-analysis needed to pull data from longitudinal study greater than 2 years of weight reduction and BP change to be helpful to the future HTN research.

### **Sedentary behavior and blood pressure.**

Lee and Wong (2015) conducted a systematic review and meta-analysis to examine the association between time spent in sedentary behaviors and BP. The 31-articles in the review were published from 2002 to 2014. Out of the 31-articles, 21 of the studies (67.7%) used SBP and/or DBP as an outcome measure; those 21 studies reported an association between sedentary behaviors and SBP ( $n = 14$ ; 66.7%) or DBP ( $n = 11$ ; 51.1%). Sedentary behavior was defined by energy expenditure ( $\leq 1.5$  metabolic equivalent task) while in a sitting or reclining posture. The study found that an additional 1 hour of time spent in sedentary behaviors per day was associated with an increase of 0.06 mmHg of SBP ( $N = 108,228$ ; 95% CI [0.01, 0.11];  $p = .01$ ) and 0.20 mmHg of DBP ( $N = 107,791$ ; 95% CI [0.10, 0.29];  $p < .001$ ). The study concluded that self-reported sedentary behavior was associated with BP elevation.

#### Strengths of the study.

(a) The title suggested the study phenomenon and identified the report as a systematic review and meta-analysis. (b) The abstract provided a clear and precise summary of the features of the study. (c) The introductory paragraph provided a clear aim and study hypothesis. (4) There was no evidence of publication bias.

#### Weaknesses of the study.

A causal relationship of sedentary lifestyle on BP was not established.

#### Knowledge gap.

More longitudinal and RCT studies are needed to establish evidence of causal relationships between sedentary behavior and BP.

### **Effects of flaxseed consumption on blood pressure.**

Khalesi and colleagues (2015) conducted a systematic review and meta-analysis to assess the effects of flaxseed consumption on BP. Eleven RCT and non-RCT articles were reviewed utilizing MEDLINE, CINAHL, and Cochrane Library Central published through July 2014. This study found that flaxseed supplementation reduced SBP (-1.77 mmHg; 95% CI [-3.45, -0.09];  $p = .04$ ) and DBP (-1.58 mmHg; 95% CI [-2.64, -0.52];  $p = .003$ ). When consuming whole flaxseed, the DBP reduction was significantly greater (-1.93 mmHg; 95% CI [-3.65, -0.21];  $p < .05$ ); for durations of 12 week or longer, the DBP reduction was even greater (-2.17 mmHg; 95% CI [-3.44, -.89];  $p < .05$ ). Conclusions indicated that flaxseed consumption lowered BP slightly and the benefit was greater when consumed as whole seed for 12 weeks or more.

#### Strengths of the study.

(a) The study title identified the report as a systematic review and meta-analysis of controlled trials. (b) The abstract provided a precise summary of the study. (c) The introductory paragraph included background information, a rationale for the review, and study objectives. (d) The methodology included the review registration number (CRD42014010248), eligibility criteria, inclusion/exclusion criteria, information sources, search strategies, process of study selection, data extraction, and quality assessment protocols. (e) Key variables were operationally defined based on JNC-7. (f) Figures and tables were clear and independent. (g) Results were detailed showing each study's sample characteristics. (h) The risk for bias was low with Rosendal scores between 50% and 93% ( $> 60\%$  = excellent) for the selected articles. (i) Individual study results were

displayed in a forest plot. (j) The review gave direction for future research. (k) The review could serve as an exemplar of systematic review and meta-analysis.

Weaknesses of the study.

The duration of flaxseed consumption (3-48 weeks) was inadequate for evaluating its long-term benefit (> 1 year) for SBP/DBP reduction.

Knowledge gap.

(a) Potential side effects of flaxseed supplement should be studied among VA and non-VA populations. (b) Qualitative study is needed to explore the mechanisms of how flaxseed influences changes in BP (Khalesi et al., 2015).

#### **Meaning of antihypertensive drug therapy.**

Hultgren and colleagues (2014) conducted a qualitative study examining the meaning of antihypertensive drug therapy among hypertensive patients at a primary care clinic in Western Sweden. The study sample consisted of a purposive sample of 10 subjects ( $N = 6$  men, 39-68 years old,  $M = 50$  years;  $n = 4$  women, 51-66 years old,  $M = 59$  years) with various occupational backgrounds and on HTN treatment from 1 1/2 months to 15 years. This study revealed that patients' experience with antihypertensive drug therapy was a process where attitudes and behaviors changed from *resistance* to medication (e.g., worry, side effects, lack of autonomy), to *rescue* medication (e.g., desire for life style changes), to *normal* medication (e.g., trust healthcare).

Strengths of the study.

(a) The articles revealed many words useful for instrument development (e.g., symptom, headache, dizziness, altered sensation, sexual impairment, side effect, dislike,

fear, knowledge, attitude, accept or resist, stroke, brain bleeding, heart infarction, worry, lack of autonomy or control, normal or perfect, confidence). (b) Information on informants clarified the sample characteristics. (c) The model presented clarified the themes developed by the study.

#### Weaknesses of the study.

(a) The description of the phenomenological study design did not include the time needed to complete the study. (b) The claim of increased validity utilizing all three authors in the analysis of data could not be confirmed without evidence of intercoder agreement or cross-checking (Creswell, 2014). (c) The discussion section included new ideas that would be more appropriate in the literature review. (d) The qualitative generalizability of the study results may be limited to Swedish population rather than U.S. veterans (Creswell, 2014).

#### Knowledge gap.

No studies have explored the meaning of antihypertensive drug therapy from the perspective of U.S. veteran patients.

#### **Meaning of adherence to antihypertensive drug treatment.**

Lahdenperä and Kyngäs (2001) conducted a qualitative study to describe hypertensive patients' treatment compliance and its deeper meaning in terms of "intention, activity, responsibility and collaboration" (p. 189). The study included 21 subjects, 9 males and 12 females ( $M = 46$  years, range 32-63 years), who were diagnosed with HTN, on either antihypertensive medication or no medication for 1 year with a diagnosis of HTN for 12 to 18 months. Patients were recruited by telephone, based on

the information from a previous study, and interviewed at either a municipal health care center or a Department of Nursing Health Administration in Finland. The study revealed four levels of compliance (i.e., subconscious, cognitive, action, attitudinal) and attitudes toward HTN treatment (i.e., careless, serious, adjusted well, frustrated). The authors recommended that healthcare professionals listen to patients' various levels of compliances and attitudes with regards to their HTN treatment.

Strengths of the study.

(a) The title suggested a phenomenon of compliance by hypertensive patients and their attitudes toward their illness. (b) The abstract provided a concise summary of the main features of the report. (c) The problem statement indicated that hypertensive patients often did not have any symptoms, did not feel ill, did not see any reason to treat themselves and provided the rationale to conduct this study. (d) The key concept of *compliance*, defined as "patients work to maintain their health in accordance with health regimens and in collaboration with healthcare professionals" (Lahdenpera & Kyngas, 2001, p. 190), emphasized that patients' responsibility was consistent with the theory of self-care agency (Renpenning & Taylor, 2003). (e) Inclusion and exclusion criteria were appropriate. (f) Sample size seemed to be adequate to gain a saturation of themes; the setting was appropriate. (g) The 45 to 60 minutes allowed for audiotaped interview was adequate. (h) The patients' definition of the nursing role was "not that of a partner in care, but that of a provider of nursing services congruent with the patient's identified goals" (Lahdenpera & Kyngas, 2001, p. 193) was consistent with self-care deficit theory (Renpenning & Taylor, 2003). (i) Consistent with the social learning theory (Bandura,



1971), the levels of compliance and attitudes toward HTN treatments were validated by the authors reviewing research materials multiple times and utilizing a two-phased categorization data analysis approach, making it trustworthy and potentially useful in the development of an adherence instrument in the future.

Weaknesses of the study.

Validity for the study could be further strengthened with triangulation.

Knowledge gap.

No qualitative study has elicited the meaning of adherence to antihypertensive drug therapy from patients and primary healthcare providers' perspectives within the VA system; these studies would be important for instrument development in the future.

#### **Family nurse practitioners' experience with pre-HTN care.**

Hernandez and Anderson (2012) conducted three-dimensional qualitative inquiries to explore family nurse practitioners' (FNP) experience of caring for pre-HTN patients. Interviewing eight FNPs, five males and three females with 4 months to 18 years of practicing experience in urban, rural, and suburban areas. This study revealed that caring for pre-HTN patients was a complex and multifaceted experience and three major themes emerged: (a) FNPs often failed to address the pre-HTN condition due to a time constraints, patients had other urgent health problems that needed to be addressed at that visit, or lack of reimbursement for addressing pre-HTN due to insurance or lack of public support; (b) FNPs experienced frustration and bewilderment with their role identity due to a conflicting practice model (holistic vs. medical), FNPs practiced the medical model almost exclusively because of reimbursement; (c) FNPs encouraged a bridging model of

hope (e.g., ability to promote cardiovascular health by being a good listener, educator, follow the JNC-7 guidelines) for pre-HTN patients despite multiple barriers (e.g., sense of betrayal by patients who promised to follow lifestyle modifications, no-show for follow up appointments); this frustration could be avoided by not addressing pre-HTN issues with non-compliant patients.

#### Strengths of the study.

The result of the study was a powerful, well-written story. (a) The methodology was appropriate for addressing the research goal. (b) The purposive sampling method provided diverse FNP experts with rich narratives. (c) Data collection was completed in 30-90 minutes in a private, mutually-agreed upon location with semi-structured interview method; an appropriate framework. (d) Results of this study were trustworthy; themes were consistent with findings of similar qualitative studies.

#### Weaknesses of the study.

It would be better if this was a mixed study design in that the magnitude of themes (e.g., patients' refusal to discuss lifestyle modification, no show at HTN follow-up clinic) may be addressed simultaneously. HTN control research needs improved data collection for precision in targeting the problem.

#### Knowledge gap.

No qualitative study of HTN detection with sample of VA patients or VA healthcare providers could be found. Evidence suggests a sufficient lack of quantitative study detecting associations between refusing lifestyle modifications and the magnitude of no shows at follow-up with SBP and/or DBP.

## **HTN Control Domain**

A search of the literature was performed utilizing the databases of Academia Premier, CINAHL plus with text, Health Source: Nursing / Academic Edition, Google Scholar, and PsychInfo within past 5 years to identify peer-reviewed journal articles pertaining to the domain of HTN control. Key terms included *hypertension, control, blood pressure, systolic, diastolic, BP, age, sex, race, ethnicity, religion, religiosity, education, health literacy, disability, insurance, copay, socioeconomic, demographic, tobacco, smoking, alcohol, DASH, exercise, caffeine, coffee, stress, job strain, OSA, diabetes, A1C, dyslipidemia, HDL, obesity, BMI, depression, anxiety, PTSD, antihypertensive, medication adherence, clinic visit, end organ damage, stroke, transient ischemic attack, heart failure, coronary heart disease, myocardial infarction, CABG, CKD, and veteran*. This approach yielded from zero to over one hundred articles under each category per the HTN control conceptual framework. After screening the abstracts, a few articles with high level of relevancy were selected for review. Additional articles were found from the reference list in the selected articles. These additions were older than 5 years, but deemed relevant and are therefore included in this review.

### **Socio-demographic variables impacting HTN control.**

#### ***Age and blood pressure.***

Presently, no credible evidence could be found to suggest a statistically significant association between age and BP utilizing either systematic review and/or meta-analysis.

***Sex and blood pressure.***

No credible evidence showing a statistically significant sex differences in SBP or DBP utilizing systematic review and/or meta-analysis.

***Racial discrimination and HTN.***

Dolezsar and colleagues (2014) conducted a comprehensive, systematic review to examine the association between racial discrimination and HTN. Discrimination was assessed utilizing three validated tools. In 44 articles averaging 742 participants per study, evidence suggested a small, significant association between perceived discrimination and HTN among hypertensive Black males with low education.

Strengths of the study.

(a) The title described the study phenomenon and identified the report as a systematic review. (b) The abstract providing a concise summary. (c) The literature review had adequate background information and rationale. (d) The study aim was clearly stated. (e) Inclusion and exclusion criteria appeared to be appropriate. (f) Tables and figures were well-defined. (7) Key study variables were operationalized.

Weaknesses of the study.

(a) The study lacked article synthesis (e.g., author's name, year of publication, population, sample size, instruments, scores, confounders, outcome measures). (b) The study lacked an objective finding describing the measurable effect of racial discrimination on SBP or DBP by mmHg. Methodological weaknesses yield less credible study findings.

Knowledge gap.

No credible evidence showing the mean office BP or 24-hour ambulatory BP differences among diversional racial and ethnic groups can be found in the literature.

***Religious service attendance and blood pressure.***

Bell and colleagues (2012) conducted a descriptive, correlational, cross-sectional study to examine the association between religious service attendance (RSA) and BP among three ethnic groups. Utilizing survey data from the 1994 National Center for Health Statistics, the study initially enrolled a total of 18,825 participants aged 20 or older through home interviews and medical examinations. After excluding participants who were pregnant, had a heart attack, CHF, CVA and those who failed to answer an interview question regarding the frequency of RSA, 12,488 remained for the final data analysis. Mean and proportional differences of RSA were compared utilizing *t*-tests and  $X^2$  tests. Associations between RSA and HTN (yes/no), as well as SBP and DBP, were examined through logistic regression modeling. The study found no relationship between RSA and HTN among Mexican-Americans, and RSA was inversely associated to SBP for all three ethnic groups (i.e., White, Black, Mexican-American), but more so for Whites and Blacks when compared with Mexican-Americans.

Strengths of the study.

The study addressed a sensitive yet important association between RSA and BP. The abstract provided a balanced summary of how the study was conducted and the research findings. The study utilized tables to explain the results, making it easier for

readers to understand the statistical analyses performed in the study. The study provided direction for future research on the topic.

#### Weakness of the study.

The study lacked clearly defined inclusion criteria and the design lacked a detailed description of (a) relevant dates (e.g., beginning and end, length of time needed to recruit 18,825 participants), (b) data collection procedures (e.g., who measured BP, brand of BP equipment), (c) 34% attrition rate, (d) confounders (e.g., social support, stress coping), (e) power analysis to justify  $N = 12,488$  for logistic regression model with three IV (i.e., ethnicity, RSA, sex), a major threat to statistical conclusion validity. The reported statistical method of *t*-test for mean SBP and DBP differences among 3-ethnic groups, gender, and religious service attendance was questionable. A more appropriate statistical analysis method should have been factorial multivariate analysis of covariance (MANCOVA). If the author group conducted multiple *t*-tests, interpretation of the results would be at a high risk for type I error. *T*-tests do not allow testing of interactions and main effects, but were reported in the tables, thereby making the chance of a type I error unlikely. Finally, the study oversimplified the complexity of religion study. It would have been more meaningful had religion construct were multidimensional rather than unidimensional as measured by church attendance only.

#### Knowledge gap.

Although much research has been conducted to examine relationships between religion and HTN, most studies have major methodological weaknesses yielding findings at high risk for bias. No systematic review or meta-analysis investigating the relationship

between religious involvement and BP could be found. Per Gallup (2016), 70% Americans identify as Christian; 53% reported that religion was very important in their lives, suggesting a need to conduct research in this area. Further study is needed to investigate the role of religion in BP control and/or HTN self-management as well as the impact of religious involvement on BP changes among VA and non-VA population comparison.

***HTN education program and blood pressure.***

Lauziere and colleagues (2013) conducted a quasi-experimental pilot study to investigate changes in SBP and DBP associated with a HTN education program. Participants were recruited from one physician's office in Southeastern Canada between September 2008 and December 2010. Participants were 20 to 70 years of age with HTN, French-speaking, no prior exposure to HTN education (e.g., HTN risk factors), and capable of participating in a HTN education program during the 6-month study. Patients with DM, CVD, renal disease, and pregnancy were excluded from the study. IVs were weight, BMI, WC, lifestyle (20-item instrument), quality of life (20-item instrument), dietary habit (15-item instrument); DVs were SBP and DBP. Covariates or confounders were age, number of years since diagnosis of HTN, gender, level of education, household income, and employment status. Statistical methods employed by the study included (a) *t*-tests and Fisher's exact tests comparing the intervention and usual care group's BP differences, (b) MLR to assess the change of BP within the HTN education intervention group from baseline to 6 months, (c) Poisson regression to assess change of physical activity and knowledge scores before and after HTN education intervention, (d)

polynomial logistic regressions to assess between group differences in smoking and alcohol use over a follow-up period. The study found a significant reduction of SBP in the intervention group compared with the regular care group ( $p < .05$ ) without between-group differences in weight, BMI, WC, lifestyle, QOL, and dietary habits.

#### Strengths of the study.

The study title indicated the study design and HTN phenomenon. The abstract provided a concise summary of the main features of the study report. The introductory paragraph provided sufficient background and rationale for the study. The purpose statement was well-defined and the methodology was described in detail.

#### Weaknesses of the study.

One obvious weakness of the study was the small sample size of the intervention group ( $n = 21$ ) and regular care group ( $n = 19$ ), which narrowed options of statistical analysis with MLR, Poisson regression, and LR models down to zero with five IVs. Lack of power associated with small sample size could explain the negative finding of between-group differences. Another weakness appears to be biased higher baseline SBP/DBP in the intervention group compared with the regular care group, associated with systematic sampling without blinding procedure, allowing for a significant reduction in BP with medication therapy in the intervention group, not the usual care group. The major confounder was not statistically controlled. Additionally, the 20-item-lifestyle, SF-36 quality of life, and 15-item-dietary habits instruments were not validated before they were used in the study. Finally, an intervention of 6 months was too short to be credible for sustained effects on SBP and DBP changes.



Knowledge gap.

The association between HTN education program and BP is limited.

***Functional disability and blood pressure.***

Qualitative study could reveal the phenomenon in which patients with functional disabilities cannot open antihypertensive pill bottles, thereby affecting one's BP control.

Quantitative study, however, has yet to associate this inability to one's BP. There has been no systematic review or meta-analysis on this topic.

***Insurance expansion impact undiagnosed and uncontrolled HTN.***

Hogan and colleagues (2015) conducted a secondary analysis utilizing data from the 1999-2012 National Health and Nutrition Examination Survey to examine associations between health insurance through the Affordable Care Act with the diagnosis and management of DM, dyslipidemia, and HTN. The study sample consisted 28,157 adults aged 20 to 64 years (52% male); 6,366 were diagnosed with HTN and 1,531 with undiagnosed HTN. Uncontrolled HTN was operationally defined per JNC-7 guideline. Diagnosed HTN was operationally defined by a "yes" answer to the question "have you ever been told by a doctor that you had high blood pressure?" (Hogan et al., 2015, p. 1555). Utilizing an epidemiologic data analysis strategy, this study found having health insurance was associated with a 9% higher probability of having a HTN diagnosis compared with uninsured people and insurance was associated with lower SBP (-2.9 mmHg) than people without insurance. IRB oversight and approval was done by the National Center for Health Statistics. The work was supported by the National

Institute of Diabetes and Digestive and Kidney Diseases (Grant No. 1R01 DK090435) and the first author was a member of the World Health Organization.

#### Strength of the study.

The abstract provided a precise summary of the features in the study report. The study methodology was described in detail. The statistical analysis method that utilized Mahalanobis' distance to match variables for reducing potential confounders and match propensity scores for reducing risks of systematic sampling bias. Confounders were statically controlled. Sensitivity analysis separated private insurance from ACA coverage or non-insurance. Results were appropriately represented.

#### Weakness of the study.

There was no power analysis to justify the sample size ( $N = 28,157$ ) for the MLR model with four IVs (i.e., controlled HTN, uncontrolled HTN, A1C, total cholesterol), a threat to statistical analysis validity. The SBP difference between insured to uninsured cases could be clinically irrelevant.

#### Knowledge gap.

No knowledge gap; however, there is a need for risk-benefit analysis associated with treating elders at BP goal (140/90 mmHg). There is also a need to analyze the benefit of treating pre-HTN and conduct a cost analysis associated with pre-HTN treatment (Moise et al., 2015).

#### ***Copayment and medication adherence.***

Sinnott and colleague (2013) conducted a systematic review and meta-analysis to quantify the risk of medication non-adherence in publicly insured populations with

copayments. This is relevant because adherence to antihypertensive medication has been associated to HTN-treatment success in RCT (Alhalaiqa, Deane, Nawafleh, Clark, & Gray, 2012). The analysis comprised four studies of Medicare insurance plans and three studies of copayment increase in the VA healthcare system in older men and women ( $M = 72$  years, Range = 65-85 years) with copayments from \$5-7\$. This study found significant evidence of non-adherence to medicines among Medicare and VA insured beneficiaries where copayments for medications were necessary (OR = 1.11, 95% CI [1.09, 1.14],  $p < .001$ ).

#### Strength of the study.

(a) The study title was a systematic review and meta-analysis. (b) The abstract provided a concise summary of the features in the study report. (c) The methodology that covered detailed eligibility criteria, information sources, search strategies, study selection, data collection processes, summary measures, synthesis of results, and risk of bias across studies. (d) Results were detailed and appropriate. (e) The discussion was detailed, balanced, and candid. (g) The study resulted in important policy implications, was trustworthy, and was relevant to the veterans' population.

#### Weakness of the study.

No major validity concerns could be seen.

#### Knowledge gap.

A new knowledge gap was identified with this systematic review and meta-analysis: the association between socioeconomic status and non-adherence to antihypertensive drugs was likely due to the lack of comprehensive socioeconomic

measures (Alsabbagh et al., 2014). To fill this gap, research for HTN control should collect actual income and copayment data rather than nominal or ordinal data as HTN has a higher prevalence in low-to-moderate socioeconomic groups.

### **Lifestyle as a variable impacting veterans' HTN control.**

#### ***Smoking and arterial stiffness.***

Scallan and colleagues (2010) conducted a systematic review to assess a combined effect of HTN and smoking on arterial stiffness, considering the role of large arteries in the circulation of blood to the periphery. In the study reviewing four articles published between 1985 and 2008 in English, HTN and smoking were independent detrimental factors for raising arterial stiffness; the combined effects were even greater.

#### **Strengths of the study.**

(a) The study addressed a public health concern. (b) The introductory paragraph provided sufficient background information and rationale for the review. (c) Inclusion criteria were clear and strict, decreasing the risk for biased outcomes. (d) Figures and tables stood alone. (e) The study reviewed both the acute and chronic effects of smoking on arterial stiffness. (f) Major confounders were statistically controlled in addition to strict inclusion criteria. (g) Conclusions included the need for future research.

#### **Weaknesses of the study.**

(a) The study title did not identify the report as a systematic review. (b) The abstract lacked description of the data source and study participants. (c) The efforts from following up the reference lists, personal contacts with experts, searching for unpublished and non-English language studies were not evident in ensuring that all important and

relevant studies were included. (d) The four articles reviewed were all cross-sectional; the study would have been stronger if at least one RCT article were included in the review. (e) The study lacked evidence of assessing individual article quality and overall publishing bias. Higher quality systematic review and/or meta-analysis on the topic would improve trustworthiness.

Knowledge gap.

Study is needed to examine smoking cessation therapy combined with the appropriate antihypertensive medication for greater improvement of arterial stiffness among veteran smokers with HTN.

#### ***Smoking and blood pressure.***

Despite smoking being listed as an independent risk factor of essential HTN by multiple JNC guidelines, no systematic review or meta-analysis has examined the association between smoking and BP among any population in the literature. Existing studies were primarily cross-sectional surveys; major findings supported the notion that smoking or chewing tobacco affected BP (Hughes, Leong, Sothy, Lun, & Yed, 1993) or did not affect BP (Li, Tong, Wang, Lin, & Zhang, 2010; Pandey, Shreevastva, & Neupane, 2014; Thuy et al., 2010). Few interventional or longitudinal studies on this topic could be found in scientific literature.

#### ***Alcohol and blood pressure.***

Briasoulis and colleagues (2012) conducted a systematic review and meta-analysis to determine the effects of dose-response alcohol consumption on the long-term risks of developing HTN among non-veteran men and women. A total of 16 prospective

studies ( $N = 33,904$  men) were chosen from the databases of MEDLINE, PubMed, Embase, and Cochrane Library for Central Register of Clinical Trials (Briasoulis et al., 2012). This study found a dose-response alcohol consumption between 10 gm /day and 11-20 gm /day tended to increase the risk of HTN (RR = 1.03, 95% CI [0.94, 1.13],  $p = .51$ ; RR = 1.15, 95% CI [0.99, .33],  $p = .06$ , respectively) and that heavy drinkers (31-40 gm/day) was significantly associated with an increased risk of HTN (RR = 1.77, 95% CI [1.39, 2.26],  $p < .001$ ).

#### Strength of the study.

(a) The study addressed a clearly-focused dose-response alcohol consumption and HTN risk. (b) The bibliographic databases used were credible and inclusive of all important studies. (c) Inclusion and exclusion criteria were included. (d) A quality assessment of all included studies was performed. (e) The authors of reviewed studies were contacted if data was unclear; publication biases were checked and found to be low risk. (f) Findings were presented with odds ratio and 95% CI, precise, and valid including consistency with several prior studies.

#### Weakness of the study.

(a) The inclusion of studies using 160/95 mmHg as HTN definition reduced the number of HTN cases, biasing results away from the null hypothesis; a threat to internal validity. (b) Measuring alcohol consumption by *grams per day* was less common than *drinks per day*; however, it is a more accurate measure. The study results are less credible due to the HTN definition; not consistent with JNC guidelines.

Knowledge gap.

(a) Excessive alcohol consumption and alcohol withdrawal could raise BP and HR significantly in patients going through alcohol overdose and detox. (b) There is a lack of consensus for measuring alcohol consumption in terms of units.

***DASH diet and blood pressure.***

Saneei and colleagues (2014) conducted a systematic review and meta-analysis of 17 RCTs with 2,561 participants to assess the magnitude of the DASH diet on adults' BP. This study reported that the DASH diet significantly reduced SBP by 6.74 mmHg (95% CI [-8.25, -5.23],  $I^2 = 78.1\%$ ), DBP by 3.54 mmHg (95% CI [-4.29, -2.79],  $I^2 = 56.7\%$ ) with the mean baseline SBP and DBP explaining 24% and 49% of the variance among the studies.

Strengths of the study.

(a) The abstract summarized the main features of the study. (b) The literature review provided sufficient background knowledge, rationale, and aims for the review. (c) The study followed a preferred reporting for systematic review and meta-analysis (PRISMA) protocol. (d) Inclusion and exclusion criteria were clearly elucidated. (e) Multiple databases were searched and the searching strategy was described clearly. (f) Figures and tables were clear and distinct. (g) The risk of publication bias was checked. (h) Results contributed significantly to HTN research databases.

Weaknesses of the study.

Minimal risks for bias or threats to validity were found in the study.

Knowledge gap.

None could be identified.

***Physical activity and blood pressure.***

Semlitsch and colleagues (2013) conducted a systematic review and meta-analysis to evaluate the long-term effects of increasing physical activity comparing with no activity in adults with essential HTN. Outcome measures were all causes of mortality, cardiovascular morbidity and mortality, end stage renal disease, quality of life, and adverse events. This study has included three high-quality, systematic reviews published between 1997 and 2009. Additionally, included were nine RCTs with at least 24 weeks of follow-up evaluation for the effects of increased physical activity on BP among adults, published by September 2012. This study was unable to form definitive conclusions regarding the effects of increasing physical exercise on BP because of the following limitations: (a) 50% of the included RCTs had small sample sizes, approximately 20 participants per group; (b) more than two-thirds of the studies included RCTs found to be at high risk for bias.

Strengths of the study.

- (a) The abstract provided a concise summary of the main features of the report.
- (b) Utilized traditional methodology without deviation from the standards for a systematic review and meta-analysis.
- (c) The presentation of results included tables that were of sufficient detail and quality.
- (d) Discussion was thorough, balanced, and candid.
- (e) Conclusions offered direction for future research.



Weaknesses of the study.

Minimal risks for bias or threats to validity were found in the study.

Knowledge gap.

Figures illustrated that high quality studies were rare; approximately 99% of studies were low in quality. Nonetheless, the effects of increasing physical activity on BP reduction among hypertensive individuals remained unknown. High quality RCTs are needed with large sample sizes to exam the effects of physical exercises on CV risks and benefits among hypertensive individuals.

***Coffee, blood pressure, and cardiovascular disease risk.***

Mesas and colleagues (2011) conducted a systematic review and meta-analysis to assess (a) the acute and long-term effect of caffeine and coffee intake on BP and (b) the association between habitual coffee consumption and risk of cardiovascular disease among hypertensive individuals. The study included five trials examining the acute effects of caffeine on BP, three trials exploring the long-term effects of coffee intake on BP, and seven cohort studies investigating the association between habitual coffee consumption and cardiovascular events, all published by April 2011. The study concluded that caffeine intake produced an acute increase in BP for 3 hours or more, but there were no association between long-term or habitual coffee consumption and an increased BP or risk of cardiovascular disease in hypertensive individuals.

Strengths of the study.

- (a) The abstract provided a precise summary of the features of the study report.
- (b) The introductory paragraph provided sufficient background information and rationale

for doing the study. (c) The study methodology followed PRISMA and MOOSE protocol. (d) The key variable of HTN was operationally defined based on JNC-7 (Chobanian et al., 2003). (e) The figures and tables were clear and independent. (f) Results were detailed and depicted each study sample's characteristics for which data were extracted. (g) The study had strong external validity with no publication bias, per Begg's funnel plot and Egger's test. (h) The conclusion that coffee intake had no long-term effect on BP was consistent with the findings of another meta-analysis (Zhang, Hu, Caballero, Appel, & Chen, 2011). (i) The study results included important practice implications, suggesting that the practitioner ask about caffeine intake prior to measuring the patient's BP.

#### Weakness of the study.

(a) The unit of coffee intake in milligrams was uncommon in the literature and difficult to measure in everyday experience. (b) Mechanisms of caffeine raising BP for 3 hours or more after ingestion (dose-response) was not elaborated further in the review.

#### Knowledge gap.

(a) The need to study the dose-response relationship between coffee intake and BP increase among VA and non-VA patients is indicated. (b) The effects of coffee or caffeine on the degree of BP control among hypertensive patients should include possible variations in the type of antihypertensive medication (e.g., ACEI, CCB, BB) as such evidence could help adapt recommendations about coffee consumption in hypertensive patients.

***Job strain and ambulatory blood pressure.***

Landsbergis and colleagues (2013) conducted a meta-analysis and systematic review to assess the relationship between job strain and ambulatory BP. The study reviewed 29 articles, including 22 cross-sectional, one case control, and three cohort studies. This study found that a single exposure to job strain was associated with higher work SBP (3.43 mmHg; 95% CI [2.02, 4.84];  $p < .001$ ;  $I^2 = 62.3$ ) and DBP (2.07 mmHg; 95% CI [1.17, 2.97];  $p < .001$ ;  $I^2 = 42.3$ ). Associations were stronger in men versus women and in studies of broad-based populations with limited occupational variance; the study suggested that job strain be assessed to reduce one's CV risk.

Strengths of the study.

(a) The title identified the main study phenomenon, meta-analysis, and systematic review. (b) The methodology followed traditional meta-analysis protocol as well as being thorough and balanced. (c) The presentation of results was clear and precise. (d) The discussion was fair and balanced. (e) Directions for future research were offered. (f) The study result is trustworthy.

Weaknesses of the study.

The abstract was missing background, objective, data source, study eligibility criteria, participants, intervention, study appraisal, and synthesis method.

Knowledge gap.

Multiple gaps exist based on suggestions by the authors.

**Secondary HTN impacting veterans' HTN control.*****Obstructive sleep apnea and systolic blood pressure.***

Kong and colleagues (2016) conducted a systematic review and meta-analysis to evaluate an association between markers of metabolic syndrome and OSA. A total of 10 articles in the review were the most up-to-date evidence published by the end of 2015. This study found that patients without OSA had lower SBP compared with those who did have OSA (pooled SMD = 0.56; 95% CI [0.40, 0.71]). The study also found that patients with OSA had lower HDL (pooled SMD = -0.27; 95% CI [-0.38, -0.16];  $p < .001$ ) and higher LDL (pooled SMD = 0.26; 95% CI [0.07, 0.45];  $p < .05$ ). In addition, OSA was associated with an increased triglyceride (pooled SMD = 0.26; 95% CI [0.07, 0.45];  $p < .05$ ) and FBG (pooled SMD = 0.35; 95% CI [0.81, 0.53],  $p < .001$ ). OSA was significantly associated, not only with SBP elevation, but also four lab components (i.e., HDL, LDL, triglyceride, FBG) suggesting that OSA is associated with metabolic syndrome.

**Strengths of the study.**

(a) The abstract described the features of the study report clearly and precisely. (b) The introductory paragraph clearly described the rationale and objectives for the review. (c) The study followed PRISMA protocol. (d) Sensitivity analysis demonstrated good reliability in study results in the relationship between OSA and SBP without publication bias. (e) Strong evidence was presented for the association between SBP and OSA.

Weaknesses of the study.

(a) There was a potential publication bias for the associations between OSA and lab parameters. (b) The form and effect size of the association between OSA and SBP were not analyzed, likely due to a small sample size.

Knowledge gap.

The relationship between SBP ( $< 140$  mmHg,  $\geq 140$  mmHg) and a diagnosis of OSA based on the ICD-9-CM code among veterans remains unknown.

### **HTN comorbidity impacting veterans' HTN control.**

#### ***Impact of exenatide (Byetta) on HgA1C, weight, and blood pressure.***

Paul and colleagues (2012) conducted a post-hoc analysis to examine the synergy between improved glycaemia, weight loss, and BP reduction in patients treated with either exenatide (Byetta®) twice daily (BID) or once weekly (OW). Byetta® was manufactured by AstraZeneca. The study sample consisted of 686 subjects (53% men;  $M_{\text{age}} = 55$  years,  $SD = 10$ ;  $M_{\text{weight}} = 95$  kg,  $SD = 20$ ;  $M_{\text{SBP/DBP}} = 130/79$  mmHg,  $SD = 15/9$ ;  $M_{\text{HgA1C}} = 8.3\%$ ,  $SD = 11\%$ ) treated with exenatide QW ( $n = 541$ ) or BID ( $n = 145$ ) over 26 weeks. Patients were divided into four groups at each visit by glycaemia and weight response; those who failed to reduce both A1C and weight below weight means became the reference group. The other three groups were A1C reduction, weight reduction, and both A1C and weight reduction. Compared with the reference group, the study reported a significant likelihood of improving SBP ( $< 130$  mmHg) by 88%, 61%, and 30% respectively. The likelihood of improving DBP ( $< 80$  mmHg) was 63%, 45%, and 13% respectively.

Strengths of the study.

(a) The study explained mechanisms of action regarding the glucagon-like peptide-1 (GLP-1) receptor agonist exenatide. (b) Tables helped the reader visualize various data distributions among groups. (c) The study explained beneficial effects of exenatide in weight reduction, reduced A1C, and reduced BP.

Weakness of the study.

(a) Exenatide has not been approved as a drug of choice by the U.S. Food and Drug Administration (FDA) for its BP lowering effect. (b) The reference group, by its design, appeared to be inappropriate as it reported exenatide more effective in the reduction of A1C and weight, more so than a true control group with no exenatide treatment; this could be misleading. (c) Exenatide had multiple side effects, was costly for patients with no health insurance or high copayments as exenatide was classified as a third-tier drug for the treatment of diabetes. (d) The likelihood of BP reduction was poorly explained.

Knowledge gap.

There was no correlational study to examine the association between A1C and SBP/DBP among veterans in the literature.

***HDL and blood pressure.***

There was no correlational study to examine the association between HDL and SBP/DBP among veterans in the literature.

***Obesity (BMI  $\geq 30$ ) and blood pressure.***

Neto and colleagues (2013) conducted a cross-sectional survey to evaluate relationships among BMI, waist circumference, waist-hip ratio, waist stature ratio, conicity index, body adiposity index and BP in northeastern Brazil. The study sample consisted of 316 community-dwelling adults aged 60–105 years old ( $M = 74$  years,  $SD = 10$ ). This study found that BMI and the body adiposity index were significantly associated with male HTN, suggesting these measures be used to screen HTN in the elderly men.

**Strengths of the study.**

(a) Research was needed for this research question. (b) The purposive sampling method was appropriate for the research questions asked. (c) The sample size was adequate for the Poisson and AUROC model used by the study.

**Weaknesses of the study.**

(a) There was a lack of evidence ensuring BP data accuracy as 20 students were used to collect the BP data. (b) The sensitivity (39.3%) and specificity (82.1%) of BMI for detecting HTN did not meet the minimum standard for a clinical measure. (c) Measurements of alcohol (i.e.,  $\geq 1$  time/week or  $< 1$  time /week) was not helpful in evaluating its impact on BP due to metabolic turnaround time. The results would be considered untrustworthy.

**Knowledge gap.**

The relationship between BMI and SBP is limited.

***BMI and BP in diverse populations.***

Abayomi (2012) conducted a meta-analysis to examine the relationship between BMI and SBP among diverse populations. The study found that the relationship between BMI and SBP could be linear or curvilinear, and was dependent upon the statistical models used. The study concluded that those relationships were weak among differing populations and age was not a confounder in that relationship.

Strengths and weaknesses of the study.

This PhD student's dissertation project was diligent and likely conducted under the supervision of academic advisors. No major methodological weaknesses were found. The study result was trustworthy.

Knowledge gap.

The relationship between BMI and SBP was weak, both linear and curvilinear, depending upon the statistical models used; an interesting starting point for this topic.

***Mental health disorder impacting veterans' HTN control.******Depression and HTN.***

A systematic review and meta-analysis found the prevalence rate of depression in patients with HTN (26.8%; 95% CI [21%, 32.3%]; Li, Li, Chen, Chen, & Hu, 2015). A second systematic review found that late-life depression, defined as a depressive illness in people aged 60 years or older, was significantly associated with hypotension rather than HTN (Briggs, Kenny, & Kennelly, 2016). There was no credible evidence showing a relationship between depression-symptom severity and BP by systematic review or meta-analysis.



### ***Anxiety and HTN.***

Pan and colleagues (2015) conducted a systematic review and meta-analysis. A total of 21 articles were reviewed as the most up-to-date evidence by November 2014. The study found a significant association between anxiety and HTN (OR 1.18; 95% CI [1.02, 1.37],  $p < .001$ ) from analyzing 13 cross-sectional studies and 8-prospective studies (adjusted HR 1.55; 95% CI [1.24, 1.9];  $p < .001$ ). This study concluded that anxiety, as an independent risk factor for HTN, required early detection and treatment among patients with essential HTN.

#### Strengths of the study.

(a) The study was a systematic review and meta-analysis. (b) The abstract described the feature of the study report clearly and precisely. (c) The introductory paragraph described the rationale and objective for the review clearly and adequately. (d) The study following the PRISMA protocol. (e) There was a strong evidence of an association between BP and anxiety. (f) The mechanisms of the relationship found by the study were discussed in detail. (g) The study suggested to use DSM-IV (GAD-7) to assess anxiety.

#### Weaknesses of the study.

(a) The study included only English- and Chinese-language articles and could have influenced pooled results. (b) The study was unable to analyze raw data, limiting adjustment to many of the factors at the granular level and ultimately could have influenced pooled results. (c) Measurement instruments for anxiety differed among the 21 studies, potentially affecting the pooled results. As 13 of 21 studies were cross-

sectional, pooling data could produce similar outcomes but be of questionable accuracy.

(d) Anxiety is a treatable disease; its impact on BP could be dynamic. Interpreting and applying study results should be done with caution.

Knowledge gap.

It is important to explore the short-term and long-term effects of anxiety on HTN in terms of BP, CV risk factor (e.g., age, smoking, alcohol, sedentary, diet), and end-organ damage (e.g., brain, heart, kidney).

#### ***PTSD and blood pressure.***

Paulus and colleague (2013) conducted a retrospective EMR data analysis to examine if patients with PTSD had higher SBP, DBP and HR compared with non-PTSD patients, as well as a relationship between trauma exposure and BP within the Iowa City VA Healthcare System. The study sample consisted of veterans with co-morbidities of depression, mood disorder, anxiety, smoking, and/or substance abuse in men ( $M_{PTSD} = 26$  years,  $n = 88$ ;  $M_{non-PTSD} = 32$  years,  $n = 98$ ). The study found significant differences in veterans in the PTSD group in DBP ( $M = 87.6$ ,  $SD = 6.3$ ) compared to the non-PTSD group ( $M = 78.4$ ,  $SD = 7.2$ ; Cohen's  $d = 1.36$  [large]) and in SBP between the PTSD group ( $M = 133.8$ ,  $SD = 8.6$ ) compared to the non-PTSD group ( $M = 122.3$ ,  $SD = 9.6$ ; Cohen's  $d = 1.27$  [large]). This study also found that trauma-exposed patients without PTSD had significantly higher BP than non-exposed ones.

Strengths of the study.

This study addressed an important topic.

Weaknesses of the study.

(a) Major confounders (e.g., anxiety, antidepressants for patients with mood disorder) were not statistically controlled, a major threat to PTSD construct validity. (b) The study lacked explicit exclusion criteria, a threat to internal validity. (c) No power analysis was reported to justify the sample size for the two-sample *t*-test and the ANCOVA, a major threat to statistical validity. (d) Key concepts were not operationally defined (e.g., PTSD by ICD-9-CM code, psychiatric medication, notes, trauma exposure), a threat to internal validity. The combination of methodological weaknesses made the study untrustworthy.

Knowledge gap.

There was no systematic review and/or meta-analysis to explore the relationship between PTSD and SBP/DBP with the most up-to-date evidence.

### **Medication impacting veterans' HTN control.**

#### ***Effectiveness of antihypertensive medication.***

Fretheim and colleagues (2012) conducted a systematic review and meta-analysis to evaluate which antihypertensive medication class was the most effective in reducing the incidence of CVD outcomes for healthy people at risk. Results from this study could assist in developing clinical recommendations for a first-line drug choice to prevent CVD supported by study findings. A total of 25 articles was reviewed with the most up-to-date RCT evidence through February 2011. The study found no particular drug to be more effective in reducing CVD risk than others and the meta-analysis concluded that there

was little or no difference between commonly used blood pressure lowering medications for primary prevention of CVD.

Strengths of the study.

(a) The study title suggested important HTN control phenomena as a systematic review and meta-analysis. (b) The abstract captured the main features of the study report. (c) The methodology followed traditional systematic review and meta-analysis protocol with clear inclusion and exclusion criteria; the study was registered (PROSPERO CRD42011001066). (d) Results included self-explanatory tables with narrative. (e) Critique of prior studies was fair and balanced; the study's own limitations were discussed in detail.

Weaknesses of the study.

No major validity concerns could be identified.

Knowledge gap.

The results appeared to conflict with the drug treatment algorithm recommended by JNC-7; however, the trustworthiness of this study is compelling.

***Providers' assessment of adherence and intensification of BP medication.***

Meddings and colleagues (2012) conducted a cross-sectional survey to answer two research questions: How often did providers correctly identify patients with poor adherence to chronic BP medication? and, how often did providers intensify BP medication regimen on patients with significant non-adherence issue when BP was uncontrolled? The sample consisted of 92 primary care providers and 1,169 veterans ( $M = 65$  years,  $SD = 11$ ) from nine different VA facilities in three Midwestern states. Data

was collected on BP, at the time of study enrollment via automated data sources; medication adherence, from VA pharmacy records 1-year prior and 90-day post-enrollment with refill history for antihypertensive medication classes; provider-survey post patient visit; and demographic questionnaire post patient's clinic visit. Medication non-adherence was based on a gold standard of continuous multiple-interval gap (CMG), where non-adherence was defined as 20% CMG or greater. The patient would be non-adherent if the medication was missed 1 in 5 doses or more on average. The study found an overall poor correlation between providers' assessment of a patient's adherence and the patient's refill adherence ( $r = .18$ ,  $p < .001$ ; Kappa = .15). The study also found that BP medications were not available for 20% or more days in medication non-adherence patients. Providers characterized 37% of 211 patients as medication non-adherence. Among 18 patients with non-adherence 50% or more of the time, the provider assessed 44% as non-adherence. Providers intensified antihypertensive medications in 451 of patients (42%) regardless their medication adherence status.

#### Strengths of the study.

(a) This study addressed a clinically significant issue. (b) Data collection was from multiple sites, increasing the external validity of study results. (c) Key variables were operationally defined. (d) Missing data were imputed to prevent sampling bias. (e) Figures and tables were clear and independent. (f) Sampling characteristics were like hypertensive veterans in Southern California in terms of age and race. The study results appeared trustworthy.

Weaknesses of the study.

There was no power analysis presented to justify the sample size for the logistic regression model employed by the study.

Knowledge gap.

The authors made multiple references for a need of a reliable, multidimensional HTN treatment adherence instrument.

***Number of doctor's office visits and HTN control.***

There were no correlational studies, systematic review, or meta-analysis to explore the relationship between the number of doctor's office visits and SBP/DBP.

***Impact of antihypertensive drug therapy on cognitive decline and dementia.***

Rouch and colleagues (2015) conducted a systematic review to examine all published studies investigating the relationship between antihypertensive drug therapy and cognitive decline or dementia). A total of 38 articles were included in the review from 1990 to 2014. A quality assessment of all articles was conducted by Jadad criteria (Pogue et al., 1996). The study concluded that antihypertensive drug therapy might decrease the incidence and progression of cognitive decline, dementia, and Alzheimer's disease, specifically calcium channel blockers and renin-angiotensin system blockers.

Strengths of the study.

(a) The study addressed the effects of antihypertensive drug therapy on cognition, dementia, and Alzheimer's disease. (b) The flowchart for the systematic review clarified the process of article selection. (c) The tables were helpful in reviewing relevant study categories systematically. (d) The article discussed reasons for variations. (e) An

explanation of the mechanisms with dementia prevention in the discussion section was extensive. (f) This study results were consistent with another meta-analysis, with one exception: antihypertensive drug use did not decrease the risk of developing Alzheimer's disease, associated cognitive decline, or cognitive impairment (Chang-Quan et al., 2011).

#### Weaknesses of the study.

(a) There was a lack of homogeneity in all the reviewed articles across study designs, patient populations, variables, duration of follow-up, and methodology quality impacting the estimation of effect size. (b) Antihypertensive medication dosage varied study-to-study and most studies did not address the medication adherence issue, creating an issue with the reliability of study findings. The overall results lacked a definitive conclusion.

#### Knowledge gap.

The effects of CCB and ACEI on cognitive function, dementia, and Alzheimer's disease with 5 years or greater follow up among veterans' and non-veteran population will be needed to confirm the study results.

#### **Uncontrolled HTN impacting veterans' quality of life.**

##### ***Impact of non-adherence on end-organ damage.***

Gosmanova and colleagues (2015) conducted a cohort study with an 8-year follow-up to examine the association between ICD-9-CM code V 15.81 (non-adherence) and end organ damage (EOD) involving the heart, brain, and/or kidneys among 312,489 veterans with newly diagnosed HTN. The study sample was obtained from a prior HTN study by including patients with the diagnosis of HTN (baseline GFR  $\geq$  60 ml/min per

1.73 m<sup>2</sup>), initiated on one or more antihypertensive drugs in the outpatient setting from October 1, 2004 through September 30, 2006, based on VA pharmacy dispensation records. Patients who used combined drug therapy, on  $\alpha$ -blocker monotherapy and with an ICD-9-CM code for CHF and tachyarrhythmia were excluded from the study. Outcome data, including demographic, laboratory, SBP/DBP, and comorbidity, were collected. Patients were divided into two groups (inadequate or < 80% vs. adequate or  $\geq$ 80%) based on their adherence to antihypertensive drug as estimated by medication possession ratio (MPR) per VA standard formula. Follow up for brain damage with stroke by ICD-9-CM codes and Current Procedure Terminology (CPT) codes, heart damage with coronary artery bypass grafting (CABG), CAD and percutaneous angioplasty, and kidney damage with GFR, study found that ICD-9-CM code V 15.81 independently predicted the incidence of stroke, CAD, CKD, and end stage renal disease.

#### Strengths of the study.

The study addressed an association between V 15.81 code and EOD among veterans with essential HTN. Major confounders were statistically controlled.

#### Weaknesses of the study.

There was no power analysis to justify the sample size for the Cox regression analysis of five independent variables (i.e., GFR, CKD, ESRD, CAD, stroke) used by the study, a major threat to statistical conclusion validity affecting the trustworthiness of the results.



Knowledge gap.

A high quality, longitudinal study of HTN-associated EOD of the brain, heart, and/or kidney with quantitative measurements of medication adherence and BP at yearly follow up intervals for 7 to 8 years is needed.

### **Summary**

In summary, several major themes emerged. First, essential HTN control is a multidimensional issue associated with (a) patients' consumption of excessive amounts of salt, alcohol, caffeine products (Briasoulis et al., 2012; Chobanian et al., 2003; Neter et al., 2003, Soltani et al., 2016), flaxseed (Khalesi et al., 2015), and lack of physical exercise (Lee & Wong, 2015), smoking related arterial stiffness (Scallan et al., 2010), illness of anxiety (Pan et al., 2015), metabolic syndrome, obesity (Kong et al., 2016), knowledge of HTN disease or HTN risk factor and external support (Lahdenperä & Kyngäs, 2001; Schmid et al., 2009), (b) providers' attitudes in following JNC-7 guideline, time constraints, frustration with patients' refusal to comply with medical advice and missing scheduled appointments, HTN treatment guideline regarding to BP treatment goal, (c) environmental factors, including health insurance, copayment (Sinnott et al., 2013), job stress (Landsbergis et al., 2013) and BP treatment goals per HTN treatment guideline, (d) antihypertensive drug effectiveness and adherence (Hultgren et al., 2014; Schmid et al., 2009) and (e) end organ damage including CVA, TIA, vascular dementia, CHF, CAD, MI, CABG, and CKD. Second, HTN-control research remains in an infancy stage as scientists continue to seek an optimal SBP goal for hypertensive individuals despite decades of research (James et al., 2013). Third, HTN-control research

lacks a theory-based, operational definition of patients' adherence to HTN-control protocol and HTN control outcomes (e.g., BP, HR, BMI, WC, cholesterol values, blood sugar values, kidney function values, CVA, TIA, CHF, CAD, MI, CKD, quality of life) based on current HTN treatment guidelines. Fourth, much of the current HTN control studies have serious methodological weakness with non-probability sampling and cross-sectional observational study design as the most commonly used ones without any theoretical or conceptual basis, producing less than credible and useful results. Fifth, most results in systematic reviews and meta-analyses were based on RCTs that lasted less than a year and requires more longitudinal RCTs in the future. Sixth, major knowledge gaps remain about the association of family history in premature CVD and how that affects offspring BP. Seventh, there is a lack of evidence in the associations between IVs (e.g., age, sex, race, religion, A1C, HDL, BMI, MDD, GAD, PTSD) and a DV (SBP) among veterans. The study was intended to address the multidimensional factors impacting veterans' HTN control to contribute to the scholarly nursing literature.

### 1. What is known?

- DASH significantly reduced weight in 8-week to 1-year by  $-1.42 \text{ kg/m}^2$  (95% CI,  $-2.03$  to  $-0.82$ ), BMI  $-0.42 \text{ kg/m}^2$  (95% CI,  $-0.64$  to  $-0.20$ ) & Waist Circumference  $-1.05 \text{ cm}$  (95% CI,  $-1.61$  to  $-0.49$ ).
- Weight reduction of  $-5.1 \text{ kg}$  (95% CI,  $-6.03$  to  $-4.25$ ) reduced SBP by  $-4.44 \text{ mmHg}$  (95% CI,  $-5.93$  to  $-2.95$ ) and DBP by  $-3.57 \text{ mmHg}$  (95% CI,  $-4.88$  to  $-2.25$ ).
- Sedentary behavior per day was associated with  $0.06 \text{ mmHg}$  increase in (95% CI,  $0.01$ - $0.11$ ,  $p < 0.05$ ) SBP and  $0.20 \text{ mmHg}$  (95% CI,  $0.10$ - $0.29$ ,  $p < 0.001$ ) in DBP.
- DASH significantly reduced SBP by  $6.74 \text{ mmHg}$  (95% CI:  $-4.29$  to  $-2.79$ ,  $I^2 = 56.7\%$ ), DBP by  $3.54 \text{ mmHg}$  (95% CI:  $-4.29$  to  $-2.79$ ,  $I^2 = 56.7\%$ ).
- Caffeine intake produces an acute increase in BP for  $\geq 3$  hours, but there were no associations between long-term or habitual coffee consumption and HTN or CVD risk.
- Patients without the OSA had a lower level of SBP compared with those who had it (pooled SMD =  $0.56$ , 95% CI,  $0.40$  to  $0.71$ ).
- Job strain is significantly associated with ambulatory BP.
- Anxiety is significantly associated with HTN.
- Alcohol consumption/AUDIT-C score is significantly associated with BP.

### 2. What is unknown?

- An optimal goal of SBP for patients with HTN.
- The association between insurance copayment and number of hypertension visit.
- The association between age and BP (forms and strengths).
- Sex difference in risk of cardiovascular disease and mortality.
- The association between racial discrimination and BP.
- The association between religious involvement and BP.
- The association between a HTN education program and BP.
- The association between veterans' functional ability and BP.
- The association between adolescents' BP and adults' BP.
- The association between number of cigarettes smoked today and BP today.
- The association between number of years smoked and BP trend by years smoked
- The association between chronic stress (job strain) and BP (office BP x 4).
- The association between MDD/PHQ-9 score and BP.
- The association between PTSD/PCL-M score and BP.
- The association between GAD/GAD-7 score and BP.

### 3. What the study adds?

- Characteristics of hypertensive veterans in a Southern California primary care clinic.
- Self-reported medication adherence is an independent predictor for one's SBP.
- Many insights into conducting secondary analysis with electronic medical records (EMRs) that may help novice researchers with this approach in the future.

Figure 3. What is known, unknown and what the study adds?

### **Chapter 3: Methodology**

This chapter presents research methodology including study design, setting, sample, and source of data for the study. It also presents sampling method, data collection procedure, sampling size with power analysis and statistical analysis procedure. The conclusion addresses issues for the protection of human subjects.

#### **Study Design**

The study is a descriptive, exploratory, cross-sectional, retrospective, convenient sampling of an EMR data set analysis. The design was approved by the researcher's dissertation committee for four reasons. First, laboratory data (i.e., A1C, HDL) cannot be obtained by interview, survey questionnaire, or other observational methods. Second, it reduces resources by utilizing a pre-existing data. Third, it is time efficient when the needed information is readily available and easily found. Fourth, research questions are in accordance with the protection of cases under study.

#### **Study Setting**

The study was conducted at a Southern California VA primary care clinic for approximately one month from October 17, 2016 through November 15, 2016.

#### **Sample and Source of Data**

The study sample comprised U.S. veterans with essential HTN based on ICD-9-CM code 401. Data used in this report were from a VA dashboard data set at a Southern California VA primary care clinic between October 17, 2014 and October 17, 2016. The data set was used by providers to identify and monitor veterans with chronic disease (e.g., HTN) as a standard feature of the EMR in the VA.

**Inclusion criteria.**

Men and women veterans of any race, 24-years-old and above with essential HTN and multiple comorbidity, with or without antihypertensive drug therapy.

**Exclusion criteria.**

Missed a baseline or final point of BP measurement, or had an organ transplant and on steroid drug therapy.

**Sampling Method**

A convenience sampling method was used as it entailed using the most readily available data to answer study questions and achieve the study objective at the time of data collection. More specifically, study cases already existed in an EMR dashboard at the time of data collection.

**Data Collection Procedure**

1. An expedited Institution Review Board (IRB) was granted because the research collected pre-existing data without any procedure involvement.
2. Study oversight was determined by IRB at the University of San Diego and the Department of Veterans Affairs VA Healthcare System, California.
3. A data extraction instrument was created based on the HTN control conceptual framework (see Appendix B).
4. Retrospective data was collected by the researcher utilizing Microsoft Excel, then uploading the raw data set directly to IBM SPSS Version 24.

5. The researchers carefully reviewed the cover sheet, problem list, medication list, order list, providers' notes, lab values, reports of BMI and BP measurement of the EMR covering two years, from October 17, 2014 through October 17, 2016.
6. Data collection took place in a private office at a Southern California VA primary care clinic began at 8:00 AM and ended 5:00 PM, Monday through Friday, from October 17, 2016 through November 15, 2016.
7. All harvested data was pre-coded to protect veteran cases' confidentiality.
8. The harvested data was then mailed to the researcher's password-protected e-mail account electronically and stored on a flash drive.
9. Data accuracy was to be ensured with a random check of 33% data by a nurse practitioner who is blinded to the study with an acceptable accuracy of Cohen's  $Kappa \geq 0.81$ .

### **Sample Size and Power Analysis**

1. The minimum sample size was 97 for the multiple linear regression (MLR) model employed by the study per a priori sample size calculator with effect size ( $r^2$ ) = 0.15, statistical power = 0.8, predictor variable = 6 (i.e., A1C, HDL, BMI, BP medications, clinic visit, baseline SBP) and probability = 0.05 (Soper, n.d.).
2. The minimum sample size was 300 for a logistic regression model (LRM) employed by the study based on 50 cases per IV principle (Polit, 2012). The LRM was utilized to explore non-normally distributed IVs (i.e., A1C, HDL, BMI, baseline SBP) associated with a dichotomous DV of veteran's final SBP control.
3. The researcher completed data analysis under the supervision of a PhD. Professor.

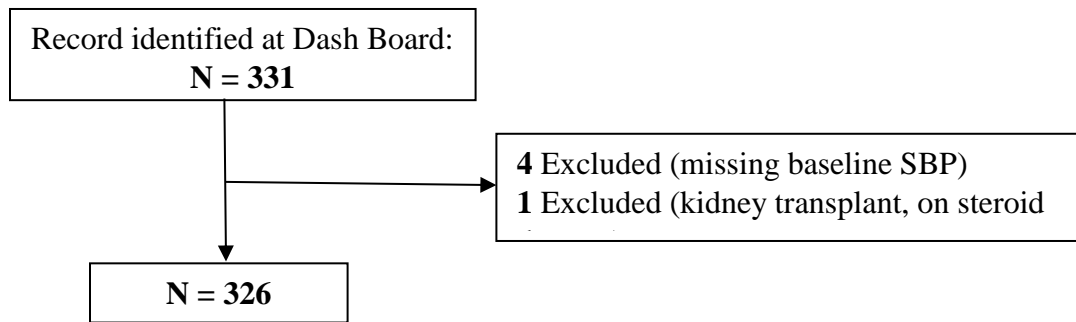


Figure 4. Data selection flow chart

### Data Analysis Procedure

1. Screen for missing data with all IVs and DVs, including age, race, religion, tobacco use, alcohol use, OSA, DM, dyslipidemia, BMI, MDD, GAD, PTSD, medication adherence, brain damage, heart damage, kidney damage, A1C, HDL, number of BP med, number of clinic visits, baseline SBP, and final SBP.
2. Screen for outliers (Mahalanobis distance).
3. Determine if data transformation would be indicated.
4. Run descriptive statistics on all IVs and DVs. Show results by number and percentage with nominal, ordinal, or categorical level of data. Show results by mean ( $M$ ), standard deviation ( $SD$ ), median, and mode for continuous levels of data.
5. Test assumption of multiple linear regression (MLR) model and run the test.
  - (1) Normality test: Histogram, box plots, skewness, kurtosis.
  - (2) Linearity: Create correlation matrix between IVs and DVs (bivariate scatterplots).
  - (3) Homoscedasticity:

- (a) Tolerance statistics with all IVs' indices  $< 0.1$  indicates no multicollinearity problem (Mertler & Vannatta, 2013).
  - (b) Variance inflation factor (VIF) for each predictor, where  $< 10$  indicates no multicollinearity problem (Mertler & Vannatta, 2013).
6. Major confounder of HTN control including BMI, Alcohol use, all medication and diagnosis of anxiety will be statistically controlled in this study.
  7. Test assumptions of LR model and run the test.
    - (1) No normality, linearity, equal variance requirement.
    - (2) Predictor variable can be continuous, scale, or dichotomous.
    - (3) All probability will be ranging from 0 – 1.
    - (4) Sensitive to multicollinearity relationships and outliers.
    - (5) The -2 Log Likelihood (goodness of fit test) index should be = 0, but no strict adherence in LR statistical analysis (Mertler & Vannatta, 2013).
  8. Run  $\chi^2$  or Fisher's exact test to represent effect size with Cramer's V for relevant variable associations with a 2 X 2 table.
    - (1) Sample size assumption: no more than 20% of the contingency cells have expected values  $< 5$  (Blaikie, 2003).
    - (2) Expected frequency cannot be  $< 1$  (Blaikie, 2003).
    - (3) In case of assumptions will be violated, Fisher's exact test would be used to interpret the test result as appropriately.
    - (4) Sample size requirement:  $10 \times 2 \times 2 = 40$  (Blaikie, 2003).



9. Summarize and interpret the results, represents results with more tables or figures as indicated.
10. Discuss the data analysis results with major limitations to the study.

### **Protection of Human Subjects**

Informed consent was not needed as the study involved collecting information that had already existed in an EMR dashboard e-database and the research presented no more than a minimal risk of harm to the study subjects. The protection of human subjects was ensured by the researcher throughout the study. Prior to data collection, the researcher completed the National Institutes of Health (NIH) module on the protection of research subjects to have a thorough understanding of the methods used to protect research participants. The activities of the researcher were monitored by the research committee chairperson. The raw data will be stored in a password protected file on a thumbnail drive by the researcher for a minimum of five years after the publication of this study if needed for auditing (American Psychological Association, 2010).

## Chapter 4: Results

### Introduction

The purpose of this study was to describe the multidimensional factors impacting veterans' HTN control. The purpose of this chapter was to present the overall results. It begins with a data management brief, proceed to a description of the study results according to research aims and questions. It concludes with a summary of the most significant result of the study.

### Data Management

Prior to statistical analysis, the researcher reviewed inclusion and exclusion criteria and screened out five ineligible electronic medical records. This resulted in a final sample size of 326. Accuracy of the data was not randomly checked due to financial and time constraints during the data collection period. Consequently, an interrater reliability of Cohen's Kappa index was not calculated as originally planned. Since the researcher was the only person who has extracted data in a consistent manner, an intra-class correlation (ICC) would not be indicated.

### Description of the Study Results

#### **Aim # 1.**

Describe the characteristics of hypertensive veterans in one Southern California VA clinic from data collected during a period of October 17, 2014 through October 17, 2016.

***Question # 1.***

What were characteristics of hypertensive veterans in one Southern California VA clinic for the seven dimensions of IVs from data collected during a period of October 17, 2014 through October 17, 2016?

The study sample had most cases (80.4%) between the ages of 45 and 76 years old with  $M_{age} = 62$  and  $SD = 13$ . Most were male veterans (95.4%) diagnosed with essential HTN and comorbidities, including dyslipidemia (68.4%) with HDL level at 33 mg/dl in most cases, obesity (56.7%) with BMI of 30 kg/m<sup>2</sup> in most cases, and diabetes (45.4%) with A1C level at 5.5 mg/dl in most cases. A large portion of cases (37.1%) had no service-connected disability rating, despite documented ratings for the remaining cases with  $M = 40\%$  and  $SD = 40\%$ . Nearly one-half (47.9%) of cases were diagnosed with OSA, one-third (32.8%) with MDD, 20.9% with PTSD, and 12.9% with GAD. Most cases (70.9%) were Christians, including 27% Roman Catholics and 43.9% non-Catholic Christians. Most cases (90.1%) served in either the U.S. Navy (63.1%) or U.S. Army (28.2%) during the Vietnam war/Korean war/World War II (47.6%). Most cases did not use tobacco (79.4%) or consume alcohol (87.8%). Approximately one-third of cases (36.5%) had an average of five to eight healthcare visits at a Southern California primary care or cardiology clinic, averaging two to four visits per year from October 17, 2014 through October 17, 2016. Most cases (42.6%) received only one antihypertensive medication with ACE inhibitors (38.3%), beta blockers (34.4%) and calcium channel blocker (30.7%) comprised the top three most commonly prescribed antihypertensive medications at the time of EMR review from October 17, 2016 to November 15, 2016.

While rates of pre-HTN rose from 43.6% to 55.5%, Stage I HTN decreased from 30.4% to 16.3% during two-year study period. Rates of Stage I HTN at baseline were 43.3%, at the final measurement were 21.2%, and the 2-year SBP control rate was 42%. Tables 1-3 provide a summary of the characteristics of HTN veterans in this Southern California primary care clinic.

Table 1  
Demographic Characteristics of Hypertensive Veterans in a Southern California Primary  
Care Clinic

	<i>N</i>	%
Age (in years) <i>M</i> = 62, <i>SD</i> = 13, <i>Median</i> = 63, <i>Mode</i> = 68	326	100.0
24 – 44	31	9.5
45 – 64	144	44.2
65+	151	46.3
Sex (Male)	311	95.4
Race/Ethnicity (missing 14 = 4.3%)		
Caucasian	200	61.3
African American	68	20.9
Asian and Other	44	13.5
Religion (missing 83 = 25.5%)		
Roman Catholic	88	27.0
Non-Catholic Christians	143	43.9
Others	12	3.7
Branch of Military Service (missing 2 = 0.6%)		
Air Force	28	8.6
Army	92	28.2
Navy	204	62.5
Time Periods of Military Service		
Peace Time Only	69	21.2
Persian Gulf War	102	31.3
Vietnam Era/Korean War/WW II	155	47.6
Education (missing 206 = 63.2%)		
≥ High School	115	35.3
< High School	5	1.5

Table 2  
Medical History of Hypertensive Veterans in a Southern California Primary Care Clinic

	<i>N</i>	%
Lifestyle		
Current Tobacco Use	67	20.6
Current Alcohol Use	43	13.2
Obstructive Sleep Apnea	156	47.9
Comorbidity		
Obesity (BMI $\geq 30$ )	185	56.7
BMI (kg/m <sup>2</sup> ) <i>M</i> = 31, <i>SD</i> = 6, <i>Median</i> = 30, <i>Mode</i> = 30		
Overweight (25 - 29.9)	103	31.6
Dyslipidemia	223	68.4
HDL (mg/dl) <i>M</i> = 43.8, <i>SD</i> = 15, <i>Median</i> = 40, <i>Mode</i> = 33		
< 40	150	46.0
40 – 49	83	25.5
50 – 59	45	13.8
$\geq 60$	39	12.0
Missing	9	2.8
A1C (mg/dl) <i>M</i> = 6.3, <i>SD</i> = 1.3, <i>Median</i> = 6, <i>Mode</i> = 5.5		
<6.5	209	64.1
6.5 – 8.4	79	24.3
$\geq 8.5$	18	5.5
Missing	20	6.1
Diabetes Milieus Diabetes	148	45.4
Mental Health Disorder		
Major Depressive Disorder	107	32.8
Generalized Anxiety Disorder	42	12.9
Post-Traumatic Stress Disorder	68	20.9
Target Organ Damage		
Brain (stroke, transient ischemia attack)	19	5.8
Heart (heart failure, coronary artery disease, heart attack, CABG)	57	17.5
Kidney (chronic kidney disease)	36	11.0
Service-Connected Disability (%) <i>M</i> = 40, <i>SD</i> = 40, <i>Median</i> = 30 <i>Mode</i> = 0		
No Disability Rating	121	37.1
10-50% Disability Rating	76	23.3
60-100% Disability Rating	129	39.6

Table 3  
Hypertensive-Related Data for Study Veterans in a Southern California Primary Care  
Clinic

Parameter	<i>N</i>	%
<b>Medications</b>		
Self-Reported Medication Non-Adherence	24	7.4
Clinic visits (visit/2-year) <i>M</i> = 6, <i>SD</i> = 4, <i>Median</i> = 6, <i>Mode</i> = 5		
0 visit in 2-year	18	5.5
1-4 visits in 2-year	104	31.9
5-8 visits in 2-year	119	36.5
≥9 visits in 2-year	85	26.1
BP medication class ( <i>M</i> = 1.6, <i>SD</i> = 1, <i>Median</i> = 1, <i>Mode</i> = 1)		
0 BP RX	25	7.7
1 BP RX	139	42.6
2 BP RX	104	31.9
3+ BP RX	58	17.8
All medications ( <i>M</i> = 8.56, <i>SD</i> = 4.6, <i>Median</i> = 8, <i>Mode</i> = 5)		
1-5 medications	96	29.4
6-10 medications	118	36.2
11-15 medications	86	26.4
≥ 16 medications	25	7.7
Baseline SBP (mmHg) <i>M</i> = 137, <i>SD</i> = 18, <i>Median</i> = 138, <i>Mode</i> = 138		
Final SBP (mmHg) <i>M</i> = 130, <i>SD</i> = 15, <i>Median</i> = 130, <i>Mode</i> = 132		
Baseline SBP (120-139 mmHg)	142	43.6
Final SBP (120-139 mmHg)	181	55.5
Two-year uncontrolled SBP (October 17, 2014 – October 17, 2016)	189	58.0

**Aim # 2.**

Examine the relationships among the predictor variables of blood glucose level (A1C), high-density lipoprotein (HDL), body mass index (BMI), number of BP medication prescribed, number of clinic visits, baseline SBP, and the outcome variable of the final point SBP.

***Question # 2a.***

Which of the possible six predictor variables were included in an equation for predicting veterans' final point SBP?

***Answer # 2a.***

Prior to conducting a stepwise MLR analysis, data was screened for missing values and outliers. The process led to an elimination of 25 outlier cases based on a Mahalanobis distance  $\leq 22.458$  at  $P < 0.001$ . Normality was assessed by visual inspection of histogram (see *Figure # 5-8*) and skewness, kurtosis per descriptive statistics (see *Figure 9*). This process led to transformation of four variables A1c, HDL, BMI, BaSBP. Homoscedasticity was assessed by tolerance statistics and VIF with all IV indices  $> 0.1$  and VIF indices  $< 10$  (see *Figure 10*) and residual plots without major clusters (see *Figure 11*) indicated no homoscedasticity problems. Linearity was assessed between IVs and DV with transformed data by scatter and residual plots (see *Figure 12*).

Only one out of six predictor variables could be included in the prediction model. The other five (A1c, HDL, BMI, BP drug class and clinic visit) could not be included in the prediction model due to a severe violation to linearity assumption of the MLR model with non-elliptical shaped scatter plots (see *Figure 12*), an indication for non-linear



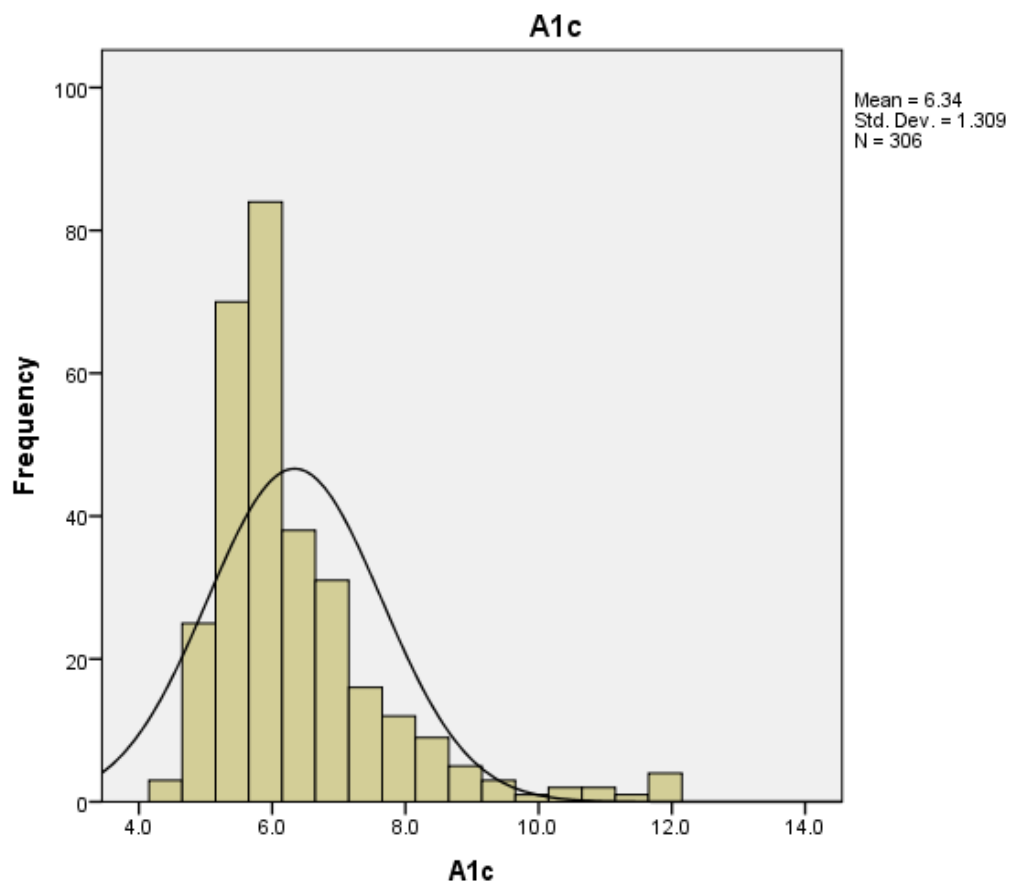
correlations between IVs and DV or disconnected scores from the center mean line without a rectangular formation on the residual plot (see *Figure 11*). At this point, a decision was made to abandon the MLR analysis for a concern that forcing it may produce a false or biased result.

***Question # 2b.***

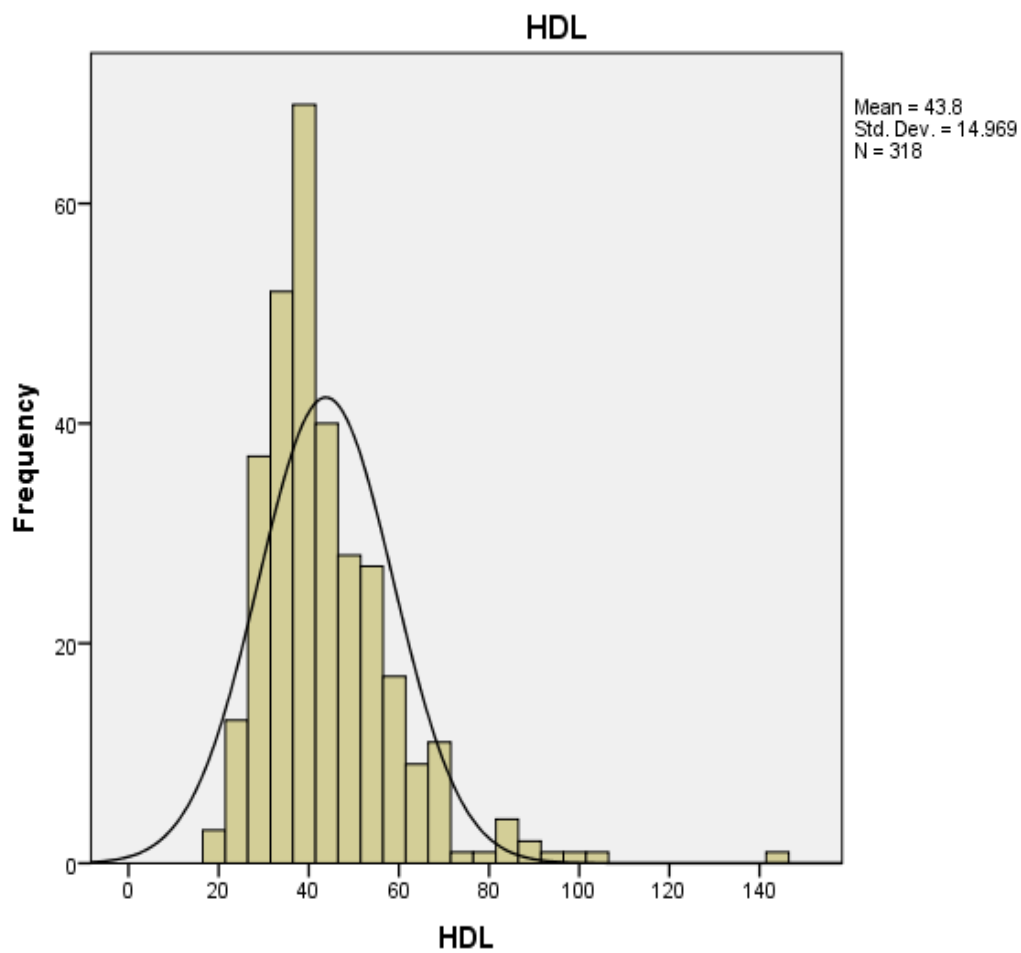
Does the obtained regression equation resulting from a subset of the six predictor variables allow us to reliably predict veterans' final point SBP?

***Answer # 2b.***

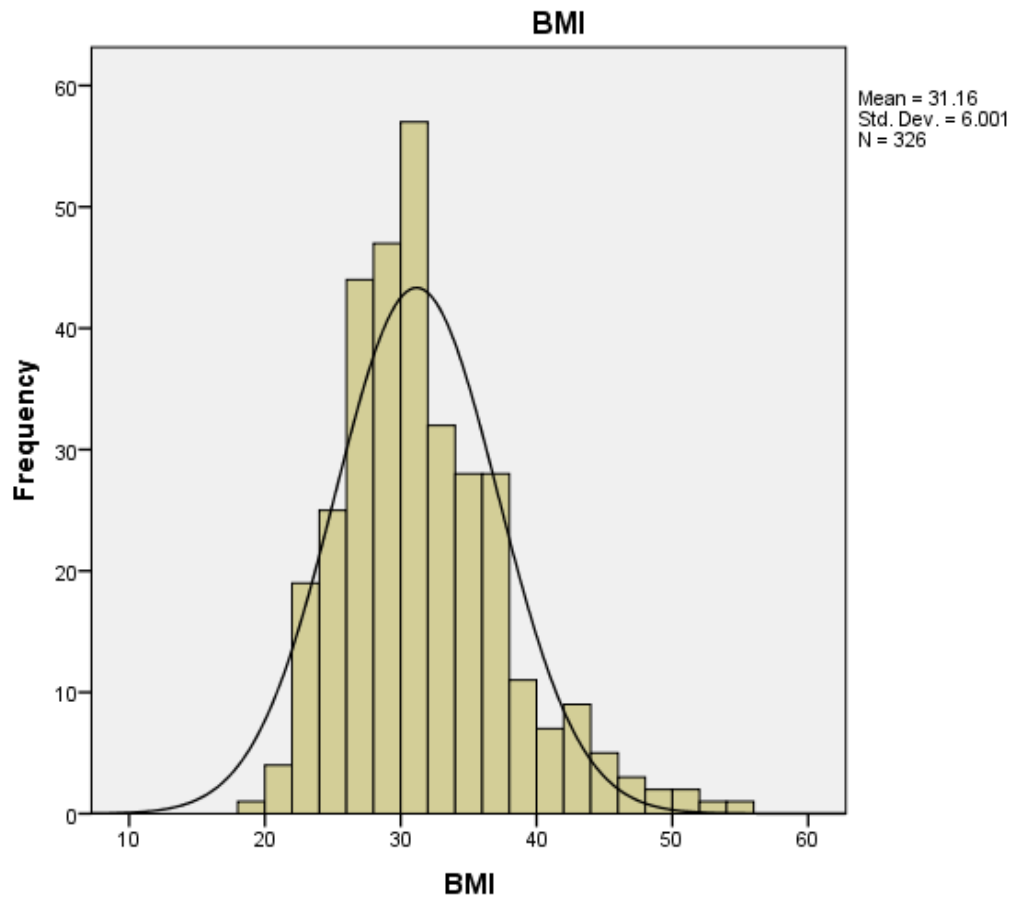
After eliminating five predictor variables from the MLR equation, baseline SBP was the only predictor variable left in the prediction model and it did not allow us to reliably predict veterans' final point SBP.



*Figure 5.* Histogram of A1C



*Figure 6.* Histogram of HDL



*Figure 7.* Histogram of BMI

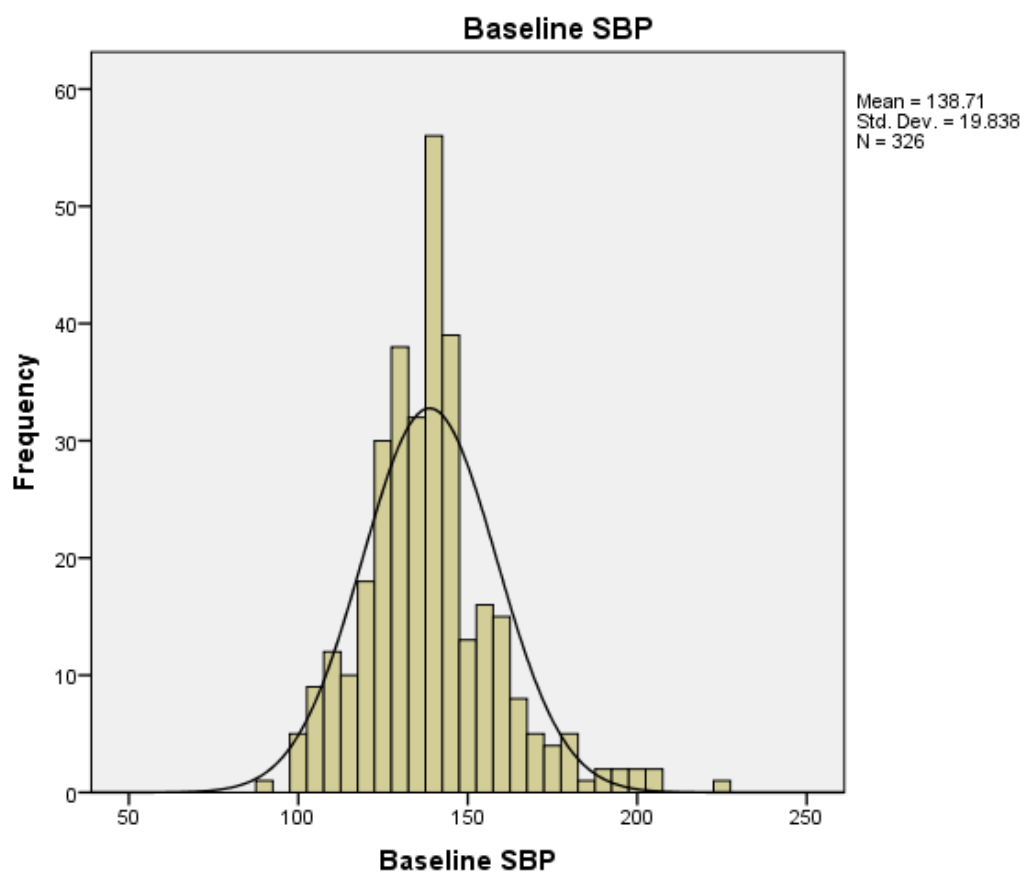


Figure 8. Histogram baseline SBP

**Descriptive Statistics**

		A1c	HDL	BMI	Baseline SBP
N	Valid	306	318	326	326
	Missing	20	8	0	0
Mean		6.337	43.80	31.16	138.71
Median		6.000	40.00	30.00	138.00
Mode		<b>5.5</b>	<b>33</b>	30	138 <sup>a</sup>
Std. Deviation		1.3086	14.969	6.001	19.838
Skewness		<b>1.982</b>	<b>1.916</b>	.914	.825
Std. Error of Skewness		.139	.137	.135	.135
Kurtosis		<b>4.961</b>	<b>7.203</b>	<b>1.164</b>	<b>1.861</b>
Std. Error of Kurtosis		.278	.273	.269	.269

Figure 9. Skewness and kurtosis of 4-variable

Model		Unstandardized		Sig.	95.0% CI for B		Collinearity Statistics	
		B	Std. Error		L. Bound	U. Bound	Tolerance	VIF
1	(Constant)	-93.128	34.914	.008	-161.841	-24.415	<b>&gt;0.1</b>	<b>&lt;10</b>
	Ig10A1c	-3.073	10.961	.779	-24.645	18.499	<b>.928</b>	<b>1.077</b>
	Ig10HDL	3.622	6.671	.588	-9.506	16.751	<b>.853</b>	<b>1.173</b>
	Ig10BMI	15.819	10.757	.142	-5.352	36.990	<b>.870</b>	<b>1.150</b>
	Ig10BaSBP	90.897	13.421	.000	64.485	117.309	<b>.973</b>	<b>1.028</b>
	BP drug class	.784	.847	.355	-.883	2.452	<b>.951</b>	<b>1.051</b>
	Clinic Visit	.100	.222	.652	-.337	.538	<b>.960</b>	<b>1.041</b>

Figure 10. Tolerance and VIF

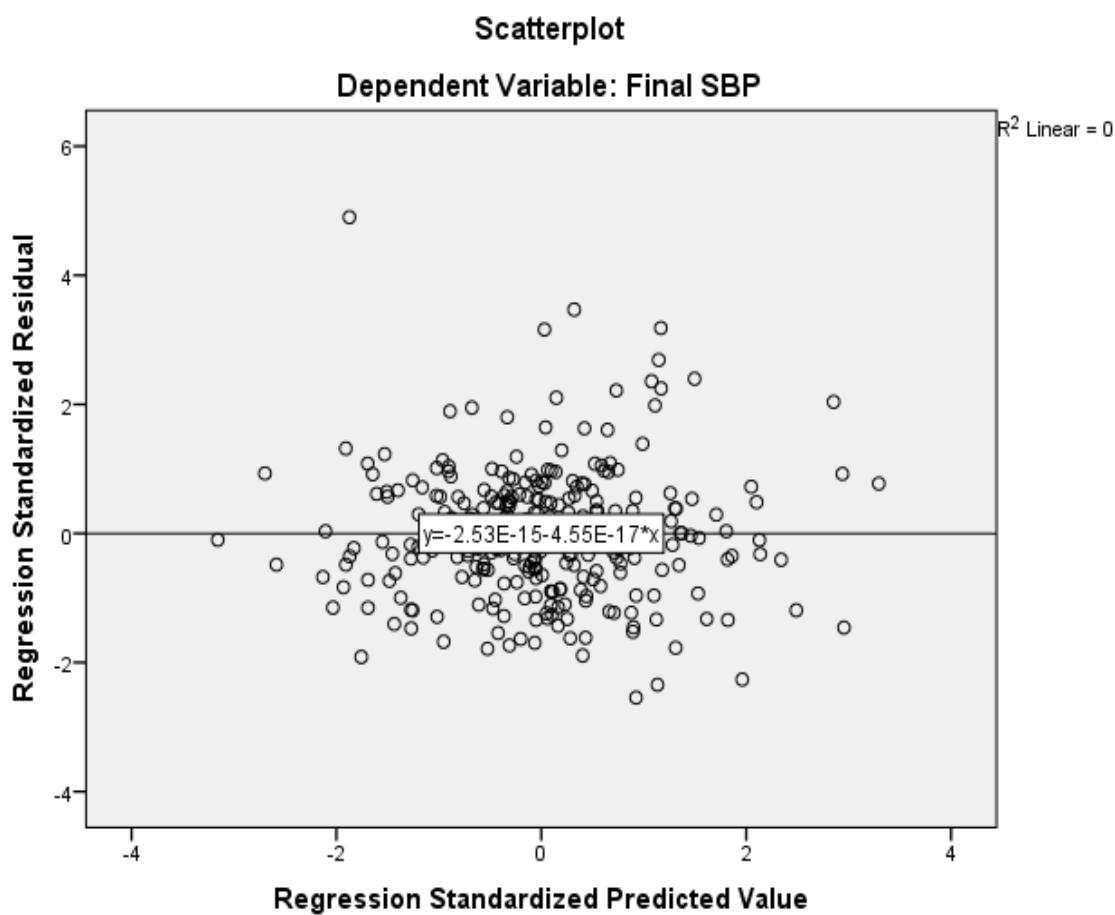


Figure 11. Residual plots

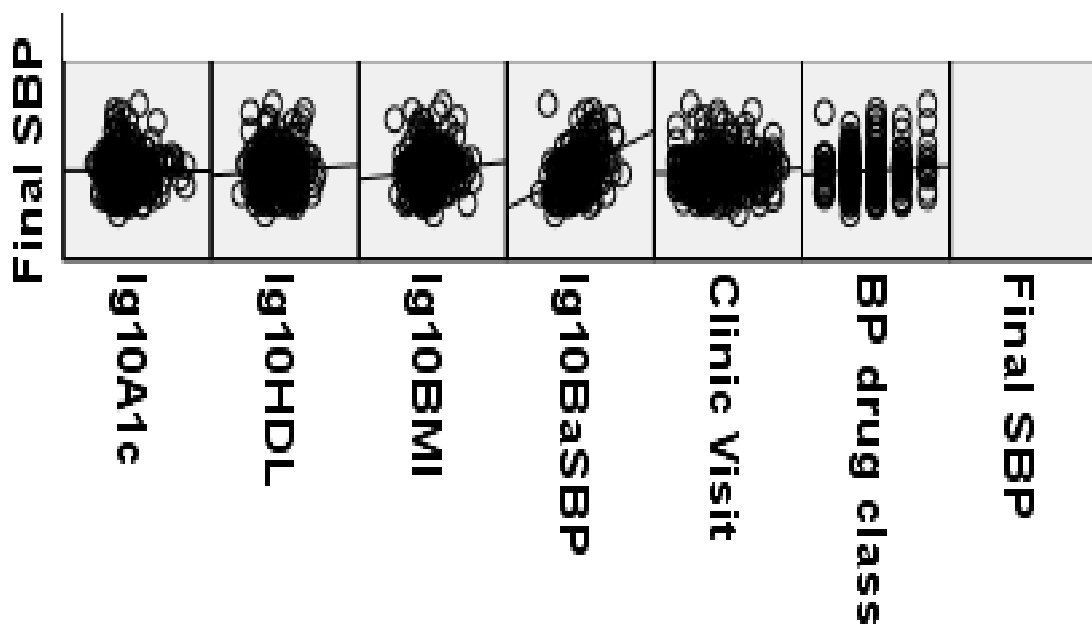


Figure 12. Scatterplots for Question # 2a

**Aim # 3.**

Describe any significant association among non-normally distributed IVs and the final SBP.

**Question # 3.**

Can status of veterans' final SBP be correctly predicted from knowledge age, A1C, HDL, BMI?

**Answer # 3.**

Since *total BP med* and *clinic visit* were normally distributed variables per histograms and descriptive statistics, they were not included in the LR model testing. *Age* was added to the LR model analysis instead.

Forward stepwise LR analysis was conducted to explore which of the four (age, A1C, HDL, BMI) were predictors of veterans' final SBP (controlling for alcohol use, all

medication and anxiety statistically). Regression results indicated that the overall model fit was good with  $-2 \text{ Log likelihood} = 405.969$  compared to  $-2 \text{ Log likelihood} = 748.595$  capable of predicting membership reliably (Mertler & Vannatta, 2013). However, none of the four IVs were entered at the step one of the forward LR model, indicated that there was not any significant correlation among them.

**Aim # 4.**

Describe any relationships between categorical predictor variables (Yes/No) and an outcome variable of final (SBP < 140) or (SBP  $\geq$ 140).

**Question # 4.**

What were the significant relationships between age ( $\geq$ 60 or <60), race (Black/non-Black), religion (yes/no), tobacco use (yes/no), alcohol use (yes/no), OSA (yes/no), DM (yes/no), dyslipidemia (yes/no), BMI ( $\geq$ 30, <30), MDD (yes/no), GAD (yes/no), PTSD (yes/no), medication adherence (yes/no), brain damage (yes/no), heart damage (yes/no), CKD (yes/no) and final SBP ( $\geq$  140, < 140)?

**Answer # 4.**

$\chi^2$  tests were conducted to determine any relationships between 15 nominal independent variables and the outcome variable. There was a strong evidence ( $p < 0.001$ ) to indicate that 1 of the 15 predictor variables (i.e., self-reported medication adherence) was significantly associated with veterans' final SBP (see Table 4).



Table 4  
Relationships between Categorical Independent Variables and Final SBP

Variable	$\chi^2$ Fisher's Exact Test	<i>p</i>	Cramer's V
Age ( $\geq 60$ / $< 60$ )	0.002	.960	.003
Race (Black/non-Black)	0.477	.490	.041
Religion (yes/no)	0.651	.722	.047
Tobacco use (yes/no)	0.004	.949	.004
Alcohol use (yes/no)	0.168	.682	.024
OSA (yes/no)	0.276	.600	.030
DM (yes/no)	0.036	.850	.011
BMI ( $\geq 30$ / $< 30$ )	1.058	.304	.059
MDD (yes/no)	1.106	.303	.059
GAD (yes/no)	0.013	.910	.007
PTSD (yes/no)	0.052	.478	.122
Med-adherence (yes/no)	80.921	< .001**	.586
Brain damage (yes/no)	1.495	.221	.070
Heart damage (yes/no)	3.385	.066	.106
Kidney damage (yes/no)	0.036	.850	.011

### Medication Adherence & Final SBP Chi-Square Tests

	Value	df	Asymptotic Significance (2- sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	103.373 <sup>a</sup>	2	.000	.000		
Likelihood Ratio	83.754	2	.000	.000		
Fisher's Exact Test	<b>80.921</b>			<b>.000</b>		
Linear-by-Linear Association	21.868 <sup>b</sup>	1	.000	.000	.000	.000
N of Valid Cases	301					

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is 1.24.

b. The standardized statistic is -4.676.

*Figure 13.* X<sup>2</sup> test / Fisher's exact test

The X<sup>2</sup> test result of medication adherence (yes/no) and SBP ( $\geq 140$ / $< 140$ ) shows that 3 cells = 50% which is  $\geq 20\%$  have expected count less than 5 with a standardized statistic of -4.667 ( $< 1$ ), indicating an assumption violation. Fisher's exact test was used to interpret the test result.

### Symmetric Measures

	Value	Approximate Significance	Exact Significance
Nominal by Nominal	Phi	.586	.000
	Cramer's V	.586	.000
N of Valid Cases	301		

*Figure 14.* Cramer's V

### Summary of Results

Utilizing a convenient sample of 331 cases to represent hypertensive veterans in the Southern California region, data was collected to explore multidimensional factors impacting veterans' HTN control. The study found a strong evidence ( $p < .001$ ) to

support that self-reported medication adherence to antihypertensive drugs was an independent predictor to veterans' final SBP level.

## Chapter 5: Discussion

The purpose of this chapter is to provide rich discussion to the study results. It begins with a summary discussion of the research design and methodology that impact the study results. It then compares these results with previous results in the area. It next discusses the study limitations. It ends with implications for future research and a conclusion.

### Summary of Research Design and Method

This was the first study that utilized a VA dashboard data set in an EMR system to explore multidimensional factors impacting U.S. veterans' final SBP. The unique research design allowed the study to provide novel insights into multiple aspects of HTN control research results for future studies. First, the descriptive statistics demonstrated a long term (2-year) uncontrolled SBP rate of 58% and an increased pre-HTN rate of 11.9% from a baseline point 43.6% to a final point of 55.5% of an EMR review. Second, the fitness test of exploratory MLR model showed five unfitted variables including A1C, HDL, BMI, BP med, clinic visit due to severe normality and or linearity violations. The unfitting variable of A1C and HDL could be associated to manipulations by DM and dyslipidemia medication therapy, making values of A1C and HDL atypical. The exploratory stepwise LR model showed a good overall model fit, no significant correlations were found between four IVs (i.e., age, A1C, HDL, Baseline SBP) and one DV (SBP), suggesting none of the four IVs from this data set were predictors for veterans' final SBP. Since A1C represents ones' average blood sugar level within past 3-month, values of A1C must match with SBP measurements in the same time periods to

have meaningful correlational outcomes. However, that was not the case in this study. The exploratory  $\chi^2$  tests showed 14 out of 15 non-significant associations between and among independent variables (i.e., OSA, DM, dyslipidemia, MDD, GAD, PTSD, brain damage, heart damage, CKD) and a dependent variable of final SBP. This is likely associated with utilizing ICD-9-CM codes that only have “yes/no” options in operational definition of many multidimensional variables by nature of utilizing retrospective data. Surprisingly, the study found strong evidence ( $p < .001$ ) of self-reported medication adherence as an independent predictor for veterans’ final SBP based on a positive Fisher exact test. Third, the cross-sectional data collection took place at a single point in time per study case and the researcher could easily over or under estimate the results, particularly in the estimation of regularly changing medication data. Fourth, the retrospective EMR review utilized pre-existing data for a research purpose that was unintended when the data was created. Nevertheless, the study had to employ available data to answer four research questions by this inquiry. In this case, the results were less robust than desired. Finally, the non-probability sampling method disqualified the study for inferential statistics by design. However, multiple parallel comparisons of characteristics of this study sample with characteristics of the previous study sample have demonstrated a high external validity of the study results.

## Comparison of Study Results

### **Aim # 1.**

Describe the characteristics of hypertensive veterans in one Southern California VA clinic from data collected during a period of October 17, 2014 through October 17, 2016.

### ***Question # 1.***

What were characteristics of hypertensive veterans in one Southern California VA clinic for the seven dimensions of IVs from data collected during a period of October 17, 2014 through October 17, 2016?

Per HTN control conceptual framework (see Figure 2), the demographic dimension included age, sex, race, religion, branch of service, time of service, education, and disability rating. The result of this study with  $M_{age} = 62$  and  $SD = 13$  was consistent with a previous study results that showed veterans of multiple states with  $M_{age} = 63.9$  and  $SD = 13.2$  (Fletcher et al., 2012) and a study result that showed non-veterans at a Southern Florida Family Clinic with  $M_{age} = 62$  and  $SD = 13$  (Koti & Roetzbeim, 2015). This study's  $M_{age}$  was also consistent with the HTN-age prevalence in the United States based on an epidemiological study by Yoon, Fryar, and Carroll (2015). Gender of this study with 95.4% male was consistent with several previous HTN studies among VA populations (Range 92% - 96%; Choma, Griffin, Kaltenbach, Greevy, & Rumine, 2012; Fletcher et al., 2012; Gosmanova, Lu et al., 2014; Gosmanova, Molnar et al., 2015). Results of race (61.3% Caucasian) was consistent with a previous HTN study (Rittmueller et al., 2015), and the proportion of African-Americans (20.3%) of this study

was consistent with another previous HTN study result (Gosmanova, Molnar et al., 2015). However, education background of this study was missing in 64.7% of the cases; yet multiple similar HTN studies reported no such information. Results of religion, branch of military service, time of military service, and service connected disability have become major strengths of this study as the combined information allowed for a more complete picture of veterans' wellbeing from multiple perspectives. Spiritually, this study shows 71% of cases were Christians, including 27% Roman Catholics and 43.9% non-Catholic Christians compared with 69% Christians in the United States (Religion, 2016). Socioeconomically, this study shows the plurality of cases (43.6%) were Vietnam veterans with most of whom were from lower working class backgrounds with three fourths had family incomes above the poverty level (Sobering Vietnam Vets as of April 2016). Functionally, this study shows 37% cases without any service-connected disability ratings compared with previous HTN studies that had no such information reported. Results of multiple parallel comparisons indicated a well-represented demographic dimension with additional strengths to the study.

Per HTN control conceptual framework (see *Figure 2*), the lifestyle dimension included tobacco use and alcohol abuse. This study shows 20.6% current tobacco and 13.2% current alcohol users, consistent with a previous study results with 22% self-reported smoker and 11% positive screen for mild alcohol misuse by AUDIT-C (Rittmueller et al., 2015). Results of the parallel comparison of two studies indicate a well-represented sampling in the lifestyle dimension.

Per HTN control conceptual framework (see *Figure 2*), the secondary HTN dimension included an OSA diagnosis. This study shows 47.9% OSA among studied cases compared with 29% of mild and 30% of moderate OSA among hypertensive non-veterans' cases in a primary care setting (Brostrom et al., 2012), indicating more veterans in the study than non-veterans in a previous HTN study suffered OSA. Since OSA is associated with metabolic syndrome (Kong et al., 2016) with much higher prevalence rates of dyslipidemia, obesity, and insulin resistance rates among veterans (Fryar et al., 2016), it is possible that veterans would have also experienced a much higher rate of OSA than civilian population. The parallel comparison of two studies indicates a much higher OSA cases in the study compared with a previous study of civilian counterpart (Brostrom et al., 2012).

OSA represents a common, treatable, metabolic syndrome significantly associated with obesity, dyslipidemia and insulin resistance (Kong et al., 2016). One component of treatment for OSA is weight loss; therefore, perhaps the time has come to debate instituting a policy that holds patients accountable for their healthcare providers' recommendations. Specifically, this policy could detail healthcare providers' rights in situations where the patient does not demonstrate efforts to lose weight, refuses to discuss weight loss options, or does not wear continuous positive airway pressure (CPAP) machine at night based on the treatment providers' best judgement. Current health policy lacks a balanced approach in the long-term management of OSA, emphasizing patients' rights and satisfactions, but no responsibilities for one's own behavioral choices.



Per HTN control conceptual framework (see Figure 2), a total of three sets of major CVD comorbidities and lab values were included in the dimension. The study shows 68.4% dyslipidemia which was higher compared with a previous HTN study results of 56.6% (Fryar et al., 2016). This study shows 56.7% obesity which was also higher compared with a previous HTN study result of 41.2% (Fryar et al., 2016). This study shows a median BMI of 30 compared with a previous HTN study result that showed median BMI of 28.2 to 31.5, depending on group assignment by age (Choma et al., 2012). The study also shows 45.4% DM which is much higher compared with a previous HTN study result that showed 16.4% among male veterans in the U. S. from 2009 to 2012 (Fryar et al., 2016). Additionally, this study result shows median A1C of 6 mg/dl compared with a previous HTN study result that showed median A1C 7.0-7.2 mg/dl depending upon group assignments by age (Choma et al., 2012). The parallel comparison of two studies indicates a well-represented sampling in cardiovascular comorbidities of HTN (dyslipidemia and obesity) with exception of DM as there were more DM cases in the study than in the previous study. Cases of DM in this study were better controlled than cases in the previous study. No parallel comparison study could be found for the HDL laboratory value in the literature.

Per HTN control conceptual framework (see Figure 2), the mental health dimension included three mental health diagnosis. This study shows 32.8% MDD which is consistent with a previous HTN study result that showed 32.5% (Wecht et al., 2016). This study shows 12.9% GAD which is much lower than the previous HTN study result that showed 25% (Wecht et al., 2016). This study shows 20.9% PTSD which is

consistent with a previous HTN study result that showed 20% (Wecht et al., 2016). The parallel comparison of two studies indicates a well-represented sampling of mental health diagnosis in MDD and PTSD.

Per HTN control conceptual framework (see Figure 2), the medication dimension included medication adherence, an average of two-year clinic visit, number of BP medication patients were receiving, top three BP medication prescription names and a mean overall prescription medications patients were receiving at the time of data collection. This study shows a self-reported non-adherence rate of 7.4%, a much lower rate than a previous HTN study result that showed  $\geq 20\%$  medication non-adherence rate (Meddings et al., 2012). The result of two-year primary and cardiology clinic visit  $M \pm SD = 6 \pm 4$ , averaging  $3 \pm 2$  per year is consistent with a previous HTN study result that showed  $M \pm SD = 4.5 \pm 2$  (Koti & Roetzbeim, 2015). This study shows 7.7% cases received no BP medication, 42.6% received one, 31.9% received two and 17.8% received three or more BP medications, consistent with a previous HTN study results that showed 41.6% received one, 26.9% received dual and 15.9% received three or more BP medications (Vincze et al., 2008). A trend of the highest percentage of cases receiving monotherapy might indicate that 42.6% cases of this study and 41.6% cases of the previous HTN study were being treated for stage 1 rather than stage 2 HTN per JNC-7 HTN treatment guideline. In addition, this study shows the top three commonly prescribed antihypertensive medications were ACE inhibitor 38.3%, beta blockers 34.4%, and calcium channel blockers 30.7% compared with a previous HTN study that showed diuretic 45%, ACE inhibitors 37.5%, and calcium channel blockers 35% in an orthostatic

hypotensive group (Wecht et al., 2016) vs. ACE inhibitor 35.5%, calcium channel blockers 29%, and diuretics 27.4% in an orthostatic hypertension group (Wecht et al., 2016). Nevertheless, BP drug class makes no difference in reducing CVD risks among hypertensive cases based on a credible systematic review and meta-analysis (Frethim et al., 2012). However, JNC-7 recommended monotherapy with diuretic for most (Chobanian et al., 2003) without a sound of scientific evidence. This study shows a bimodal (see *Figure 15*) distribution in the total number of overall medications with two peaks at 5 and 10 indicating most study cases took either 5 or 10 kinds of prescription medications per day, a phenomenon of polypharmacy. Unfortunately, the bimodal shape of the total number of overall medications prevented the variable from participating in both MLR and LR analysis due to a concern that the data might bring about false or biased results. However, a previous HTN study result that showed “a higher number of prescribed medication ( $sr^2 = 0.06$ ,  $t = 2.42$ ,  $p < .05$ ) and lower medication adherence ( $sr^2 = 0.07$ ,  $t = -2.60$ ,  $p < .05$ ) were statistically significant determinants” of an increased SBP among Chinese American immigrants (Li, Wallhagen, & Froelicher, 2010). Results of the parallel comparisons indicate a well-represented sampling in total number of clinic visit and BP medication, but not medication adherence and total number of an overall medication in the medication dimension.

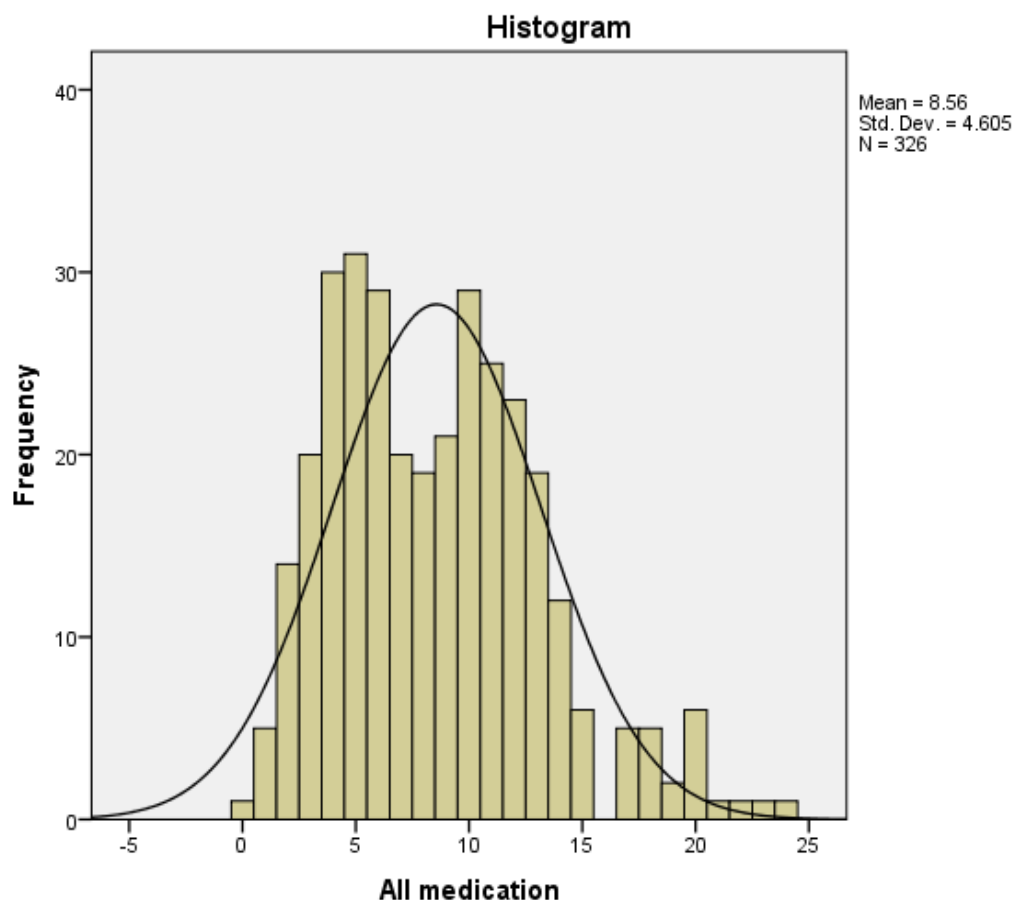


Figure 15. Bimodal distribution

Per HTN control conceptual framework (see Figure 2), the uncontrolled HTN dimension included baseline and final SBP as well as end-organ damage. Despite seven-point mean SBP decrease from the baseline 58% to the final point of 42%, the study shows a lower long term (two-year) SBP control rate of 42% (see *Table 1*) compared with the HTN control rate of 61.2%, a goal set by the Healthy People 2020 (Gillespie & Hurvitz, 2013). The study shows 11.9% increase in pre-HTN cases from a baseline (43.6%) to a final point (55.5%) of an EMR review ( $z = 3.2897, p < .001$ ).

JNC-7 highlighted that “pre-hypertensive individuals require health promoting lifestyle modifications to prevent the progressive rise in BP and cardiovascular disease” (Chobanian et al., 2003, p. xiv) because risk for CVD doubles in increments of 20/10 mmHg beginning at 115/75 mmHg (Chobanian et al., 2003). Nurse practitioners with the best training in health promotion and disease prevention are well positioned to provide counseling services to patients for lifestyle changes if deemed to be necessary. However, literature indicates that healthcare providers are not reimbursed for time spent on addressing lifestyle issues in patients with pre-hypertension (Hernandez & Anderson, 2012). This problem needs to be resolved at the federal level to include these services in Medicare and Medicaid coverage.

This study shows HTN-associated brain damage in 5.8% study cases compared with a previous HTN study results that showed 4.2% to 4.5% depending upon a BP treatment goal (“JATOS,” 2008), heart damage (17.5%) compared with the previous HTN study results (5.4% to 11.8%) depending upon levels of alcohol consumption (Rittmueller et al., 2015) and kidney damage (11%) compared with the JATOS Study Group results that showed 9.8% to 10% (2008) at a baseline.

In summary, multiple parallel or non-parallel comparisons of this study’s characteristics with prior studies helps to determine an external validity of an overall research results. Primarily, this study’s results could be generalizable to the target population of U.S. veterans given that the sample’s characteristics are highly representative of this group in terms of age, gender, ethnicity, lifestyle factors, comorbidities, mental health diagnosis and BP medication classes.

**Aim # 2.**

Examine the relationships among the predictor variables of blood glucose level (A1C), high-density lipoprotein (HDL), body mass index (BMI), total number of BP medication prescribed, total number of clinic visits, baseline SBP and the outcome variable of the final point SBP.

***Question # 2a.***

Which of the possible six predictor variables (i.e., A1C, HDL, BMI, clinic visit, BP med class, baseline SBP) were included in an equation for predicting veterans' final point SBP?

***Question # 2b.***

Does the obtained regression equation resulting from a subset of the six predictor variables allow us to reliably predict veterans' final point SBP?

Five out of six predictor variables were excluded from the MLR model due to severe linearity violations to the model assumption. As such, baseline SBP was the only predictor variable remaining in the MLR prediction model. Since veterans' SBP fluctuated throughout the day and can also be affected by confounders of lifestyle (e.g., alcohol, diet, exercise, caffeine, stress) and medication factors, a single baseline SBP would not have allowed us to predict veterans' final SBP reliably as multiple confounders were unaccounted by the prediction model. There are other factors that could have impacted A1C's model fitness. First, A1C values lack variance when most (64.1%) DM cases were well controlled by medication therapy as evidenced by A1C mode = 5.5 mg/dl and kurtosis = 4.961, making it unfit to the prediction model with severe linearity

violation to the MLR model assumption. Second, A1C represents an average of blood sugar level in the past three months and it must be associated with final SBP measurements within the same time periods for a meaningful outcome. However, that was not the case in this study.

While there is no evidence of a study examining an association between HDL and SBP in the literature, this study failed to find any association between the two variables. Nevertheless, HDL mode = 33 mg/dl was well below the normal values of  $\geq 40$  mg/dl for men and  $\geq 50$  mg/dl for women, this could indicate that HDL values are difficult to change with or without medication therapy. Moreover, HDL Kurtosis = 7.203 was unfit to a normal bell curve due to a severe violation to MLR model assumption. The non-linear association between HDL and SBP based on scatter plots (see *Figure 12*) was another violation to MLR model assumption. Although no evidence of a study examining the association, a previous HTN study found a positive association ( $p < 0.01$ ) between the ratio of total cholesterol (TC) to HDL or TC/HDL and BP alternatively (Okosun, Choi, Hash, & Dever, 2001).

While no evidence of a study examining an association between number of clinic visits and SBP, this study failed to detect any association between the two variables due to a severe violation of linearity assumption to the MLR model. While a previous systematic review and meta-analysis found no significant differences between BP medication class and BP reduction for primary prevention of DVD (Frethim et al., 2012), this study failed to detect any association between the two variables due to a severe violation of linearity assumption to the MLR model.

**Aim # 3.**

Describe any significant association between and among non-normally distributed IVs and the final SBP.

***Question # 3.***

Can status of veterans' final SBP be correctly predicted from knowledge of age, A1C, HDL, BMI?

Considering the review of relevant literature that found no statistically significant association between age and SBP, this study failed to detect it despite a previous epidemiology study showing an evidence that a relationship between age and SBP did exist (Yoon et al., 2015). Considering a previous systematic review and meta-analysis which found a weak linear association between BMI and SBP (Abayomi, 2012), this study failed to detect it in a LR model analysis. Failing to detect BMI and SBP association could be attributed to the strength of  $R^2$  values that ranged from 0.083 (weak) for males to 0.203 (weak) for females in the meta-analysis (Abayomi, 2012) with a good overall LR model fit background. Although weak associations could be detected with a high power by increasing a sample size, it was not the case in this study.

**Aim # 4.**

Describe any relationships between categorical predictor variables (Yes/No) and an outcome variable of final controlled (SBP < 140) or uncontrolled (SBP  $\geq$ 140).

***Question # 4.***

What were the significant relationships between age ( $\geq$ 60 or <60), race (black/non-black), religion (yes/no), tobacco use (yes/no), alcohol use (yes/no), OSA



(yes/no), DM (yes/no), dyslipidemia (yes/no), BMI ( $\geq 30$ ,  $<30$ ), MDD (yes/no), GAD (yes/no), PTSD (yes/no), medication adherence (yes/no), brain damage (yes/no), heart damage (yes/no), CKD (yes/no) and final SBP ( $\geq 140$ ,  $<140$ )?

This study shows a strong evidence ( $P < 0.001$ ) that self-reported medication adherence is an independent predictor for veterans' SBP. These results support a previous HTN study that showed habit-based medication adherence was not only the most effective predictor for BP outcomes, but also the most effective intervention in reducing BP by a systematic review and meta-analysis (Con, Ruppar, & Chase, 2016).

Although age 60 is a cut off point for a new set of BP treatment goals per JNC-8 (James et al., 2013), this study shows no significant association between age ( $\geq 60$  /  $<60$ ) and SBP ( $\geq 140$  /  $<140$ ). Still, 60 seem to be an age of high HTN prevalence in multiple epidemiology studies. However, it is the inferential statistics showing a statistically significant association between age and SBP with a p-value ( $<0.05$ ) that matters. So far, there is no previous study with a finding of a significant association between age and BP in the literature.

This study shows no significant association between race (black / non-black) and SBP ( $\geq 140$  /  $<140$ ), inconsistent with a previous systematic review that showed a small effect size, but significant association between perceived racial discrimination among hypertensive black males with low education level and HTN (Dolezsar, McGrath, Herzig, & Miller, 2014).

This study shows no significant association between religion (yes / no) and SBP ( $\geq 140$  /  $<140$ ) compared with a previous study that showed religious service attendance is inversely associated to SBP among white, black and Mexican-American ethnic groups (Bell et al., 2012). There is no systematic review and or meta-analysis exploring a relationship between religious involvement and SBP to the best of my knowledge.

This study shows no significant association between tobacco use (yes / no) and SBP ( $\geq 140$  /  $<140$ ), consistent with a previous cross-sectional study that showed tobacco use had no effect on BP (Li et al., 2010; Pandey et al., 2014; Thuy et al., 2010). However, there is no systematic review and or meta-analysis exploring an association between tobacco use and SBP to the best of my knowledge.

This study shows no association between alcohol use (yes / no) and SBP ( $\geq 140$ ,  $<140$ ) compared with a previous systematic review and meta-analysis that showed an association between dose-response alcohol consumption and risk of HTN (Briasoulis et al., 2012). Specifically, drinking alcohol  $<10$  gm/day to 11-20 gm/day has a trend toward an increased risk of HTN (RR 1.03, 95% CI, 0.94 -1.13,  $p = 0.51$ ) and (RR 1.15, 95% CI, 0.99-1.33,  $p = 0.06$ ) respectively, and that men with heavy drinking of alcohol at 31- 40 gm/day is significantly associated with an increased risk of HTN (RR 1.77, 95% CI, 1.39-2.26,  $P<0.001$ ). However, that systematic review and meta-analysis demonstrated an inclusion of articles defining HTN as BP  $\geq 165/95$  mmHg rather BP  $\geq 140/90$  mmHg, which was inconsistent with the JNC-7 guideline.

This study shows no association between OSA (yes / no) and SBP ( $\geq 140$  /  $<140$ ), consistent with a reviewing of relevant literature that found no association between OSA and BP by systematic review and or meta-analysis to the best of my knowledge.

This study shows no association between DM (yes / no) and SBP ( $\geq 140$  /  $<140$ ), consistent with a review of relevant literature that found no association between DM and BP by systematic review and or meta-analysis to the best of my knowledge.

This study shows no association between dyslipidemia (yes / no) and SBP ( $\geq 140$  /  $<140$ ), consistent with a review of relevant literature that found no association between dyslipidemia and BP by systematic review and or meta-analysis to the best of my knowledge.

This study shows no association between BMI ( $\geq 30$  /  $<30$ ) and SBP ( $\geq 140$  /  $<140$ ), inconsistent with findings from two previous HTN studies that showed BMI was not only significantly and positively associated with SBP and DBP (Zhang, Wang, Yan, Gong, & Guo, 2013), but also linearly or curvilinearly associated with SBP by a meta-analysis despite the relationship was rather weak (Abayomi, 2012).

This study shows no association between MDD (yes / no) and SBP ( $\geq 140$  /  $<140$ ), consistent with a review of relevant literature that found no association between a diagnosis of MDD and SBP to the best of my knowledge.

This study shows no association between GAD (yes / no) and SBP ( $\geq 140$  /  $<140$ ), inconsistent with a previous systematic review and meta-analysis result that

showed a significant association between anxiety and HTN with OR 1.18, 95% CI, 1.02 to 1.37,  $P < 0.001$  (Pan et al., 2015).

This study shows no association between PTSD (yes / no) and SBP ( $\geq 140$  /  $<140$ ), consistent with a review of relevant literature that found no association between PTSD diagnosis and SBP to the best of my knowledge.

This study shows a strong evidence ( $P < 0.001$ ) of self-reported medication adherence to antihypertensive medication (yes / no) and is an independent predictor to veterans' SBP ( $\geq 140$  /  $<140$ ), inconsistent with a review of relevant literature that found no systematic review and or meta-analysis exploring such a relationship to the best of my knowledge. Therefore, the finding of such a significant association could be viewed as innovative and the result must be confirmed by systematic review and or meta-analysis utilizing RCT and longitudinal studies in the future. However, current medication adherence construct lacks an association with BP control outcome which makes it difficult to associate two variables of medication adherence and BP in one entity. Clearly, there is a need for an operational definition of patients' adherence to antihypertensive medication that are associated with BP outcomes in one entity.

Finally, this study shows no association between brain damage (yes / no), or heart damage (yes / no) or kidney damage (yes / no) and SBP ( $\geq 140$  /  $<140$ ), inconsistent with two previous Japanese study results that showed brain damage, or heart damage or kidney damage were significantly associated with SBP ("JATOS," 2008; Ogihara et al., 2010). However, this Japanese study did have serious methodological weaknesses. It

would be better if evidence of significant associations between and among brain, heart, kidney damages and SBP were found from a couple of systematic review and or meta-analysis, however such evidence was not found by this review of relevant literature.

Comparing this study results that utilized MLR, LR and  $X^2$  statistical analysis models with previous HTN study results via systematic review and or meta-analysis may seem to be unparalleled. However, this is the best way for truth finding if researchers want the most efficient way about it. First, systematic review and or meta-analysis are research designs with the highest level of study quality (Crowther, Lim, & Crowther, 2010). Second, systematic review and or meta-analysis produces results with less biases (Crowther et al., 2010) compared with results from cross-sectional studies.

### **Limitation**

There are several limitations to this study. First, there were noteworthy issues with the operational definition of key study variables including A1C, tobacco dependence, alcohol abuse or misuse, MDD, GAD, PTSD, OSA, DM, dyslipidemia, Obesity, CVA, TIA, CHF, CAD, MI, CABG and CKD, resulting in an inadequate assessment of correlations between these variables and final SBP. Future studies should pay attention to the special features of A1C values and consider using validated multidimensional instruments in relationship studies. Specifically, ensuring A1c values matches BP measurements within three-months window time frame for meaningful correlational outcomes is important. Moreover, using patients' Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001) for assessing MDD, Generalized Anxiety Disorder scale (GAD-7; Plummer, Manea, Trepel, & McMillan, 2016) for GAD, and

PCL-5-M (Keane et al., 2014) for PTSD are more meaningful than using ICD-9-CM codes with “yes / no” operational definition in relevant relationship studies. Second, there were major barriers to data accuracy assessment regarding primary data manipulation and data collection. Specifically, primary data of A1C and HDL values were manipulated by medication therapy for approximately 96.3% veterans and the impact of manipulation to the overall statistical model fit was difficult to estimate. Additionally, funding and time constraints prohibited random check blindly on collected data. Consequently, the inter-rater agreement Kappa was not calculated to confirm the accuracy of the data collected.

### **Implication for Future Research**

Although this study finds self-reported medication adherence is an independent predictor to a veteran’s final SBP level, validity of self-reported medication adherence can be influenced by multidimensional factors including patients-related factors (e.g., age, sex, race, education level, knowledge, self-care ability, patient-satisfaction, self-efficacy, attitude, cognition, perceived stress), provider-related factors (e.g., prescription of medication, communication style, attitude toward adhering to current HTN treatment guideline, role modeling, teaching consistency and content) and environment-related factors including health policy (e.g., insurance, copayment, BP treatment goal per HTN management guideline) and healthcare system (e.g., access to care, communication system) (Viswanathan et al., September 2012). Therefore, future HTN control research should focus on *multidimensional determinants of self-reported patients’ adherence to antihypertensive medications fully*. Since all medications have side effects in context

that some patients are not on antihypertensive medication therapy for treatment of HTN and that lifestyle modification works for BP reduction (Briasoulis et al., 2012; Landsbergis et al., 2013; Mesas, Leon-Munoz, Rodriguez-Artalejo, & Lopez-Garcia, 2011; Saneei et al., 2014; Semlitsch et al., 2013), future HTN research should focus on multidimensional determinants of self-reported patients' adherence to HTN treatment fully *to broaden the scope of coverage*. Since current definition of patients' adherence to HTN treatment lacks an association with HTN outcomes based on extensive review of relevant literature, future HTN control research should focus on *operationally defining adherence and BP control outcomes in one entity*. Since HTN definition can affect HTN control outcomes, future HTN control study should *use a consistent HTN definition defined by JNC-7* rather than JNC-8. Since self-reported HTN treatment may be influenced by not only patients, but also healthcare providers, future HTN control studies should *assess this construct for both patients and healthcare providers simultaneously so that two-way outcome feedback could be accomplished*. Since theory can help to make predictions of ones' BP levels possible (Bandura, 1971) when an operational definition of patients' adherence to HTN treatment is defined with BP outcome in one entity, future HTN control research should focus on some *theory-guided operational definitions linking patients' adherence to HTN treatment and outcomes (e.g., primary, secondary and or tertiary)*.

Ideally, patients' adherence to HTN treatment should be assessed by a scaled measure that takes into consideration multidimensional factors impacting BP control rather than self-reported adherence utilizing "yes/no" options when it can be quickly and

easily done in the real world. However, it may subject veterans' to recall bias and reading level. Therefore, future theory guided operational definitions of self-reported adherence to HTN treatment will be challenged by these limitations. It is therefore, vitally important to consider using the future tense in the sentence construction and reading level with some theory-guided operational definitions linking patients' and providers' adherence to HTN treatment and outcomes. Multiple field tests and pilot studies would be necessary in the process of developing a reliable theory-guided instrument measuring self-reported patients' and providers' adherence to a standardized HTN treatment protocol in the future.

Since the rate of pre-HTN increased from the baseline to final point per EMR review, associating risks of pre-HTN with CVD or benefit with pre-HTN could also guide future research. Since current research is not only limited on the topic, but also with multiple methodological weaknesses in the research design based on a review of relevant literature, utilizing a random sampling method in longitudinal studies to explore any relationships would be helpful in contributing potential new knowledge to the existing nursing research database.

## **Conclusion**

The study explored multidimensional factors impacting veterans' HTN control with a descriptive, exploratory, cross-sectional, retrospective and non-probability sampling design. Despite the limited data in essential areas, the study found a strong evidence ( $p < 0.001$ ) through fisher exact test to support that self-reported medication adherence to antihypertensive medication therapy was an independent predictor to



veterans' final SBP. Future HTN control research may focus on exploring some theory-guided multidimensional determinants of patients' and providers' adherence to HTN treatments (e.g., lifestyle modification and antihypertensive drug therapy), rather than unidimensional medication adherence, and HTN control outcomes fully (e.g., BP, quality of life, target organ damage), utilizing a consistent HTN definition defined by JNC-7.

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## Appendices

### Appendix A: SPSS Code for Exploring Factors Impacting Veterans' Hypertension Control

Variable	Variable Description	Measure	Values
1. Age	Index date per EMR review ( $\geq 60$ , $<60$ ) for $\chi^2$ test.	Continuous, Categorical, Dichotomous	1 = 24 – 44, 2 = 45 – 64, 3 = 65+
2. DisRat	Disability rating by percentage of service connected disability	Continuous & Categorical,	0 = 0 %, 1 = 10 - 50%, 2 = 60 - 100%,
3. A1C	HgA1C (mg/dl)	Continuous & Categorical,	0 = $< 6.5$ , 1 = 6.5 – 7.4 2 = 7.5 – 8.4, 3 = 8.5 -9.4 4 = $\geq 9.5$ , 99 = missing
4. HDL	HDL (mg/dl)	Continuous & Categorical,	1 = $< 40$ , 2 = 40-49 3 = 50-59, 4 = $\geq 60$ 999= missing
5. BMI	BMI (kg/m <sup>2</sup> )	Continuous & Categorical,	0 = 18.5-24.9, 1 = 25.0-29.9 2 = 30.0-34.9, 3 = 35.0-39.9 4 = $\geq 40.0$
6. BPRX	Total number of BP medication prescription at the time of EMR review	Continuous & Categorical,	0 = 0 BP RX 1 = 1 BP RX 2 = 2 BP RX 3 = $\geq 3$ BP RX
7. AmT	All medication total	Continuous & Categorical,	1 = 1-5 pills 2 = 6-10 pills 3 = 11-15 pills 4 = $\geq 16$ pills
8. ClinVist	Total number of primary & cardiology clinic visit	Continuous & Categorical,	0 = 0 visit in 2-year 1 = 1-4 visits in 2-year 2 = 5-8 visits in 2-year

	during the 2-year study period		3 = $\geq 9$ visits in 2-year
9. BaSBP	Baseline systolic BP at the time of EMR review	Continuous & Categorical,	0 = < 120, 1 = 120-139 2 = 140-159, 3 = $\geq 160$
10. BaDBP	Baseline diastolic BP at the time of EMR review	Continuous & Categorical,	0 = < 80, 1 = 80-89 2 = 90-99, 3 = $\geq 100$
11. FiSBP	Final systolic BP at the time of EMR review	Continuous & Categorical,	0 = < 120, 1 = 120-139 2 = 140-159, 3 = $\geq 160$
12. FiDBP	Final diastolic BP at the time of EMR review	Continuous & Categorical,	0 = < 80, 1 = 80-89 2 = 90-99, 3 = $\geq 100$
13. Sex	Men or Women	Nominal	1 = Men, 2 = Women
14. Race	Race/Ethnicity of case	Nominal	1 = Caucasian 2 = African American 3 = Other or missing
15. Religion	Religious affiliation of cases	Nominal	1 = Roman Catholic 2 = Non-Catholic Christian 3 = other or missing
16. Branch	Branch of military serviced	Nominal	1 = Air Force, 2 = Army 3 = Navy
17. Time	Time periods of service	Nominal	0 = Peace time only 1 = Persian Gulf War 2 = Vietnam Era/Korean war/WW II
18. Edu	Highest education level attained	Ordinal	1 = < High School, 2 = $\geq$ High School, 99 = missing
19. Tobacco	current smoke/chew tobacco per MD's note/ICD-9-CM code	Nominal	0 = no 1 = yes

20. Alcohol	current drink alcohol per ICD-9-CM code & MD's note	Nominal	0 = no 1 = yes
21. MDD	MDD per ICD-9-CM code	Nominal	0 = no, 1 = yes
22. GAD	GAD per ICD-9-CM code	Nominal	0 = no, 1 = yes
23. PTSD	PTSD per ICD-9-CM code	Nominal	0 = no, 1 = yes
24. OSA	OSA per ICD-9-CM code	Nominal	0 = no, 1 = yes
25. ACEI	ACE inhibitor	Nominal	1 = Yes, 0 = No
26. ARB	Angiotensin Receptor Blocker	Nominal	1 = Yes, 0 = No
27. $\alpha$ -block	$\alpha$ -blocker (Prazosin)	Nominal	1 = Yes, 0 = No
28. BB	BB (Atenolol)	Nominal	1 = Yes, 0 = No
29. CCB	CCB (Amlodipine, diltiazem, Verapamil, Nifedipine)	Nominal	1 = Yes, 0 = No
30. CA $\alpha$ A	Centrally acting $\alpha$ -Agonist	Nominal	1 = Yes, 0 = No
31. ComDrug	Combination drugs	Nominal	1 = Yes, 0 = No
32. Diuretic	Diuretic	Nominal	1 = Yes, 0 = No
33. HydraZin	Vasodilator/hydralazine	Nominal	1 = Yes, 0 = No
34. Spiro	Spironolactone	Nominal	1 = Yes, 0 = No
35. Iso	Nitrates/Isosorbide	Nominal	1 = Yes, 0 = No
36. MedAdh	Medication adherence	Nominal	0 = Medication Non-adherence 1 = Medication Adherence 99 = missing
37. EOD-brain	EOD-brain: TIA/CVA/dementia	Nominal	0 = no, 1 = yes
38. EOD-heart	EOD-heart CHF/CAD/MI/CABG	Nominal	0 = no, 1 = yes
39. EOD-kidney	Chronic kidney disease (CKD)	Nominal	0 = no, 1 = yes
40. Dyslip	Dyslipidemia	Nominal	0 = no, 1 = yes
41. DM	HTN comorbidity of DM	Nominal	0 = no, 1 = yes
42. FinalSBP	For LR analysis	Dichotomous	0 = $\geq 140$ 1 = $< 140$
43. FinalDBP	For LR analysis	Dichotomous	0 = $\geq 90$ 1 = $< 90$

## Appendix B: Data Abstraction Instrument (Microsoft Excel in Word Format)

	1	2	3	4	5	6	7
ID	Age	DisRat	A1C	HDL	BMI	BPmT	AmT
A0097, RIC							

	8	9	10	11	12	13	14
ID	ClinVist	BaSBP	BaDBP	FiSBP	FiDBP	Sex	Race
B0245, ROG							

	15	16	17	18	19	20	21
ID	Religion	Branch	Time	Edu	Tobacco	Alcohol	MDD
C0051, ROC							

	22	23	24	25	26	27	28
ID	GAD	PTSD	OSA	ACEI	ARB	a-Block	BB
D0583, LAR							

	29	30	31	32	33	34	35
ID	CCB	CAaA	CombDrug	Diuretic	HydroZin	Spiro	Iso
E1605, LIS							

	36	37	38	39	40	41	42
ID	MedAdhe	EODbrain	EODheart	EODkidney	Dyslip	Obesity	DM
F1586, JAM							

### Appendix C: Theoretical and Operational Definition of Key Study Concept

**Age:** is defined by the date of birth (DOB) on the day of an EMR review.

**Sex:** is categorized by male or female per EMR review.

**Race/ethnicity:** is classified as Caucasian, African American, Other or missing per EMR review.

**Religion:** is classified by Roman Catholic, non-Catholic Christian, Other or missing per EMR review.

**Branch of military service:** is classified as Air Force, Army or Navy per EMR review.

**Time periods of military service:** is classified as Peace time only, Persian Gulf war, Vietnam Era / Korean war / WW II per EMR review.

**Education:** is classified as  $\geq$  high school or missing or  $<$  high school based on multidisciplinary “note” per EMR review.

**Service connected disability:** is operationally measured from 0 to 100% per EMR review.

**Current tobacco use:** is operationally measured by presence (yes) or absence (no) of tobacco dependence ICD-9-CM code 305.1 and primary healthcare providers’ “note” indicating current use per EMR review.

**Current alcohol use:** is operationally measured by presence (yes) and absence (no) of alcohol abuse ICD-9-CM code 305.00 and primary healthcare providers’ “note” indicating current consumption of alcohol per EMR review.

**OSA:** is operationally measured by presence (yes) or absence (no) of OSA ICD-9-CM code 327.23 per EMR review.

**DM:** including type I and II, is operationally measured by presence (yes) or absence (no) of DM ICD-9-CM code 250.00 per EMR review.

**A1C:** referring to an average blood sugar level for the past three months, is operationally measured by the latest (toward the end of a EMR review) A1C (mg/dl) value from October 17, 2014 through October 17, 2016 per EMR review.

**HDL:** referring to a high-density lipoprotein level, is operationally measured by the latest (toward the end of chart review) HDL value (mg/dl) from October 17, 2014 through October 17, 2016 per EMR review.

**Dyslipidemia:** referring to an abnormal blood lipid level, is operationally measured by presence (yes) or absence (no) of dyslipidemia ICD-9-CM code 272.4 per EMR review.

**BMI (body mass index):** is operationally measured by the latest measurement (toward the end) from Oct 17, 2014 through Oct 17, 2016 per EMR review.

**MDD (major depressive disorder):** is operationally measured by presence (yes) or absence (no) of MDD ICD-9-CM code 298.0 per EMR review.

**GAD (generalized anxiety disorder):** is operationally measured by presence (yes) or absence (no) of GAD ICD-9-CM code 300.02 per EMR review.

**PTSD (post-traumatic stress disorder):** is operationally measured by presence (yes) or absence (no) of PTSD ICD-9-CM code 309.81 per EMR review.

**BP medication:** is operationally measured by a numeric number from 0 – 4 of BP medication class among ACEI, ARB,  $\alpha$ -blocker,  $\beta$ -blocker, CCB, centrally acting  $\alpha$ -agonist, Combination drug, Diuretic, Vasodilator, Spironolactone and Nitrates case per EMR review.



**Clinic Visit:** is operationally measured by a numeric number from 0 – 15 primary care and cardiology clinic visits during a period of October 17, 2014 and October 17, 2016 based upon the total number of BP measurements generated from those office visits.

**Baseline and final BP measurement:** are continuous variable in “mmHg” by *toward the beginning* and *toward the end* of the EMR review from October 17, 2014 through October 17, 2016.

**Essential HTN:** is operationally defined as BP elevation without identifiable cause with seated BP  $\geq 140/90$  mmHg at two or more office visits or current use of BP-lowering medication with ICD-9-CM code of 401 regardless their awareness of it (Chobanian et al., 2003; James et al., 2013).

**Controlled HTN:** is operationally defined as BP  $< 140/90$  mmHg at both the baseline and the final points of a EMR review.

**Uncontrolled HTN:** is operationally defined as BP  $\geq 140/90$  mmHg at both the baseline and the final points of a EMR review.

**Medication adherence:** is operationally measured by primary healthcare providers’ note (e.g., patient was non-adherent to antihypertensive drug therapy, or patient refused to antihypertensive drug therapy) per EMR review.

**End organ damage of brain:** is operationally measured by presence (yes) or absence (no) of TIA, CVA and dementia ICD-9-CM code of 433.1 for TIA, 434.91 for CVA and 290.42 for vascular dementia per EMR review.

**End organ damage of heart:** is operationally measured by presence (yes) or absence (no) of CHF CAD, MI, CABG ICD-9-CM codes of 428.0 for CHF, 414.01 for CAD, 410.9 for MI and V45.81 for CABG per EMR review.

**End organ damage of kidney:** is operationally measured by presence (yes) or absence (no) of CKD ICD-9-CM code of 585.9 per EMR review.



**SIGNATURE PAGE**

All applicable signature lines MUST be signed. If any required lines are left blank, the application will be returned to the principal investigator.

\_\_\_\_\_  
**Researcher (signature)** Department/School and Date

Jian Hua Liu, PhDc, MSN, SON PhD Student

\_\_\_\_\_  
**Researcher (printed)** REQUIRED: email Phone

\_\_\_\_\_  
**Faculty Advisor (signature)** Department/School and Date

(Only required if PI is a USD Student.)

Joseph F. Burkard, DNSc, CRNA

\_\_\_\_\_  
**Faculty Advisor name (printed)** REQUIRED: email Phone

\_\_\_\_\_  
**USD Sponsor (signature)** email Phone

(Only required if PI is NOT a USD student/faculty. The USD sponsor must be a full-time employee of USD).

\_\_\_\_\_  
**USD Sponsor name (printed)** Department/School and Date

\_\_\_\_\_  
**School/College IRB Representative** Date

(ALL applications must obtain this signature, whether your unit has a designated IRB representative or not. Contact the IRB Chairperson if you need guidance.)

\_\_\_\_\_  
**Dean/His/Her Representative (signature)** Date

*The project described above has been approved by the USD Institutional Review Board.*

\_\_\_\_\_  
**Chair or Administrator to IRB (signature)** Date