THE PROGNOSTIC VALUE OF RELATIVE GRIP STRENGTH IN ASSESSING HYPERTENSION RISK

by

Ebony C. Gaillard

A dissertation submitted to the faculty of
The University of North Carolina at Charlotte
in partial fulfillment of the requirements
for the degree of Doctor of Philosophy in
Biology

Charlotte

2023

Approved by:

____
Dr. Reuben Howden

____
Dr. Adam Reitzel

____
Dr. Eugenia Lo

____
Dr. Joseph Marino

____
Dr. Jeanette M. Bennett

ABSTRACT

EBONY C. GAILLARD. The Prognostic Value of Relative Handgrip Strength in Assessing Hypertension Risk. (Under the direction of DR. REUBEN HOWDEN).

More than 1.3 billion people are affected by hypertension (HTN) globally. Research has shown that Black women have the highest prevalence of hypertension worldwide compared to women of other racial/ethnic backgrounds. Although attempts have been made to reduce prevalence of HTN among Black women through non-pharmacological and pharmacological interventions, blood pressure control remains suboptimal. Handgrip strength, a measure of overall muscular strength, has been associated with risk of hypertension, cardiovascular-related mortality, and all-cause mortality. Currently, there is conflicting evidence on the predictive value of relative handgrip strength in assessing hypertension risk in women, specifically Black women. We conducted three studies to investigate the utility of relative handgrip strength to predict hypertension risk in US and South African women. Study 1 was conducted to establish whether there was a cross-sectional relationship between relative handgrip strength and hypertension in a nationally representative sample of US Black and white women (NHANES). We determined that there was an inverse association between relative handgrip strength and hypertension in women, and there was no statistical difference in the association found between Black and white women. Study 2 assessed the longitudinal association between relative handgrip strength and hypertension in an age-matched sample of middle-aged and older US Black and white women (MIDUS). We found no significant relationship between relative handgrip strength and hypertension in both Black and white women. Study 3 investigated the cross-sectional and longitudinal associations between relative handgrip strength and hypertension in a cohort of middle aged and older Black South African women (HAALSI). No longitudinal association was found between relative handgrip strength and hypertension in middle-aged and older Black South African women. The results of this dissertation can provide guidance on strategies to identify women at risk for HTN earlier and to improve blood pressure management.

DEDICATION

In Loving Memory of My Grandmas Nancy and Mozelle and Grandpa Richard.
Thank you for all your love and wisdom to cherish for a lifetime.

ACKNOWLEDGEMENTS

I would like to thank my advisor Dr. Reuben Howden for your mentorship and guidance throughout my dissertation. Thank you for all your support throughout my graduate school matriculation and providing me the space to explore my research and career interests. I would also like to thank my committee members Dr. Adam Reitzel, Dr. Eugenia Lo, Dr. Joseph Marino, and Dr. Jeanette M. Bennett for the time and effort dedicated to helping me though this project. Additionally, thank you for going above and beyond your role and providing me the guidance, expertise and help to complete my project. Special thanks to Dr. Soma Nag for your assistance helping me learn SAS and developing my data analytic skills. I would also like to express my gratitude to Dr. Yvette Huet for her mentorship and support throughout my graduate school program. To my parents, Kevin and Donna, for always being there for me and for all the sacrifices you have made for me to be here today. Thank you for being a shoulder to lean on during the most challenging days and always being present to celebrate my biggest victories. To my sister, Jasmine, thank you for always believing in me and recognizing my potential. Thank you for your unwavering support, laughter shared, and your endless song recommendations. Thank you, Grandpa Leroy, for being an exemplary example of what can be accomplished with hard work and providing me wisdom throughout my educational journey. Lastly, my acknowledgements would not be complete without thanking my grandparents who have transitioned, Grandma Nancy, Grandma Mozelle, Grandpa Richard. Thank you for your teachings, love, and steadfast support. I hope I have made you proud.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACC: American College of Cardiology

AHA: American Heart Association

BP: Blood Pressure

CVD: Cardiovascular Disease

DBP: Diastolic Blood Pressure

SBP: Systolic Blood Pressure

HCP: Health Care Provider

HGS: Handgrip Strength

HAALSI: Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa

HTN: Hypertension

MIDUS: Midlife in the United States

NHANES: National Health and Nutrition Examination Survey

PWV: Pulse Wave Velocity

RBP: Resting Blood Pressure

WHO: World Health Organization

INTRODUCTION

Brief Overview of Hypertension and Influencing Factors

Hypertension (HTN, defined as resting blood pressure (RBP) ≥ 130 and/or ≥ 80 mmHg) is a chronic medical condition characterized by higher-than-normal blood pressures against the arterial walls. It is global health concern that affects more than 1 billion people worldwide and over 100 million United States adults (Benjamin et al., 2019; James et al., 2014). Hypertension represents a major modifiable risk factor for cognitive decline and numerous cerebrovascular and cardiovascular diseases (CVD) including heart failure, stroke, myocardial infarction, and sudden death (Brook et al., 2013).

Treatment guidelines for HTN emphasize the importance of risk reduction for future adverse CVD outcomes. The American College of Cardiology (ACC) and American Heart Association (AHA) guidelines recommend implementing lifestyle modifications alone or concurrently with pharmacological therapy as an optimal treatment strategy for lowering blood pressure (BP) in adults (Wenger et al., 2018; Whelton et al., 2018). Unfortunately, many individuals are unable to achieve or sustain the recommended BP levels , with only 1/3 of hypertensive adults achieving BP control (Fryar et al., 2017). Early detection of HTN risk to identify individuals more susceptible to HTN-related CVD conditions is very important. Implementing effective blood pressure-lowering interventions to reduce or even avoid the health consequences of HTN should be a public health priority.

Hypertension is a multifactorial disease with a complex pathophysiology. Although both men and women develop HTN, there are gender differences in the etiology, incidence, pathophysiology, and severity (Lombardi M, 2017). Women experience unique phases across their lifespans that may explain the sexual dimorphism in BP control (Maas, 2019; Samad et al., 2008). HTN-related CVD risk factors specific to women include menarche, menstrual cycling, pregnancy, menopause, hormone replacement therapy, and oral contraception use (Samad et al., 2008; Wenger et al., 2018; Yoder et al., 2009). Despite the major health complications associated with HTN, HTN awareness, treatment and control remain suboptimal among women so appropriate interventions are needed to reduce HTN-related morbidity and mortality in women (McDonald et al., 2009).

Globally, HTN disproportionately affects minority populations especially people of African descent (Mills et al., 2016). In this dissertation, Black is a racialized term used to describe people of African ancestral origin, independent of nationality (Agyemang 2005). I use the term African American solely to reference research studies that have described this population as such. In the United States, prevalence of HTN is significantly higher among African Americans and disease onset occurs at an earlier age compared to white men and women (Muntner et al., 2017). Additionally, US Black women experience lower BP control rates than their white counterparts (Ahmad & Oparil, 2017). The rise of HTN prevalence observed globally is primarily occurring in low- and middle-income countries (LMICs) (Mills et al., 2020; Schutte et al., 2021). Growth of the hypertensive population in LMICs is attributed to urbanization, unhealthy diet, aging, physical inactivity, obesity, and development of other cardiometabolic disorders (Mohsen Ibrahim, 2018). Specifically, South Africa is an upper middle-income country experiencing a rise in HTN prevalence in women, increasing from 25% to > 40% within the last decade (Hendriks et al., 2012; Kandala et al., 2021; Lloyd-Sherlock et al., 2014; National Department of Health & ICF, 2019). Urgent attention needs to be focused on creating easy and affordable techniques to identify HTN in Black women across various clinical and community settings.

Handgrip strength (HGS), a surrogate for measuring overall muscular fitness, has shown utility as an index for general health (McGrath et al., 2018). A growing body of evidence suggests that weak HGS is related to an increased risk of a variety of health conditions, including HTN and CVD (Peterson et al., 2017). Currently, there is a dearth of literature that examines the association between grip strength and HTN risk in Black women (Lee et al., 2016; Sola-Rodríguez et al., 2021). The HGS test is an affordable, portable, and non-invasive tool, allowing for simple integration into clinical practice and various community settings (Brown et al., 2020). It is crucial to understand the utility of HGS as a method to predict HTN risk among Black women across various populations in order to identify at risk individuals earlier and reduce the population burden of HTN. My dissertation aimed to better understand how HGS could be used for early HTN detection in order to reduce the overall burden of HTN-related conditions in Black women.

Background and Literature Review

Blood pressure regulation

Arterial blood pressure, simply referred to as blood pressure, is the pressure exerted along the walls of arteries. There are 2 measures for BP measurement, systolic blood pressure (SBP) and diastolic blood pressure (DBP). Systolic blood pressure is the pressure exerted on the walls of the artery when the heart contracts and DBP is the pressure applied to the artery walls when the heart relaxes between heartbeats (Desai, 2020). Blood pressure is tightly regulated around a “set point” via short term and long-term adaptations to provide adequate blood flow to vital organs and maintain homeostasis (Parati et al., 2020). Blood pressure is influenced by cardiac output (heart rate x stroke volume), and total peripheral resistance. Blood pressure is regulated by making acute and circadian adjustments to these components. Extended periods of reduced blood pressure, called hypotension (BP < 90/60 mmHg) can compromise oxygen delivery to peripheral tissues, impact organ function, and cause orthostatic intolerance (Freeman et al., 2018; Sanders et al., 1989). Conversely, prolonged periods of elevated high blood pressure (HBP) can lead to tissues end-organ damage (Mensah, 2016). Various physiological, pathological and environmental variables can influence BP homeostasis throughout the day such as exercise, standing, and stress (Joyner et al., 2015; Raven & Chapleau, 2014).

The regulation of optimal blood pressure is a complex process involving several mechanisms and interactions of various organ systems (Shahoud et al., 2022). Short-term BP regulation is accomplished by the baroreceptor reflex (Joyner & Limberg, 2014; Wehrwein & Joyner, 2013). Baroreceptors are a type of mechanoreceptor found in blood vessels that respond to the state of vessel wall stretch. High-pressure baroreceptors are located in the carotid sinus and aortic arch. They are stimulated when the arterial wall is stretched. When arterial blood pressure rises, there is a subsequent increase in baroreceptor activity which in turn increases the transmission of afferent neural feedback to the brain's medullary cardiovascular center (Fahim, 1998). In response to the increase in sensory feedback, the parasympathetic nerve response is activated while the efferent sympathetic outflow is inhibited (Joyner et al., 2015). This results in vasodilation, decreased cardiac output and a subsequent reduction in BP. Low-pressure baroreceptors located in the venous system, pulmonary arteries, right atrium and ventricle are also responsible for blood pressure control by detecting changes in blood plasma volume and utilizing several methods to influence arterial pressure (Armstrong et al., 2022).

The renal system plays an essential role in maintaining BP homeostasis by regulating extracellular fluid volume through sodium and water excretion(Coffman & Crowley, 2008; Guyton, 1991). The regulation of salt and water excretion/absorption, as well as peripheral vascular tone occurs via several neurohumoral mechanisms (Wadei & Textor, 2012). Increases in arterial blood pressure lead to subsequent increases in renal perfusion pressure, resulting in the increase of sodium and water excretion, reducing vascular fluid volume and restoring normal blood pressure (Ivy & Bailey, 2014). This phenomenon is called pressure natriuresis and is the main mechanism for long-term blood pressure control. The renin-angiotensin-aldosterone system (RAAS) is an important mechanism maintaining pressure natriuresis and achieves this through its regulation of the hormone renin. Renin is responsible for the conversion of angiotensinogen to angiotensin I which is then converted into angiotensin II by the angiotensin-converting enzyme (ACE). Angiotensin II contributes to blood pressure regulation by causing vasoconstriction, and the release of aldosterone which reduces renal salt and water excretion, resulting in an increase in blood pressure (Fountain & Lappin, 2022). Abnormal RAAS function can lead to the development of HTN and subsequent target organ damage(Coffman & Crowley, 2008; Muiesan et al., 2018; Muiesan et al., 2013).

Antidiuretic hormone (ADH), also known as vasopressin, is synthesized by the hypothalamus and released by the posterior pituitary increasing water reabsorption and vasoconstriction (Inoue et al., 2001; Shahoud et al., 2022). ADH is released when a reduction of blood volume is detected to maintain normal blood volume. Conversely, the cardiac hormone atrial natriuretic peptide (ANP) acts to reduce blood volume using several mechanisms including modulating the effects of ADH on salt and water retention, vasodilation, and short-term increase in vascular permeability causing the reduction in blood pressure (Curry, 2005; Shahoud et al., 2022). Several other hormones are involved in regulating vascular tone via vasoconstriction or vasodilation, including epinephrine, norepinephrine angiotensin II, and endothelin (vasoconstrictors) and bradykinin and prostacyclin (vasodilators) (Mannelli et al., 2018; Sharma, 2009). Abnormal functioning of the mechanisms involved in renal sodium handling can result in salt-sensitivity (Choi et al., 2015).

Local control of blood pressure occurs involves the intrinsic regulation of blood flow by blood vessels and specialized tissues (Clifford, 2011). The two main methods of local blood flow regulation are myogenic control and metabolic control. Local blood flow to adjacent tissues and organs is not constant and instead adjustments are made depending on the current requirements of the target organs/organ systems delivered by microcirculation (Reglin & Pries, 2014). Arterioles and feed arteries are the main sites of local blood flow regulation and reacts independently of neurohumoral influences of the sympathetic and parasympathetic nervous system (Clifford, 2011).

To summarize, the blood pressure regulatory systems highlighted above are a part of a complex system with a main goal of maintaining blood pressure homeostasis under various physiological conditions. The mechanisms responsible for blood pressure regulation may be different across demographic backgrounds due to genetic and non-genetic factors (Bosworth et al., 2008; Ehret et al., 2016). Dysregulation of these mechanisms can ultimately lead to the development of HTN (Pagani & Lucini, 2001). Over time, additional exertion on the blood vessel wall with defective BP regulation can damage the internal arterial walls, reducing their elasticity and therefore decreasing the flow of blood and oxygen to the body (Martinez-Quinones et al., 2018). Reduced blood flow and oxygen delivery can cause detrimental consequences to general health. Complications of uncontrolled HTN include increased risk for heart attack, heart failure, kidney disease, vision loss, and dementia(Fuchs & Whelton, 2020). Using many of the mechanisms for BP regulation mentioned above, numerous anti-hypertensive medications have been developed, but their long-term success has been limited. Therefore, despite the potential for pharmaceutical manipulation of BP dysregulation, HTN rates continue to rise, highlighting the need for early HTN detection and efficacious anti-hypertensive interventions.

Hypertension – principle influencing factors

There are two main forms of HTN, primary and secondary HTN. Primary HTN, also called essential HTN, is the most common form that accounts for approximately 90% of cases and is a major modifiable risk factor for CVD (Carretero & Oparil, 2000). In individuals with primary HTN, the chronic increase BP is idiopathic and due to an unknown cause(Carey et al., 2018; Carretero & Oparil, 2000). Conversely, secondary HTN is high BP caused by a preexisting medical condition or side effect of medication and is responsible for about 5-10% of cases (Carey et al., 2018; Rimoldi et al., 2014; Viera & Neutze, 2010). Common conditions that cause secondary HTN include chronic kidney disease (CKD), obstructive sleep apnea, and adrenal disease (Charles et al., 2017).

HTN is a complex condition in which its precise pathophysiological mechanism has not been fully elucidated. Elevations in blood pressure are theorized to be caused by the dysregulation of multiple mechanisms originally designed to maintain optimal BP control (Raven & Chapleau, 2014). Often called the “silent killer”, HTN can become life-threatening if not identified in a timely manner (Messerli Franz et al., 2017; Wajngarten & Silva, 2019). Delays in treatment can further exacerbate the condition, so it is important to understand the risk factors associated with HTN (Staessen et al., 2004). There are two types of risk factors for HTN, modifiable and non-modifiable risk factors. Non-modifiable risk factors for HTN are factors that cannot be changed or are difficult to change (family history, age, demographic characteristics, and sex) while modifiable risk factors are factors that we are able to control (body weight, smoking, alcohol consumption, diet, physical activity and other lifestyle behaviors) (van Oort et al., 2020). Comorbidities can be either modifiable or non-modifiable risk factors. Awareness of both non-modifiable and modifiable risk factors can assist in prevention strategies to reduce risk and the development of targeted treatment strategies for blood pressure control.

Blood Pressure Measurement Methods

Accurate blood pressure measurement is important to the diagnosis of HTN and BP management. Multiple methods are available to measure blood pressure in both office and out-of-office settings with each having their own strengths and weaknesses. Blood pressure can be measured directly using intra-arterial catheterization, but this method is invasive and impractical for clinical use (Saugel et al., 2020). Instead, non-invasive methods such as auscultatory and oscillometric techniques are commonly used in clinical practice (Muntner et al., 2019; Pickering et al., 2005; Whelton et al., 2018). In recent years, manual BP measurement techniques have been widely replaced by automated BP measurement devices in office and clinical settings to improve the quality and accuracy of BP measurements and reduce the white coat-effect (Myers et al., 2012) The ACC/AHA guidelines recommend that BP is estimated by the averaging of ≥ 2 BP readings on ≥ 2 occasions in an office setting (Whelton et al., 2022). Although office BP readings remain essential in identifying HTN risk and BP management, clinical guidelines are increasingly suggesting the use of out-of-office BP monitoring techniques in order to increase the prognostic value of BP (Townsend, 2020).

Blood pressure fluctuates throughout the day due to a multitude of internal and external factors (Degaute et al., 1991; James et al., 2014; Mena et al., 2017; Townsend, 2020). For example, daily activities including the sleep cycle, eating and drinking, and physical activity contribute to the rise and fall of diurnal BP (Ahuja et al., 2009; Calhoun & Harding, 2010; Chen & Bonham, 2010). The ability to detect long-term variations in BP for an extended period is beneficial to identify trends in BP could have an impact on cardiovascular health (Cohen & Cohen, 2016; Weber et al., 2014). Out-of-office BP assessment can be used as a supplement to clinical assessment to confirm HTN diagnosis and monitor BP at home (Townsend, 2020). Two methods that are commonly used are 24-hour ambulatory blood pressure monitoring and home-based BP measurements (Shimbo et al., 2015). The studies in this dissertation measured BP by using both auscultatory and oscillometric methods measured in a clinical setting.

To measure blood pressure accurately, whether employing in office or out-of-office methods, requires adequate training and experience (Whelton et al., 2018). Proper training of both health care professionals and patients is essential to prevent common errors that can negatively impact BP monitoring (Ogedegbe & Pickering, 2010). Several errors that can occur during a BP measurement include incorrect patient positioning, improper selection and placement of upper-arm cuff, and use of a non-calibrated or non-validated device (Pickering et al., 2005). It is crucial to measure BP correctly to avoid an inappropriate diagnosis of HTN, which can affect a patient's quality of life (Muntner et al., 2019). Barriers to HTN control will be discussed further in a later section below.

Recommendations for Hypertension Management

During the past several decades, guidelines for HTN management have been modified several times to provide health professionals with up-to-date information on the best practices to diagnose, detect, and manage HTN. The guidelines are created and updated regularly to reduce the risk of cardiovascular, cerebrovascular and renal diseases and overall mortality. The positive correlation between high BP and increased total CVD risk is well documented, beginning at 115/75 mmHg. Furthermore, CVD risk doubles with each increment of SBP (20mmHg) and DBP (10mmHg)(Lewington et al., 2002). Therefore, it is important to identify populations at risk for HTN to determine specific BP management options. HTN diagnosis is based on arbitrary BP thresholds that are used to inform treatment decisions in clinical practice (Poulter et al., 2015).

In 2013 and 2014, most major guidelines for defining HTN were updated to exclude a lower threshold of ≥130/80 mmHg for patients with underlying CVD, diabetes or high risk for HTN due to the lack of evidence supporting the added benefit of the lower threshold for this population (Mancia et al., 2013). At that time, the BP target for the general population was <140/90 mmHg. (Chobanian et al., 2003; James et al., 2014; Seedat et al., 2014; Weber et al., 2014). A joint report published in 2017 by the American College of Cardiology (ACC), American Heart Association, and 9 other American health-related professional societies redefined HTN as ≥130 mmHg SBP and/or ≥80 mmHg DBP, elevated BP at 120-129 mmHg SBP and <80 mmHg DBP and with normal BP at <120 mmHg SBP and <80 mmHg DBP (Figure 1). Additionally, the guideline recommends a BP target of <130/80 mmHg for adults prescribed antihypertensive medications (Whelton et al., 2018).

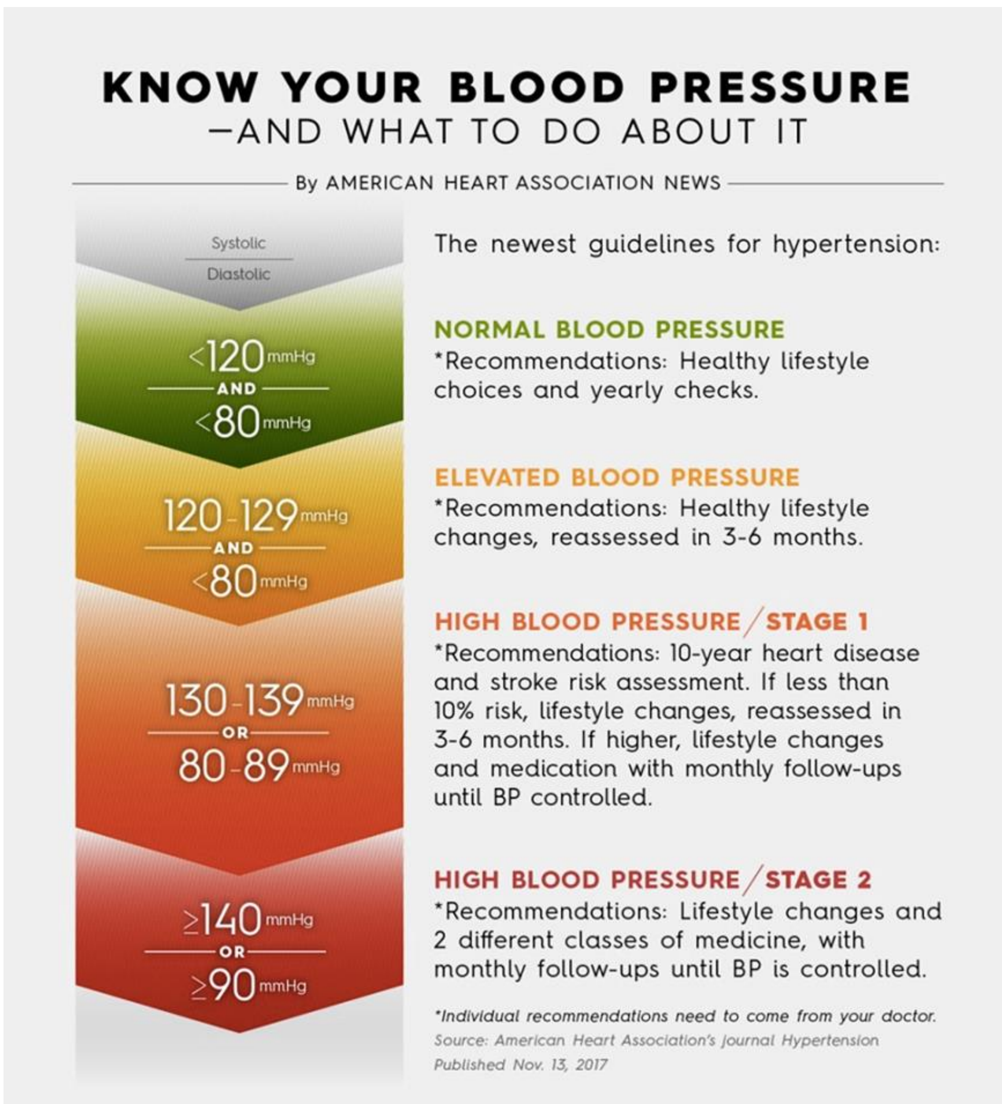


Figure 1.1 Blood pressure Categories based on 2017 ACC/AHA guidelines.
Adapted from American Heart Association News

The intentions for reducing the threshold for HTN diagnosis by 10 mmHg in the guidelines were to implement intensive BP-lowering interventions earlier with the goal of reducing overall HTN burden. The 2017 ACC/AHA guidelines classified BP into four categories: Normal as <120 SBP and <80 DBP, Elevated as 120-129 mmHg SBP and <80 mmHg, Hypertension Stage 1 as 130-139 mmHg or 80-89 mmHg, and Hypertension Stage 2 as ≥ 140 mmHg or ≥ 90 mmHg (Whelton et al., 2018). This dissertation defines HTN using self-reported questionnaire data that reports a diagnosis of HTN or HBP by a physician and/or other healthcare professional (Gómez-Olivé et al., 2018; Radler, 2014).

For the diagnosis of HTN, the 2017 ACC/AHA guidelines recommend that health care providers (HCP) evaluate patients by conducting a physical examination and basic laboratory testing and gathering personal and family medical history (Whelton et al., 2022). The goal of the comprehensive patient evaluation is to determine CVD risk which includes target organ damage, identify potential secondary causes of HTN, and develop an adequate HTN treatment regimen based on patient's medical needs (Whelton et al., 2018). In older adults, the patient evaluation also includes assessment of fragility and other conditions commonly associated with aging (Whelton et al., 2022). During this evaluation process, it is important to consider the time required for treatment and alternative strategies of BP management.

These new changes in the guidelines have been controversial due to the potential consequences of lowering the BP target by -10 mmHg worldwide and have been criticized by other global HTN societies and organizations (Leung et al., 2017; Poulter et al., 2018; Rayner et al., 2019). Researchers have argued that the rise in HTN prevalence due to the new threshold would increase health care utilization and place additional burden on already fragile healthcare systems in many communities (Kirkland et al., 2018). A study reported that the 2017 ACC/AHA BP cut offs resulted in a substantial increase in HTN prevalence among US adults ≥ 20 years from 31.9 to 45.6 percent, about a 14 percent increase (Muntner et al., 2019).

The 2017 ACC/AHA update of BP threshold is largely based on the results of the Systolic Blood Pressure Intervention Trial (SPRINT), a randomized controlled trial conducted at over 100 clinical sites across the US (Wright et al., 2015). A total of 9361 individuals with high-risk of CVD were enrolled the study and randomized into either the intensive BP target group of <120/80 mmHg or the standard BP target group of <140/90 mmHg (Wright et al., 2015). The initial design of the SPRINT study anticipated a maximum follow- up of 6 years but ended early due to the significantly reduced risk of negative CVD outcomes in the intensive BP target group. Despite this overall finding, limited evidence supports the efficacy of intensive BP intervention for women. Concerns over study design, lack of enrollment of women participants, underrepresentation of elderly women, and the exclusion of women with other underlying cardiometabolic conditions undermine the applicability of these findings for HTN control in women (Wenger 2016).

The change in guidelines by the ACC/AHA mean many individuals are diagnosed with HTN and starting antihypertensive treatments at younger ages without enough evidence supporting pharmacological intervention effectiveness in younger adults (Muntner et al., 2018; Rayner et al., 2019; Tsioufis et al., 2018). In the SPRINT study, achieving the lower <120/80 mmHg BP threshold required on average 3 antihypertensive medications, compared to 2 antihypertensive medications in the standard treatment group. Further reliance on pharmacological interventions to reduce BP could affect patient adherence to a HTN treatment regimen, potentially increasing the possibility of adverse events from polypharmacy, and make HTN control even less attainable for Black women (Aggarwal et al., 2021; Tsioufis et al., 2018). Furthermore, this practice may subject patients who previously were categorized as "normotensive" to unnecessary medications that have undesirable adverse effects. Nevertheless, early detection and implementation of individualized, targeted management strategies are very important in reducing the burden of HTN and CVD. Lifestyle modifications such as diet and exercise and pharmacological interventions are recommended to reduce BP (Chobanian et al., 2003; James et al., 2014; Whelton et al., 2018).

Lifestyle modifications

Improvements in healthy behaviors are typically the initial treatment strategy for HTN management (Bushman, 2018). Lifestyle modifications such as weight loss, reducing alcohol and sodium consumption, increasing dietary potassium and increasing physical activity are examples of strategies used for HTN prevention and reduction of BP and CVD risk (Appel, 2003; Brook et al., 2013). Numerous research studies support the positive impact of implementing lifestyle modifications alone or along with pharmacological treatments for HTN management (James et al., 2014; Liguori, 2021; Whelton et al., 2018). Hypertension prevention and control can be accomplished through both population-based and targeted, individualized treatment strategies (Cazabon et al., 2022; Kotchen, 2010; Mayfield et al., 2022). Physical activity and weight loss will be discussed in further detail.

Physical activity is a major modifiable risk factor for the development of HTN. Substantial literature has highlighted the health benefits of physical activity and incorporation of dynamic aerobic exercise, dynamic resistance training, and static isometric exercise into weekly lifestyle (Cornelissen & Smart, 2013; Pescatello et al., 2004; Pescatello et al., 2015). For example, data shows that regular participation in aerobic exercise among hypertensive individuals result in an average 5-7 mmHg reduction of SBP and DBP (Cornelissen & Smart, 2013; Smart et al., 2019). The American College of Sports Medicine (ACSM) recommends that adults should participate in moderate-intensity aerobic activity for at least 150 minutes per week along with 2-3 days per week of resistance training and flexibility exercises (Bushman, 2018; Liguori, 2021).

Recent studies have identified isometric exercise training (IET) as a promising non-pharmacological treatment for effective management or prevention of HBP (Cornelissen & Smart, 2013; Inder et al., 2016; Smart et al., 2019). IET has been found to lower resting blood pressure (RBP) (Baross et al., 2012; Carlson et al., 2014; Inder et al., 2016; Peters et al., 2006; Smart et al., 2019; Taylor et al., 2003; Wiley et al., 1992). Reductions in RBP after IET interventions have been observed in individuals of various age groups and HTN status (normotensive, elevated/pre-hypertensive, and hypertensive) (Smart et al., 2019). Moreover, IET has been shown to decrease blood pressure equally or to a greater extent compared to observed with dynamic aerobic and resistance exercise training programs (Cornelissen & Smart, 2013). Isometric exercises are practical and typically require minimal equipment, which allows for implementation in either lab or home setting and equipment is inexpensive and easy to transport with a lower time commitment than traditional workouts.

Improved physical fitness is also a benefit of performing regular physical activity, which can better overall health. Physical fitness is defined as an individual's ability to perform daily physical activities with optimal performance, endurance and strength (Caspersen et al 1985, Campbell et al 2013). Physical fitness is comprised of multiple components and are categorized as being performance related or health related. The five subcategories of health-related fitness include morphological, muscular, motor, cardiorespiratory, and metabolic (Bouchard, Blair and Haskwell, 2006). Muscular and cardiorespiratory fitness, and body composition are commonly evaluated using epidemiologic techniques to estimate the overall physical fitness of a population (Caspersen et al 1985). Muscular fitness is commonly measured for epidemiological and research purposes using a handheld device called a hand dynamometer.

Pharmacotherapy

Individuals unable to reduce their BP through lifestyle modifications alone are typically prescribed antihypertensive medications. The combination of pharmacological therapy and lifestyle modifications can be effective in BP management (Whelton et al., 2018). Due to the complex nature of HTN pathophysiology, HTN can be difficult to treat. For HCPs, it may be hard to initially determine the mechanism contributing to rise in BP so there is trial and error in prescribing medications and dosing until an effective treatment regimen is identified. Several antihypertensive agents are primarily recommended for HTN treatment such as thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, and renin angiotensin system blockers angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs)(Chobanian et al., 2003; James et al., 2014; Whelton et al., 2018). If monotherapy is ineffective, dosage may be increased, or additional pharmacological agents are added to the treatment regimen.

The Eighth Joint National Committee (JNC 8) and ACC/AHA guidelines provide HCPs a pharmacological management algorithm to assist with determining appropriate treatment options. After

HTN diagnosis, physicians will establish a BP goal and prescribe BP medications by considering age and patient history of diabetes or chronic kidney disease (CKD) (James et al., 2014). Current HTN guidelines suggest differential considerations of first line monotherapy recommendations based on racial background and CVD risk (Whelton et al., 2018) . Health care providers are advised to limit first line treatment options to thiazide diuretic and CCB medication classes for Black HTN patients without CKD (James et al., 2014; Muntner et al., 2018). Comparatively, guidelines for non-Black HTN patients include ACE inhibitors and ARBs (Muntner et al., 2018).

These guidelines are based on results from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), which reported poorer BP lowering response in Black participants using ACE inhibitors and a higher risk of stroke using ACE Inhibitors compared to using CCBs(Wright et al., 2005; Wright et al., 2015). On the contrary, thiazide diuretics for monotherapy were shown to have the best BP response for Black hypertensives (Wright et al., 2015). A meta-analysis that examined the difference in BP lowering capability of ACE inhibitors between Black and white adults also found that ACE inhibitors did not lower both SBP and DBP as effectively in Black adults than white adults. The study did note though that more variability in BP response to ACE inhibitors was recorded within race groups compared to between races(Peck et al., 2013). Despite the contrasting recommendations, blood pressure control among Black hypertensive patients remain suboptimal while disparities in HTN control are exacerbated (Williams et al., 2016). Although these interventions have been shown to be effective at reducing BP in studies, many individuals are unable to achieve ideal BP levels or sustain the results long-term (Fryar et al., 2017). Unfortunately, only 1 in 5 adults can control their HTN with current blood pressure management methods (Wenger et al., 2018). Additionally, because most hypertensive individuals require two or more medications to control adequately, the monotherapy guidelines may not be applicable to most of the population (Flack et al., 2009; Guerrero-García & Rubio-Guerra, 2018). The unique phenomenon of HTN prevalence, presentation, and prescribing in Black Americans will be discussed further in the Race/Ethnicity and HTN section.

Alternative approaches to reaching BP goals are essential to promote both clinically significant reductions in RBP and maintenance of healthy BP, thereby lowering CVD risk. Strategies that are safe, easy to perform and less time consuming will make it easier to incorporate interventions into a hectic schedule and aid in maintaining results. Identifying barriers and facilitators to HTN control can provide information on ways to improve current guidelines and improve BP control for various populations.

Barriers and facilitators in hypertension control

Barriers to the prevention and management of HTN exist on the patient, HCP and health care system-levels (Borzecki, 2005;). Patient-related barriers may include poor adherence to antihypertensive medication, limited awareness of HTN symptoms, cultural and social factors, and consequences of disease progression, cost of health care, lack of health insurance, aging and frailty, absence of motivation to modify lifestyle, accessibility of medical facilities for physician follow up, fear of injury exercising, and lack of trust in HCPs (Abel & Efird, 2013; Bosworth et al., 2008; Odedosu et al., 2012; Rimando, 2015). Health care provider-related barriers include the ways HCPs provide care to their patients that unintentionally promote gaps in HTN control in different groups of patients. Examples of HCP-related barriers to HTN control are failure to adhere to HTN treatment guidelines or intensify drug therapy when appropriate and treating patients without considering their health history, health literacy on HTN, and preferences, and disinterest to adapting practice techniques based on evidence-based strategies (Green et al., 2022; Odedosu et al., 2012). Equally important, health system barriers impact patient-physician relationships and quality of patient care because it affects delivery of medical care to patients and affect the quality of HCP's interactions with patients. A meta-analysis examined important HTN control barriers reported by both patients and HCPs found that health system-related barriers were the most discussed HTN control barrier category for patients and HCPs (Khatib et al., 2014). For providers, the study cited overwhelming workloads, limited resources and inadequate time spent with patients. On the contrary, patients mentioned access to primary care centers, pharmacies, gyms, grocery stores, and healthy eating options influence their ability to control their HTN. Although there are numerous barriers that could negatively affect BP management, studies have also identified several facilitators that encourage HTN management. These include an unexpected diagnosis, accessibility to health care services, knowledge of personal and family of HTN and CVD-related risk factors, and social support (Ogedegbe, 2008).

Interventions designed to promote reductions in BP and HTN risk typically focus on patient and provider-level barriers. Common approaches used to target these patient-level barriers are improving patient awareness and education, self-monitoring of BP at home, and behavioral health counseling. Handgrip strength is a promising method BP management by identifying potential risk of HTN through grip strength measurements.

Hypertension and women

Hypertension is responsible for 1 in 5 deaths in women worldwide (Wenger et al., 2018). Compared to hypertensive men, hypertensive women are at a higher risk of developing serious CVD-related conditions such as left ventricular hypertrophy, heart failure, diastolic dysfunction, and a steep age-related increase in arterial stiffness (Gudmundsdottir et al., 2012; Hage et al., 2013). Compared to normotensive women at age 50, hypertensive women live 5 years less on average (Hage et al. 2013). Although the mechanisms that regulate blood pressure are similar in men and women, the physiological pathways that contribute to the disparities in HTN development, onset, prevalence, disease severity, and response to treatment between men and women are not fully understood (Kauko et al., 2021; Lau et al., 2019; Sandberg & Ji, 2012). Both biological sex differences and gender differences influence HTN risk and mortality (Maranon & Reckelhoff, 2013). Despite these differences in disease etiology and presentation in men and women, there are currently no female-specific guidelines for the prevention, detection, and management of HTN (Cífková & Strilchuk, 2022).

There is a common misconception that women are at a lower risk of developing HTN than men. Research suggests a significant sex-related heterogeneity in the onset and presentation of HTN between women and men(Lombardi M, 2017). The risk of developing HTN increases as women reach their 60th year of life, and prevalence rates begin to surpass age matched men(Ramirez & Sullivan, 2018). Hypertension is more common in men than women among individuals younger than 45 years of age but after 65 years old, prevalence becomes higher in women than men (Maranon & Reckelhoff, 2013, Mozaffarian et al. 2016). Between the ages of 45 to 64 years, the percentage of men and women with HTN are similar (Mozaffarian et al. 2016). Increases in blood pressure are seen decades before the onset of HTN. For women, the progression of elevated BP occurs earlier in life compared to age-matched men. By the age of 30, women experience steeper increases in blood pressure compared to men and this trend remains throughout the life course (Ji et al., 2020). Meta-analyses have reported that an incremental 10 mmHg increase in blood pressure was associated with a 25% higher risk of CVD compared to just 15% higher risk in men (Ghazi and Bello, 2021; Wei et al., 2017). Understanding the unique biological mechanisms that contribute to increased HTN risk in women is important to tailor interventions and treatment for the most optimal strategies of BP lowering for women. Due to the complex and extensive nature of research of the mechanisms that influence sex differences in BP control and HTN in the literature that are beyond the scope of this dissertation, I will just highlight the differences in risk factors and hormonal influences on HTN prevalence and control in men and women.

There is a common misperception that HTN is an asymptomatic condition, which could lead to missing signs of abnormal activity related to BP control. This is evident especially in young and middle-aged women, who are more prone to these symptoms (Maas, 2019). For example, elevated BP can cause chest pain and/or tightness that can last for minutes to hours and spread to the jaw, arm, and shoulder blades. Further, researchers have identified several other symptoms/signals such as headaches/migraines, blurred vision, hot flushes, palpitations, and fluid retention (Vogel et al., 2021). Many of these symptoms are similar to the vasomotor symptoms experienced during menopause and can increase risk of CVD (Maas, 2019).

Age plays a major role in the differences in BP regulation and cardiovascular function and subsequent CVD development between men and women. Women tend to live longer than men and they have a lower mortality rate at any age compared to men. Globally, the life expectancy at birth is longer for women than men, 74.2 years vs 69.8 years, respectively (WHO, 2019). Sex differences in smoking rates, alcohol consumption which increase the risk for noncommunicable conditions like CVD may partially explain the higher mortality rates across the lifespan for men (Crimmins et al., 2019). Moreover, differences exist in the types of risk factors for HTN between men and women. In a study by Tziomalos et al., (2014) they found that traditional risk factors for BP control such as tobacco use, and hyperlipidemia were more common in men while nontraditional risk factors like chronic kidney disease and abdominal obesity were more prevalent in women than men. During childhood, blood pressure for males and females are similar(Barba et al., 2008; Reckelhoff, 2007). By the onset of puberty, studies have seen a steeper rise in blood pressure in males versus females (Syme et al., 2009). This may be partially attributed to the rise in androgen levels during adolescence in males (Reckelhoff 2001). In the literature, testosterone has been shown to have both pro-HTN and anti-HTN properties which provides conflicting evidence on the influence of testosterone and HTN. As men age, there is a reduction in bioavailable testosterone which is inversely associated with arterial blood pressure and the onset of HTN (Sandberg and Ji, 2012, Zimmerman and Sullivan 2013). On the contrary, testosterone replacement therapy is not related to lower BP. A study found that in women, higher total testosterone was associated with higher blood pressure (Ziemens et al., 2013).

The prevalence of HTN is higher in men and postmenopausal women compared to premenopausal women. Postmenopausal women are at a higher risk of CVD complications compared to premenopausal women and are diagnosed with coronary heart disease later in life than men (Brahmbhatt et al., 2019; Modena, 2014). Some research suggests that there may be protective pathways related to the female sex hormone estrogen that are responsible for the lower prevalence of HTN among younger, premenopausal women (Ahmad & Oparil, 2017; Ghazi & Bello, 2021). Several studies have reported that women with early-onset menopause (<45 years old) were at higher risk of coronary heart disease and heart failure (Khoudary et al. 2020). The presence of estrogen (estradiol) before menopause may not fully explain the cardioprotection that is provided to premenopausal women. Several studies investigating the impact of hormone-replacement therapy (HRT) on BP in pre- and postmenopausal women found that HRT had a limited influence on BP (Ghazi and Bello, 2021). Pregnancy is another unique female-specific risk factor for essential HTN and CVD morbidity. Pregnancy-related hypertensive disorders include chronic HTN gestational HTN, preeclampsia, and chronic HTN with superimposed preeclampsia (Ghazi and Bello, 2021). Sex differences are also present in the organ systems responsible for managing blood pressure regulation. These systems include the sympathetic nervous system, renal system and the vasculature. More research is needed to determine in the future beneficial effects for estrogen and testosterone to reduce HTN and CVD risk.

Despite the personal and societal impact of HTN, awareness, treatment and control remain suboptimal amongst women (Ahmad & Oparil, 2017). Increased representation of women in clinical trials focused on HTN and implementation of appropriate BP interventions for women are needed to reduce HTN-related morbidity and mortality in women worldwide.

Race/Ethnicity and HTN

Racial and ethnic disparities also exist in the prevalence and incidence of HTN in the United States. Although HTN affects many groups, prevalence is significantly higher among African Americans and onset of HTN occurs at earlier ages than white men and women (Muntner et al., 2017). Prior studies have noted that the disparity in blood pressure levels among African Americans arises during childhood years (Carson et al., 2011; Chen et al., 2015; Fuller-Rowell et al., 2017; Hardy et al., 2021) Additionally, lifetime prevalence of HTN is higher for African American participants than in white and Asian participants. In middle aged and older African American adults, the 40-year risk of developing HTN was greater than 90%, higher than white, Asian, and Hispanic adults (Carson et al. 2011). The disparity in HTN diagnosis creates an additional burden for CVD-related conditions.

Substantial research has been conducted to provide insight of the factors contributing to disparities in outcomes between black and white adults. Research has not found a definitive cause to explain why HTN is more common among black adults. Previous studies have investigated the role of genetics and social and physical environmental factors that are instrumental in health disparities (Carey et al., 2018). Most of these studies conclude disparities in HTN are still present after adjustment for socioeconomic, behavioral and biomedical risk factors (Mueller et al., 2015). Recent research suggest that chronic stress is not only linked to HTN and CVD but an important determinant of racial/ethnic disparities in HTN disease burden (Hicken et al., 2014).

Factors that influence HTN prevalence in US Black women

Obesity is a modifiable risk factor for several health conditions including HTN. Evidence from the Framingham Heart Study suggest that 65% of primary HTN diagnoses among women were attributed to excess weight gain (Hall et al 2015). Excess weight in the form of abdominal adiposity in particular, measured by waist circumference, has been shown to increase risk for HTN development (Rhee et al 2018; Jayedi et al. 2018) Black women have the highest rates of obesity compared to other racial/ethnic groups in the United States (Flack et al., 2010; Mensah et al., 2005). Body mass index (BMI) is a commonly used measure to estimate adiposity and serves as a marker of disease risk (Heymsfield et al. 2016). Numerous researchers have challenged the use of BMI as a universal health marker for several reasons. First, BMI does not account for body composition leading to inaccurate classifications of individuals in BMI categories. Secondly, the foundational research that helped the development of BMI categories only includes the profiles of white men), which leaves out a large portion of the population (Heymsfield et al. 2016). This is problematic because this can lead to the overestimation obesity among racial/ethnic groups with varying body composition. In 2013-2016, more than 80% of African American women in the US were classified as being overweight or obese, which is defined as having a body mass index (BMI) of 25 or more (Health, United States 2018). Recently, studies have suggested the reclassification of BMI categories to account for the differences in the relationship between health risk and obesity observed across several racial/ethnic groups. For instance, the standard BMI cutoff of >30 kg/m^2 has been shown to not be applicable in Asian adults because of the higher risk of CVD and metabolic diseases seen at lower BMI categories (Wildman 2004, Pan 2004). Biologically linked approaches to determine BMI cut offs that account for differences in body shape and composition phenotype seen across various groups would be more ideal to better gauge actual risk profiles(Stanford et al., 2019) . Stanford et al. (2019) recommends increasing the BMI cutoffs for women with the highest category personalized BMI cut offs based on sex and race/ethnicity which would increase the cut off for most Black women to 31 kg/m^2. Consideration of differences in body composition and muscle mass in Black women compared to other groups of women would be beneficial in order to accurately calculate the risk of HTN in this group.

Currently, more than half of US Black women are categorized as hypertensive based on current US HTN guidelines (Tsao et al., 2022; Whelton et al., 2018). In a study conducted by Chen et al.(2019), cumulative lifetime risk estimates for HTN were calculated for white and African American men and women from three contemporary study cohorts using both the JN7 and ACC/AHA BP thresholds. ACC/AHA guideline updates resulted in a significant increase in cumulative lifetime risk for all groups. Notably, the estimated cumulative lifetime risk for HTN in African American women was significantly higher than white women (86% vs 69%, respectively) and similar to both white and African American men (Chen et al., 2019) . As US Black women have historically been burdened by HTN and CVD risk, the lower threshold for BP target could negatively impact the already suboptimal BP control rates among this group (Tsioufis et al., 2018).

Barriers for HTN control are persistent among Black women. For Black women, race-based prescribing of first-line antihypertensive medications may limit the treatment options for Black women patients, delay treatment, exacerbate other comorbidities and contribute to overall poor HTN control in Black women. Healthcare system barriers related to health care accessibility, affordability of medications, socioeconomic status, health literacy impact Black women at higher rates than other groups of women, affecting the quality of care and ability to follow up with HCP (Hall et al., 2015). Furthermore, these barriers overlap to make HTN control particularly difficult for Black women. (Bosworth 2008). Despite Black women having higher awareness of having HTN compared to women of other racial/ethnic backgrounds, there are major disparities in BP control and HTN management. Reducing blood pressure and maintaining BP control is essential to reducing the burden of HTN and HTN-related health outcomes among Black women.

Hypertension in Sub Saharan Africa and South Africa

While high income countries worldwide overall have seen a steady decline in the prevalence of HTN, low- and middle-income countries (LMICs) instead have noticed a rise in adults with HTN. More than 80% of worldwide HTN-related disease burden is located in LMICs. The rise in prevalence of HTN that observed in low- and middle-income countries (LMICs) is attributed to the epidemiological shift from communicable to noncommunicable diseases (Lloyd-Sherlock et al., 2014). Particularly, HTN has become a serious public health concern in sub-Saharan Africa, where historically public health agencies have prioritized infectious and noncommunicable diseases, nutritional deficiencies, and maternal and infant mortality because of the high prevalence in the region (Addo 2007; Twagirumukiza 2011) . Unfortunately, the challenge of simultaneously dealing with the impact of multiple public health epidemics with limited financial resources and health centers has made it difficult to provide adequate care of these conditions (Maimela et al., 2016).

Currently, South Africa is amid a substantial epidemiological health transition from communicable conditions such as HIV/AIDS, malaria, and tuberculosis to noncommunicable diseases, specifically HTN. The development and availability of antiretroviral therapy (ART) and other medications have extended the lives of individuals in South Africa, which has contributed to the growth in the older population. As more South African adults are living to an older age, a larger portion of the population is becoming susceptible to development of CVD-related conditions. In a South African national survey from 2011 to –2012, age-standardized national prevalence of HTN was 35.1% for South

Africans 15 years and older, with only 8.9% of hypertensive population maintaining blood pressure control. Recently, HTN prevalence has rose to over 40% in South Africa, highlighting the urgency of monitoring trends in CVD risk in South Africans in order to inform health policy and reduce population burden of HTN (Lloyd-Sherlock et al., 2014). The population estimates for HTN in the studies highlighted were based on use of the 140/90–mm Hg threshold for the definition of HTN. Prevalence of HTN would have been higher if the current ACC/AHA's 130/80 mm Hg cut point been used. In addition, awareness of BP status and HTN control in South Africa is suboptimal so there is an urgent need for strategies to detect HTN risk early and implement BP treatment on a wide scale.

South Africa has experienced a rise in CVD risk factors such as HTN, obesity, alcohol consumption, and tobacco use among black South African adult women. Changes in lifestyle and health behaviors along with reported economic growth and urbanization in the region have heightened the burden of HTN in South Africa (Owolabi EO 2017). Black women residing in rural areas of South Africa had a lower risk of developing HTN compared to urban-dwelling Black South African women (Steyn, 2008; Twagirumukiza 2011). Another study reported urban-rural differences in predictors of HTN prevalence among Black South African women residing in Limpopo Providence, South Africa (Mphekgwana et al 2020). For example, poor eating habits (high consumption of meat and salty foods, low fruit intake), family history, and physical inactivity was significantly associated with an increased risk of HTN in semi-urban Black South African women, while diabetic status, high salty food intake, and waist-to-ratio was related in rural Black South African women (Mphekgwana et al 2020). Currently, there is an unmet need in South Africa for simple and affordable HTN interventions that can provide insight on HTN risk early and allow for early detection and prevention of more serious CVD conditions.

Muscle function and grip strength

Handgrip strength (HGS), a surrogate for muscular fitness, has shown utility as an index for general health (Soysal et al., 2021). Research has found that HGS is a predictor of total muscle function across a wide range of ages (Wind et al., 2010). Several studies have reported a positive relationship between muscular strength and body weight measures (Cooper et al., 2022; Lad et al., 2013). Researchers have proposed that grip strength adjusted by body size (relative grip strength) is better than just grip strength (absolute grip strength) in predicting morbidity and mortality (Fowles et al. 2014). The factors that influence HGS have been categorized in several studies. These factors include age, physical activity level, sex, socioeconomic status, body mass, race/ethnicity and morbidity (Hairi et al., 2010; Silva et al., 2018; Thorpe et al., 2016) The aging process is characterized by the progressive loss of skeletal muscle mass, strength, and function, called sarcopenia. Handgrip strength is a tool used to diagnose sarcopenia (Lee & Gong, 2020) A study found that men and women with higher education and wealth status had higher HGS (Thorpe et al., 2016). Racial differences in HGS have been reported in HGS between Black and white women. Black women have been reported to have higher HGS (Rantanen et al., 1998). This may be due to the difference in body mass between Black women and white women. Therefore, using grip strength is beneficial in measuring total muscle function and is a useful indicator for overall health.

Grip Strength as a Health Marker

A growing body of evidence suggests HGS is related to an increased risk of a variety of health conditions, including CVD, but with conflicting results. (Chang et al., 2022; Gubelmann et al., 2017; Ji et al., 2018; Lawman et al., 2015; Peterson et al., 2017; Taekema et al., 2011). Although most studies report an inverse relationship between relative grip strength and HTN or BP, others have reported no relationship or a positive relationship (Ji et al., 2018; Taekema et al., 2011). Notably, low HGS was found to be a stronger predictor of cardiovascular outcomes than resting BP (Leong et al., 2015; Sayer & Kirkwood, 2015). The differences in results are potentially due to the use of absolute grip strength, instead of accounting for body size which is called relative grip strength. Adjusting HGS with a body mass measure has been suggested to evaluate muscular health (Studenski et al., 2014). Several studies have noted that relative grip strength had a stronger association to CVD risk factors compared to absolute grip strength (Lawman et al., 2015; Lee et al., 2016). Higher relative HGS has been associated with favorable cardiometabolic risk including blood pressure, but not dominant HGS in women (Lee et al., 2016). Currently, there is a lack of evidence on relationship between relative HGS and HTN in women and with conflicting results (Ji et al., 2018; Lawman et al., 2015; Lee et al., 2016; Sola-Rodríguez et al., 2021).

The HGS test is an affordable, portable, and non-invasive tool, allowing for simple integration into clinical practice and community settings (Brown et al., 2020). Currently, there is a dearth of literature that examines the association between grip strength and HTN risk in Black women (Lee et al., 2016; Sola-Rodríguez et al., 2021). It is crucial to understand the utility of HGS as a method to predict HTN risk among Black women in order to identify at risk individuals earlier and reduce the population burden of HTN.

To summarize, this dissertation will primarily focus on the relationship between grip strength and primary HTN in Black women, a group understudied in CVD research and disproportionally impacted by HTN-related medical conditions. Black women, in both the US and South Africa, are dealing with the consequences of HTN and the negative implications on their health. The US, a high-income country, has been dealing with the HTN epidemic for decades while HTN in South Africa has been a more recent development because of the advancements and accessibility of ART and other lifesaving therapies for communicable diseases. Two countries and groups of people at different stages of the HTN epidemic but both are not achieving ideal BP control. My goal for this dissertation is to compare the benefit of using HGS as an indicator for HTN diagnosis in Black women in both the US and South Africa. Identifying easy, cost effective, and accessible interventions to identify risk in both groups are essential to curb the impact of HBP on health outcomes for Black women globally.

Black women are disproportionally impacted by HTN and at earlier ages, so the need to intervene earlier with prevention or treatment strategies is crucial. It is not well understood whether that relationship is different between white women and Black women. In determining whether there is a relationship between these two variables and the direction of the relationship, grip strength measurements could be implemented into clinical practice or in community settings to help identify individuals at higher risk for HTN and establish strategies to prevent/treat and reduce risk of developing CVDs.

Specific Aims

Specific Aim 1/Study 1: To establish whether there is a cross-sectional relationship between grip strength (relative and absolute grip strength) and HTN in Black and white women. This analysis was completed using data from NHANES data from years 2011-2014. We hypothesized that lower relative hand grip strength and absolute grip strength would be associated with higher risk of HTN. Also, I hypothesized that there would not be a significant difference in the relationship between Black and white women.

Specific Aim 2/Study 2: To investigate the longitudinal relationship between handgrip strength and HTN diagnosis among middle age/older adult Black and white women. We tested this aim by using data from MIDUS data. The primary objective was to determine whether baseline (M2) grip strength (relative and absolute GS) was related to diagnosis of HTN at follow up (M3) for Black and white women. The secondary analysis looked at the within-group and between group relationship between HTN and grip strength by race. We hypothesized that low baseline GS at baseline will predict future HTN diagnosis at M3 in both Black and white women.

Specific Aim 3/Study 3: To determine the longitudinal relationship between grip strength and HTN diagnosis among South African Black women. We tested this aim by utilizing data from the HAALSI study. The primary objective was to examine whether Black women residing in South Africa had similar relationships in grip strength and HTN diagnosis compared to American Black women. In addition, we also studied the factors that contribute to an increased risk of HTN in South African Black women. We hypothesized that in South African women, there would be a negative association between HGS and HTN status.

Article 1: The association between relative handgrip strength and hypertension status in US Black and white women: 2011-2014 National Health and Nutrition Survey

Introduction

Hypertension is a chronic condition that affects approximately 58.4 million (42.8%) U.S. women (Tsao et al., 2022). Hypertension is a major risk factor for cardiovascular disease (CVD), which was the leading cause of death for American women in 2019 (Tsao et al., 2022). Female-specific factors across the lifecycle such as menarche, use of oral contraception, polycystic ovarian syndrome (PCOS), pregnancy, and menopause have been associated with increases in blood pressure contributing to hypertension (Gauci et al., 2022; Vogel et al., 2021; Wenger et al., 2018).

Black women have the highest burden for hypertension in the U.S. For example, the age-adjusted prevalence of hypertension among U.S. non-Hispanic Black females was 55.3%, compared to 38.1% in U.S. non-Hispanic white females in 2015-2018 (Tsao et al., 2022). Black women experience an earlier onset of hypertension and more severe blood pressure elevation compared to white women (Lackland, 2014; Nesbitt, 2005; Thomas et al., 2018). In the Coronary Artery Risk Development in Young Adults (CARDIA) study, racial disparities in hypertension incidence appeared before the age of 30 (Thomas et al., 2018). This prolonged period of elevated blood pressure over the lifespan increases the risk of cardiovascular disease prevalence and mortality in this demographic (Carnethon et al., 2017). Despite U.S. Black women having the highest awareness of their hypertension diagnosis, they are unfortunately experiencing poor hypertension control through available treatment options (Aggarwal et al., 2021).

Influencing factors such as genetics, diet, smoking, obesity, and physical inactivity only partially explain the disparity in hypertension prevalence among U.S. women. Socioeconomic factors like access to health care, literacy, and income, in addition to the various and unique sources of stress experienced by Black women also contribute to the higher rates of hypertension (Carnethon et al., 2017). Therefore, it is necessary to initiate screening for hypertension risk and implement effective prevention and management strategies for hypertension to reduce its burden in U.S. Black women.

Handgrip strength (HGS) has been used as a method to measure overall muscular fitness (Wind et al., 2010). The HGS test is inexpensive, easy to perform, and non-invasive method to measure muscular fitness, allowing simple integration into clinical practice across various populations/demographics. A growing body of evidence has indicated the utility of HGS as an index for general health (Bohannon, 2019). HGS has been associated with fragility (Chainani et al., 2016) ,quality of life (Kang et al., 2018), nutritional status (Flood et al., 2014), all-cause mortality (Leong et al., 2015; Prasitsiriphon & Pothisiri, 2018), CVD incidence and mortality (Leong et al., 2015), diabetes (Lee et al., 2021; Mainous et al., 2015), depression (Mutz & Lewis, 2021) , and metabolic syndrome (Churilla et al., 2020; Sayer et al., 2007; Yi et al., 2018). Specifically, weak HGS has been associated with an increased risk of cardiometabolic disease (Kim et al., 2021; Leong et al., 2015; Liu et al., 2021; Peterson et al., 2017). In the Prospective Urban Rural Epidemiology (PURE) study, handgrip strength was found to be a stronger predictor of cardiovascular outcomes compared to blood pressure (Leong et al., 2015; Sayer & Kirkwood, 2015). HGS adjusted for body mass index (BMI) has been recommended to account for the covariance between body mass and muscular strength and referred to as relative grip strength (Fowles et al., 2014). Several studies have noted that relative grip strength had a stronger association to CVD risk factors compared to absolute grip strength (Lawman et al., 2015; Lee et al., 2016). Currently, there is a lack of evidence on relationship between relative handgrip strength and hypertension in women and with conflicting results (Sola-Rodríguez et al., 2021). To our knowledge, no studies have investigated the association between relative grip strength and hypertension with a white women reference group. It is essential to understand the utility of HGS as a prognostic tool for hypertension risk among Black women, a demographic disproportionately affected by hypertension.

The primary purpose of this study was to examine the cross-sectional associations between relative hand grip strength and hypertension diagnosis in US Black and white women using data from the National Health and Nutrition Examination Survey (NHANES) 2011-2014. Sub-analyses investigate the possible differences between US Black and white women. We hypothesized that there is a significant inverse association between relative handgrip strength and hypertension prevalence in Black and white women, and the relationship will be similar between the two groups. Future implications of this study include the potential of earlier detection of hypertension risk and inform future intervention strategies in this susceptible demographic.

Method

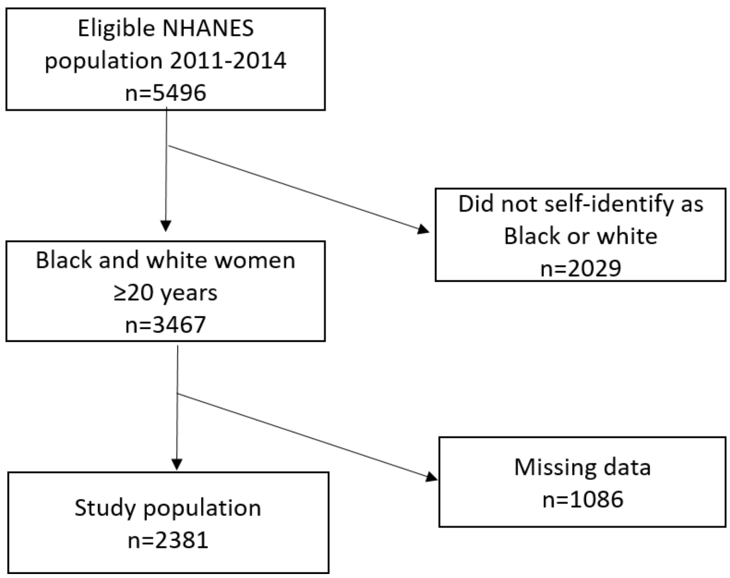
Survey description

Cross-sectional data from the National Health and Nutrition Survey (NHANES) 2011-2012 and 2013-2014 waves were used for this study. NHANES is a program run by the National Center for Health Statistics that utilizes a complex sampling design to create a nationally representative sample of the U.S. civilian non-institutionalized population. NHANES oversamples various subgroups of the US population including Hispanics, non-Hispanic Blacks, non-Hispanic Asians, non-Hispanic white adults ≥ 80 years, and low-income non-Hispanic whites/other persons. NHANES data is collected via an in-home interview and physical examination. In-home interviews collected demographic and health-related information. On a different visit, physical examinations were conducted in a Mobile Examination Center (MEC) and collected laboratory and anthropometry data. The National Center for Health Statistics Research Ethics Review Board approved the protocols used for this study and informed consent was obtained for all participants.

Study Population

Non-pregnant female participants aged ≥ 20 years were eligible for the study. Among the 5,496 participants eligible, participants who were missing data (grip strength, blood pressure, hypertension diagnosis, covariates, etc.), have had surgery on their hands or wrists for arthritis or carpal tunnel syndrome, or did not identify as Black or White race/ethnicity were excluded from the analysis. A total of 2,381 participants (797 Black female participants, 1584 White female participants) were included in the final analysis (Figure 2.1).

Figure 2 Study population for the NHANES cross-sectional study



Measures

Handgrip Strength:

Orthostatic handgrip strength was measured by a trained research assistant using the Takei Digital Grip Strength Dynamometer (Model T.K.K.5401). The test was done in a seated position if required. Prior to the handgrip strength test, participants performed a warmup for their hands and fingers and the hand dynamometer was adjusted to their grip size. The second joint of the participant's index finger was set to a 90-degree angle to set the proper grip. Handgrip strength was measured in kilograms (kg) over three trials, alternating hands between each trial, with a 60-second rest period between measurements on each hand. Missing grip test data occurred for various reasons (such as no time, arrived late/left early refusal, illness, emergency, or equipment failure). Less than 10% of participants had missing grip strength data for both hands. Absolute grip strength (kg) was the mean grip strength measurements from both left and right hands. Relative grip strength is calculated by using the equation: absolute grip strength (kg) divided by body mass index (BMI) (kg/m^2).

Blood Pressure measurement:

Blood pressure was measured during the one-time examination visit at the MEC. A participant's blood pressure was measured in their right arm unless it was necessary to use the left arm due to an underlying condition or the participant requested to not use right arm for blood pressure measurements. Blood pressure was measured after a seated 5 min rest period with the elbow slightly flexed and the arm at heart level supported by a table or arm rest. Three consecutive blood pressure readings were obtained by the oscillatory or auscultatory method with a 30 second period between each measurement. If a blood pressure measurement was incomplete or interrupted, a fourth measurement was taken. The average systolic and diastolic blood pressures across 3 measurements were used to analyze the relationship between grip strength and blood pressure.

Hypertension diagnosis definition:

Participants were considered hypertensive if they answered "Yes" to the question "[Have you/ Has study participant (SP)] ever been told by a doctor or other health professional that [you/s/he] had hypertension, also called high blood pressure?"

Anthropometry:

Anthropometry data was collected by a health technologist and data recorder in the MEC and entered into the Integrated Survey Information system (ISIS) anthropometry computer application. Height data was measured using a stadiometer with a vertical backboard connected to an acrylic head piece and recorded as centimeters (cm). Weight was measured using a digital weight scale and recorded in kilograms. BMI was calculated as weight in kilograms divided by meters squared (kg/m^2) and was reported as a continuous variable.

Sociodemographic and Health Covariates:

Covariates for this study included age, race/ethnicity, education, self-reported cardiovascular and non-cardiovascular-related conditions, and lifestyle indicators (physical activity, alcohol consumption, smoking status). Age in years was reported as a continuous variable. Physical activity was calculated as the number of minutes per week of moderate or vigorous work or recreational activity and reported as a continuous variable. Smoking status was assessed by self-reported questionnaire data and is separated into two categories: smoker or non-smoker. Alcohol consumption was coded as a dichotomous variable (yes/no) and defined as participants consuming at least 12 alcoholic drinks in 1 year. Self-reported medical history data was used to categorize number of cardiovascular and non-cardiovascular-related conditions. Cardiovascular related conditions (CVD) included stroke, heart attack, heart failure, coronary heart disease and angina pectoris. Non-cardiovascular related conditions included COPD, cancer, diabetes, asthma, and obesity. A comorbidity score was created for the number of CVDs and non-CVDs (none, one, two, three or more) diagnosed by a physician to explore whether the number of comorbidities influence the relationship between grip strength and hypertension diagnosis.

Statistical analysis

The analyses were conducted using SAS Version 9.4 (SAS Institute, Cary, NC). Data were summarized using mean and standard deviations for continuous variables and frequency and percentages for categorical variables. Differences in these characteristics were calculated using one-way analysis of variance (ANOVA) for continuous variables and chi-squared tests for categorical variables. Logistic regressions were used to examine the associations between hypertension diagnosis and relative grip strength and examine potential racial/ethnic differences. Pearson correlation coefficient analysis was used to analyze the relationship between handgrip strength, systolic blood pressure and diastolic blood pressure. A p-value of 0.05 was considered significant for this analysis.

Results

Descriptive characteristics of the study participants are summarized in Table 2.1. The present study included a total of 2,381 women aged 20 years or older that had complete data on handgrip strength, hypertension diagnosis, BMI and other sociodemographic variables. Mean age of participants was 50.0 ± 17.5 years with a BMI of 30.2 ± 8.1 kg/m^2. Significant differences between Black and white women were observed for several variables. Black women had a higher mean handgrip strength (28.8 ± 6.0 kg, 26.2 ± 5.6 kg p<0.0001) with higher BMIs (32.4 ± 8.5, 29.1 ± 7.6, p<0.0001) than white women. When grip strength was adjusted for BMI, relative grip strength was similar in Black and white women (0.93 ± 0.95 ± 0.3, p=0.3). Also, Black women were more likely to have less than a college education and health insurance. Overall, 40.9 % of participants reported a physician diagnosis of hypertension. Black women in this study were younger but had higher systolic blood pressure and diastolic blood pressure (Tables 2.2 and 2.3). Additionally, 48.6% of Black women had a physician diagnosis of HTN compared to only 37.0% of white women (p value <.0001).

Table 1.1: Descriptive statistics for NHANES study sample

	Total Population	Black	White	p-value
n	2381	797 (33.5%)	1584 (66.5%)	
Age	50.0 ± 17.5	48.0 ± 16.4	51.0 ±18.0	<.0001
Age Categories				
20-39	744 (31.2%)	259 (32.5%)	485 (30.6%)	0.01
40-59	835 (35.1%)	301 (38.0%)	534 (33.7%)	
60+	802 (33.7%)	237 (29.7%)	565 (35.7%)	
BMI (kg/m2)	30.2 ± 8.1	32.4 ± 8.5	29.1 ± 7.6	<.0001
Mean Handgrip strength (kg)	27.1 ± 5.9	28.8 ± 6.0	26.2 ± 5.6	<.0001
Relative grip strength	0.94 ± 0.3	0.93 ± 0.3	0.95 ± 0.3	0.3
Blood Pressure (mmHg)				
Mean Systolic Blood Pressure	122.8 ±18.7	125.8 ± 19.4	121.2 ± 18.2	<.0001
Mean Diastolic Blood Pressure	69.8 ±11.8	70.6 ± 13.2	69.4 ± 11.0	0.02
Education level				
Less than High School	327 (13.7%)	131 (16.4%)	196 (12.4%)	<.0001
High School	508 (21.3%)	186 (23.3%)	322 (20.3%)	
Some College	893 (37.5%)	314 (39.4%)	579 (36.5%)	
College graduate or above	654 (27.4%)	166 (20.8%)	487 (30.7%)	
Smoker				
Yes	550 (23.1%)	167 (21.0%)	383 (24.2%)	0.08
Hypertension				
Yes	973 (40.9%)	387 (48.6%)	586 (37.0%)	<.0001
Consume Alcohol				
Yes	1669 (70.1%)	501 (62.9%)	1168 (73.7%)	<.0001
Cardiovascular-Related Comorbidities Score				
0	2151 (90.4%)	721 (90.5%)	1430 (90.3%)	0.01
1	136 (5.7%)	52 (6.5%)	84 (5.3%)	
2	51 (2.1%)	19 (2.4%)	32 (2.0%)	
3+	42 (1.8%)	5 (0.6%)	37 (2.3%)	
Non-Cardiovascular-Related Comorbidities Score				
0	745 (31.3%)	259 (32.5%)	486 (30.7%)	0.80
1	764 (32.1%)	255 (32.0%)	509 (32.1%)	
2	522 (21.9%)	171 (21.5%)	351 (22.2%)	
3+	350 (14.7%)	112 (14.0%)	238 (15.0%)	
Health Insurance				
Yes	2010 (84.4%)	648 (81.3%)	1362 (86.0%)	0.003
Minutes of Physical activity/week	452.4 ± 684.0	462.5 ± 703.5	447.2 ± 674.1	0.61

Table 1.2 Descriptive statistics for NHANES subgroup-white women

	Total	Hypertension	No Hypertension	
n	**1584**	586 (37.0%)	998 (63.0%)	**p-value**
Age	51.0 ±18.0	61.0 ± 15.1	45.1 ±16.9	<0.0001
Age Categories				
20-39	485 (30.6%)	60 (10.2%)	425 (42.5%)	<0.0001
40-59	534 (33.7%)	181 (30.9%)	353 (35.4%)	
60+	565 (35.7%)	345 (58.9%)	220 (22.0%)	
BMI (kg/m2)	29.1 ± 7.6	31.3 ± 7.9	27.8 ± 7.2	<0.0001
Mean Handgrip strength (kg)	26.2 ± 5.6	24.0 ± 5.9	27.5 ± 5.0	<0.0001
Relative grip strength	0.95 ± 0.3	0.80 ± 0.2	1.0 ± 0.3	<0.0001
Blood Pressure (mmHg)				
Mean Systolic Blood Pressure	121.2 ± 18.2	130.8 ± 19.3	115.6 ± 15.0	<0.0001
Mean Diastolic Blood Pressure	69.4 ± 11.0	69.9 ± 12.6	69.1 ± 9.9	0.15
Education level				
Less than High School	196 (12.4%)	97 (16.5%)	99 (9.9%)	<0.0001
High School	322 (20.3%)	142 (24.2%)	180 (18.0%)	
Some College	579 (36.5%)	229 (39.1%)	350 (35.1%)	
College graduate or above	487 (30.7%)	118 (20.1%)	369 (37.0%)	
Smoker				
Yes	383 (24.2%)	136(23.2%)	247 (24.8%)	0.49
Consume Alcohol				
Yes	1168 (73.7%)	375 (64.0%)	793 (79.5%)	<0.0001
Cardiovascular-Related Comorbidities Score				
0	1430 (90.3%)	468 (79.9%)	962 (96.5%)	<0.0001
1	84 (5.3%)	62 (10.6%)	22 (2.2%)	
2	32 (2.0%)	24 (4.1%)	8 (0.8%)	
3+	37 (2.3%)	32 (5.5%)	5(0.5%)	
Non-Cardiovascular-Related Comorbidities Score				
0	486 (30.7%)	85 (14.5%)	401 (40.2%)	<0.0001
1	509 (32.1%)	164 (28.0%)	345 (34.6%)	
2	351 (22.2%)	177 (30.2%)	174 (17.4%)	
3+	238 (15.0%)	160 (27.3%)	78 (7.8%)	
Health Insurance				
Yes	1362 (86.0%)	527 (89.9%)	835 (83.7%)	0.0005
Minutes of Physical activity/week	447.2 ± 674.1	368.6 ± 647.2	493.4 ± 685.5	0.0004

Table 1.3 Descriptive statistics for NHANES subgroup-Black women

	Total	Hypertension	No Hypertension	p-value
n	**797 (33.5%)**	387 (48.6%)	410 (51.4%)	<.0001
Age	48.0 ± 16.4	55.5 ± 14.4	40.9 ±14.9	<.0001
Age Categories				<.0001
20-39	259 (32.5%)	62 (16.0%)	197 (48.0%)	
40-59	301 (38.0%)	143 (37.0%)	158 (38.5%)	
60+	237 (29.7%)	182 (47.0%)	55 (13.4%)	
BMI (kg/m2)	32.4 ± 8.5	34.2 ± 9.0	30.7 ± 7.6	<.0001
Mean Handgrip strength (kg)	28.8 ± 6.0	27.7 ± 6.3	29.9 ± 5.3	<.0001
Relative grip strength	0.93 ± 0.3	0.85 ± 0.3	1.0 ± 0.2	<.0001
Blood Pressure (mmHg)				
Mean Systolic Blood Pressure	125.8 ± 19.4	134.4 ± 19.6	117.8 ± 15.8	<.0001
Mean Diastolic Blood Pressure	70.6 ± 13.2	72.5 ± 14.8	68.9± 11.2	
Education level				
Less than High School	131 (16.4%)	83 (21.4%)	48 (11.7%)	0.0002
High School	186 (23.3%)	96 (24.8%)	90 (22.0%)	
Some College	314 (39.4%)	143 (37.0%)	171 (41.7%)	
College graduate or above	166 (20.8%)	65 (16.8%)	101 (24.6%)	
Smoker				
Yes	167 (21.0%)	79 (20.4%)	88 (21.4%)	0.73
Consume Alcohol				
Yes	501 (62.9%)	218 (56.3%)	283(69.0%)	0.0002
Cardiovascular-Related Comorbidities Score				
0	721 (90.5%)	324 (83.7%)	397 (96.8%)	<.0001
1	52 (6.5%)	42 (10.8%)	10 (2.4%)	
2	19 (2.4%)	17 (4.4%)	2 (0.5%)	
3+	5 (0.6%)	4 (1.0%)	1 (0.2%)	
Non-Cardiovascular-Related Comorbidities Score				
0	259 (32.5%)	66 (17.0%)	193 (47.0%)	<.0001
1	255 (32.0%)	125 (32.3%)	509 (31.7%)	
2	171 (21.5%)	107 (27.7%)	64 (15.6%)	
3+	112 (14.0%)	89 (23.0%)	238 (5.6%)	
Health Insurance				
Yes	648 (81.3%)	342 (88.4%)	306 (74.6%)	<.0001
Minutes of Physical activity/week	462.5 ± 703.5	352.9 ± 630.4	566.1 ± 752.2	<.0001

Pearson correlation coefficient was computed to assess the relationship between blood pressure and relative grip strength. There was a moderate negative association between mean systolic blood pressure and relative grip strength ($r=-0.275$, $p<0.0001$). Diastolic blood pressure was not significantly related to relative handgrip strength ($r=-0.0188$, $p=0.172$). When analyzing absolute handgrip strength, higher absolute handgrip strength was associated with higher diastolic blood pressure ($r=0.123$, $p<0.0001$). There was a negative correlation between systolic blood pressure and absolute grip strength ($r=-0.225$, $p<0.0001$).

Hypertension diagnosis was associated with relative handgrip strength, age, education, health insurance (yes/no), non-CVD conditions, and CVD conditions (Table 2.4). Lower relative handgrip strength was associated with higher risk of hypertension in both Black and white women. To assess if the relationship between relative grip strength and hypertension differed by race, an interaction term was included in the logistic regression model. The interaction between race and relative handgrip strength was not significant ($p= 0.4414$). Individuals with more comorbidities, non-CVD and CVD conditions, had a higher risk of being diagnosed with hypertension. Black women had 2.45 times higher odds of being diagnosed with hypertension by a physician compared to white women after adjusting for age, smoking status, alcohol consumption, education, health insurance, minutes of weekly physical activity, non-CVD conditions and CVD conditions. There were differences in the factors associated with Black and white women. For white women, lower education was significantly associated with hypertension diagnosis ($p= 0.0006$) while for Black women, this variable almost reached statistical significance ($p= 0.0541$). When using absolute handgrip strength and controlling for BMI in addition to the other sociodemographic factors, absolute grip strength had a weaker association to hypertension diagnosis than relative grip strength ($p=0.0579$). Higher BMI was strongly associated with hypertension risk, after controlling for lifestyle behaviors, education, age and comorbidities (Table 2.5).

Table 1.4 Association between hypertension diagnosis (yes/no) and handgrip strength (absolute and relative) from logistic regression adjusted model, >20 years and older from NHANES 2011-2014

Relative Grip Strength

Variable	Odds Ratio	Lower Limit	Upper Limit	*p*- Value
Relative grip strength	0.18	0.12	0.29	<0.0001
Black women	2.45	1.87	3.22	<0.0001
Age	1.04	1.04	1.05	<0.0001
Smoker	1.22	0.85	1.75	0.278
Consume Alcohol	1.03	0.77	1.39	0.821
Min of Physical Activity	1.00	1.00	1.00	0.293
Education	0.81	0.73	0.91	0.001
Health insurance	1.54	1.03	2.30	0.037
# Non CVD conditions	1.49	1.32	1.69	<0.0001
# CVD conditions	1.45	1.09	1.93	0.013

Absolute Grip Strength

Variable	Odds Ratio	Lower Limit	Upper Limit	*p*- Value
Absolute Grip Strength	0.972	0.945	1.001	0.0579
BMI	1.061	1.042	1.081	<0.0001
Black women	2.278	1.7	3.052	<0.0001
Age	1.051	1.042	1.061	<0.0001
Smoker	1.261	0.888	1.793	0.1876
Consume Alcohol	1.027	0.765	1.379	0.853
Min of Physical Activity	1	1	1	0.3694
Education	0.804	0.722	0.896	0.0002
Health insurance	1.592	1.061	2.389	0.0261
# Non CVD conditions	1.433	1.243	1.652	<0.0001
# CVD conditions	1.477	1.101	1.98	0.0108

Discussion

This study examined the relationship between relative handgrip strength and hypertension status in a nationally representative sample of Black and white women ≥ 20 years old from NHANES 2011-2014. The primary finding from the study was that relative handgrip strength was significantly associated with relative handgrip strength for both Black and white women, with higher handgrip strength being related to lower risk of hypertension. The results of this study suggested that relative handgrip strength had a more significant association to hypertension diagnosis than absolute grip strength and hypertension in a general population of US women. The study did not find a racial difference in this relationship between Black and white women. Also, lower systolic blood pressure was related to higher relative handgrip strength, but there was no relationship found for diastolic blood pressure.

This study's findings expand on previous research by analyzing the relationship between hypertension risk and relative handgrip strength exclusively in Black and white women. Black women are commonly a demographic underrepresented in cardiovascular and exercise-related studies, which limits quality information for hypertension management strategies in this population. Results of the cross-sectional analysis found that relative grip strength, not absolute grip strength, had a significant inverse association with hypertension. The results of our study are consistent with findings from several studies (Lawman et al., 2015; Leong et al., 2015; Mainous et al., 2015; Peterson et al., 2017; Sola-Rodríguez et al., 2021).

Several studies have suggested the importance of considering body composition (e.g. BMI, waist to hip ratio, body weight) when examining the associations between handgrip strength and hypertension in different age groups. A study of middle-aged Chinese community residents compared the predictive value of absolute handgrip strength and four adjusted handgrip strength measurements corrected for body size measures (body weight, BMI, lean body mass, and muscle mass) for CVD risk factors and found that handgrip strength adjusted for BMI (absolute handgrip strength/BMI) or body weight (absolute handgrip strength/body weight) were better predictors of CVD risk factors than absolute handgrip strength alone (Gao et al., 2022). A recent study of women with systemic lupus erythematosus found that higher relative handgrip strength (adjusted by BMI) was associated with lower systolic blood pressure, yet no significant association was found for diastolic blood pressure (Sola-Rodriguez et al. 2021). Studies that have forgone adjustment of handgrip with a body composition measure when studying the association between grip strength and hypertension risk factors have had diverging conclusions. For example, a study conducted by Zhang et al. (2020), higher dominant handgrip strength was associated with lower risk of hypertension in middle-aged and elderly females. Conversely, Ji et al. (2018) found that higher absolute handgrip strength was associated with higher diastolic blood pressure in both men and women but not systolic blood pressure. The variation in results between studies may be attributed to important role body size plays in muscle function and increased cardiovascular disease risk. This is especially important to consider when studying the relationship between grip strength and hypertension risk in US Black women, a group with the highest prevalence rates of obesity compared to women of other racial/ethnic backgrounds (Agyemang & Powell-Wiley, 2013)**.** Using BMI to adjust absolute grip strength can be useful when comparing relative grip strength values from different studies because BMI is a common index utilized in research (Kim et al., 2021). Most research studies have reported a positive relationship between muscular strength and BMI. A study that utilized longitudinal data from the 1970 British Cohort Study found that higher BMI during childhood and later life stages was associated with higher grip strength at midlife than non-obese individuals (Cooper et al., 2022). The increased absolute muscular strength observed in obese individuals is because of the additional body mass and therefore muscle mass typically observed in obese individuals compared to normal-weight individuals (Tomlinson et al., 2016). When grip strength is adjusted by BMI, individuals of higher BMI categories have lower relative grip strengths compared to normal weight individuals (Keevil et al., 2015; Lawman et al., 2015) One disadvantage of using BMI is that it does not account for body fat distribution throughout the body nor can distinguish between fat, muscle or bone mass. Body mass index has been criticized by researchers for not being inclusive for women of different ethnic backgrounds with varying body compositions (Stanford et al., 2019). Central obesity, characterized by additional fat around the abdomen and measured by waist circumference, has been shown to be a better predictor of cardiovascular disease mortality Keevil et al. (2015) found that every 10 cm increase in waist circumference corresponded to 1.00 kg lower grip strength in women. Despite the concerns of using BMI to adjust for handgrip strength, relative grip strength (absolute grip strength/BMI) is still a valuable tool in better understanding the association between grip strength and hypertension risk among a large cohort of women.

Previous studies have highlighted the differences in strength in association between grip strength and hypertension diagnosis or cardiometabolic risk in males and females. Chon et al. (2020) found that there were statistically significant associations between four grip strength categories (low, middle low, middle high, and high) and hypertension diagnosis in female participants while no significant association was found in males during a subgroup analysis. When relative handgrip strength was analyzed, the relationship was only significant in the low grip strength group in females, but statistically significant for all groups for males (Chon et al., 2020) A study by Lee et. al (2016) that examined the association between cardiometabolic risk factors and relative handgrip strength found that low systolic blood pressure was associated with higher relative grip strength in men, but not in women. Our study found that in both Black and white women, relative grip strength was inversely associated with hypertension risk. The differences in the reported results from these studies may further highlight the importance of additional research to better elucidate the association between grip strength and hypertension risk in women.

The strengths of this study were that we used data from a nationally representative sample of Black and white women in the US which provided a reasonable cohort of Black women with sociodemographic, self-report, and physical exam data. To our knowledge, this is the first study that examines racial differences in the relationship between handgrip strength and hypertension in US women. Additionally, we compare relative grip strength to absolute grip strength. Despite these strengths, our study had several limitations. First, there were almost twice as many white women in the study compared to Black women, which may influence the relationships found in the current study. Second, our definition of hypertension for the study only included individuals with a self-reported physician's diagnosis of hypertension and individuals with a blood pressure ≥ 130/80 mmHg without a previous diagnosis of hypertension were excluded. This could be excluding an important population, undiagnosed hypertensive individuals. Lastly, this is a cross-sectional study design which cannot establish a causal relationship. Future studies should investigate the longitudinal relationship between relative handgrip strength and hypertension.

Our findings indicate lower relative grip strength is associated with hypertension among both Black women and white women with no difference by race. These results may have utility in a community setting for early detection of hypertension risk among Black women, a group disproportionately impacted by hypertension and CVD.

References

Aggarwal, R., Chiu, N., Wadhera, R. K., Moran, A. E., Raber, I., Shen, C., Yeh, R. W., & Kazi, D. S. (2021). Racial/Ethnic Disparities in Hypertension Prevalence, Awareness, Treatment, and Control in the United States, 2013 to 2018. *Hypertension*, *78*(6), 1719-1726. https://doi.org/10.1161/hypertensionaha.121.17570

Agyemang, P., & Powell-Wiley, T. M. (2013). Obesity and Black Women: Special Considerations Related to Genesis and Therapeutic Approaches. *Curr Cardiovasc Risk Rep*, *7*(5), 378-386. https://doi.org/10.1007/s12170-013-0328-7

Bohannon, R. W. (2019). Grip Strength: An Indispensable Biomarker For Older Adults. *Clin Interv Aging*, *14*, 1681-1691. https://doi.org/10.2147/cia.S194543

Carnethon, M. R., Pu, J., Howard, G., Albert, M. A., Anderson, C. A. M., Bertoni, A. G., Mujahid, M. S., Palaniappan, L., Taylor, H. A., Jr., Willis, M., Yancy, C. W., American Heart Association Council on, E., Prevention, Council on Cardiovascular Disease in the, Y., Council on, C., Stroke, N., Council on Clinical, C., Council on Functional, G., Translational, B., & Stroke, C. (2017). Cardiovascular Health in African Americans: A Scientific Statement From the American Heart Association. *Circulation*, *136*(21), e393-e423. https://doi.org/10.1161/CIR.0000000000000534

Chon, D., Shin, J., & Kim, J. H. (2020). Consideration of body mass index (BMI) in the association between hand grip strength and hypertension: Korean Longitudinal Study of Ageing (KLoSA). *PLoS One*, *15*(10), e0241360. https://doi.org/10.1371/journal.pone.0241360

Churilla, J. R., Summerlin, M., Richardson, M. R., & Boltz, A. J. (2020). Mean Combined Relative Grip Strength and Metabolic Syndrome: 2011-2014 National Health and Nutrition Examination Survey. *J Strength Cond Res*, *34*(4), 995-1000. https://doi.org/10.1519/jsc.0000000000003515

Cooper, R., Tomlinson, D., Hamer, M., & Pinto Pereira, S. M. (2022). Lifetime body mass index and grip strength at age 46 years: the 1970 British Cohort Study. *J Cachexia Sarcopenia Muscle*, *13*(4), 1995-2004. https://doi.org/10.1002/jcsm.12992

Flood, A., Chung, A., Parker, H., Kearns, V., & O'Sullivan, T. A. (2014). The use of hand grip strength as a predictor of nutrition status in hospital patients. *Clinical Nutrition*, *33*(1), 106-114. https://doi.org/https://doi.org/10.1016/j.clnu.2013.03.003

Fowles, J., Roy, J., Clarke, J., & Dogra, S. (2014). Are the fittest Canadian adults the healthiest? *Health Rep*, *25*(5), 13-18. https://www.ncbi.nlm.nih.gov/pubmed/24850392

Gao, Y., Huang, H., Ni, C., Feng, Y., Yu, J., Huang, Y., Luo, L., Jiang, Y., & Wang, A. (2022). Comparison of Five Expressions of Handgrip Strength for Predicting Cardiovascular Disease Risk Factors in Chinese Middle-Aged Community Residents. *Front Public Health*, *10*, 903036. https://doi.org/10.3389/fpubh.2022.903036

Gauci, S., Cartledge, S., Redfern, J., Gallagher, R., Huxley, R., Lee, C. M. Y., Vassallo, A., & O'Neil, A. (2022). Biology, Bias, or Both? The Contribution of Sex and Gender to the Disparity in Cardiovascular Outcomes Between Women and Men. *Curr Atheroscler Rep*, *24*(9), 701-708. https://doi.org/10.1007/s11883-022-01046-2

Kang, S. Y., Lim, J., & Park, H. S. (2018). Relationship between low handgrip strength and quality of life in Korean men and women. *Qual Life Res*, *27*(10), 2571-2580. https://doi.org/10.1007/s11136-018-1920-6

Keevil, V. L., Luben, R., Dalzell, N., Hayat, S., Sayer, A. A., Wareham, N. J., & Khaw, K. T. (2015). Cross-sectional associations between different measures of obesity and muscle strength in men and women in a British cohort study. *J Nutr Health Aging*, *19*(1), 3-11. https://doi.org/10.1007/s12603-014-0492-6

Kim, J. Y., Park, H. Y., Kim, J., & Lim, K. (2021). Body mass index and relative handgrip strength are associated with the prevalence of hypertension in Korean elderly: Korean national fitness assessment in 2019. *Phys Act Nutr*, *25*(2), 26-32. https://doi.org/10.20463/pan.2021.0012

Lackland, D. T. (2014). Racial differences in hypertension: implications for high blood pressure management. *Am J Med Sci*, *348*(2), 135-138. https://doi.org/10.1097/MAJ.0000000000000308

Lawman, H. G. P., Troiano, R. P. P., Perna, F. M. P., Wang, C.-Y. P., Fryar, C. D. M., & Ogden, C. L. P. (2015). Associations of Relative Handgrip Strength and Cardiovascular Disease Biomarkers in U.S. Adults, 2011–2012. *American journal of preventive medicine*, *50*(6), 677-683. https://doi.org/10.1016/j.amepre.2015.10.022

Lee, K., Lee, J. Y., & Kim, Y. H. (2021). Low Grip Strength and Muscle Mass Increase the Prevalence of Osteopenia and Osteoporosis in Elderly Women. *Healthcare (Basel)*, *9*(4). https://doi.org/10.3390/healthcare9040476

Lee, W. J., Peng, L. N., Chiou, S. T., & Chen, L. K. (2016). Relative Handgrip Strength Is a Simple Indicator of Cardiometabolic Risk among Middle-Aged and Older People: A Nationwide Population-Based Study in Taiwan. *PLoS One*, *11*(8), e0160876. https://doi.org/10.1371/journal.pone.0160876

Leong, D. P., Teo, K. K., Rangarajan, S., Lopez-Jaramillo, P., Avezum, A., Jr., Orlandini, A., Seron, P., Ahmed, S. H., Rosengren, A., Kelishadi, R., Rahman, O., Swaminathan, S., Iqbal, R., Gupta, R., Lear, S. A., Oguz, A., Yusoff, K., Zatonska, K., Chifamba, J., . . . Yusuf, S. (2015). Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*, *386*(9990), 266-273. https://doi.org/10.1016/s0140-6736(14)62000-6

Liu, G., Xue, Y., Wang, S., Zhang, Y., & Geng, Q. (2021). Association between hand grip strength and stroke in China: a prospective cohort study. *Aging*, *13*(6), 8204-8213. https://doi.org/10.18632/aging.202630

Mainous, A. G., 3rd, Tanner, R. J., Anton, S. D., & Jo, A. (2015). Grip Strength as a Marker of Hypertension and Diabetes in Healthy Weight Adults. *Am J Prev Med*, *49*(6), 850-858. https://doi.org/10.1016/j.amepre.2015.05.025

Mutz, J., & Lewis, C. M. (2021). Lifetime depression and age-related changes in body composition, cardiovascular function, grip strength and lung function: sex-specific analyses in the UK Biobank. *Aging*, *13*(13), 17038-17079. https://doi.org/10.18632/aging.203275

Nesbitt, S. D. (2005). Hypertension in Black Patients: Special Issues and Considerations. *Curr Hypertens Rep*(7), 244-248.

Peterson, M. D., Duchowny, K., Meng, Q., Wang, Y., Chen, X., & Zhao, Y. (2017). Low Normalized Grip Strength is a Biomarker for Cardiometabolic Disease and Physical Disabilities Among U.S. and Chinese Adults. *J Gerontol A Biol Sci Med Sci*, *72*(11), 1525-1531. https://doi.org/10.1093/gerona/glx031

Prasitsiriphon, O., & Pothisiri, W. (2018). Associations of Grip Strength and Change in Grip Strength With All-Cause and Cardiovascular Mortality in a European Older Population. *Clinical Medicine Insights. Cardiology*, *12*, 1179546818771894. Retrieved 2018, from https://doi.org/10.1177/1179546818771894

Sayer, A. A., & Kirkwood, T. B. L. (2015). Grip strength and mortality: a biomarker of ageing? *The Lancet*, *386*(9990), 226-227. https://doi.org/https://doi.org/10.1016/S0140-6736(14)62349-7

Sayer, A. A., Syddall, H. E., Dennison, E. M., Martin, H. J., Phillips, D. I. W., Cooper, C., Byrne, C. D., & Hertfordshire, C. (2007). Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. *QJM : monthly journal of the Association of Physicians*, *100*(11), 707-713. https://doi.org/10.1093/qjmed/hcm095

Sola-Rodríguez, S., Vargas-Hitos, J. A., Gavilán-Carrera, B., Rosales-Castillo, A., Sabio, J. M., Hernández-Martínez, A., Martínez-Rosales, E., Ortego-Centeno, N., & Soriano-Maldonado, A. (2021). Relative Handgrip Strength as Marker of Cardiometabolic Risk in Women with Systemic Lupus Erythematosus. *Int J Environ Res Public Health*, *18*(9). https://doi.org/10.3390/ijerph18094630

Stanford, F. C., Lee, M., & Hur, C. (2019). Race, Ethnicity, Sex, and Obesity: Is It Time to Personalize the Scale? *Mayo Clin Proc*, *94*(2), 362-363. https://doi.org/10.1016/j.mayocp.2018.10.014

Thomas, S. J., Booth, J. N., 3rd, Dai, C., Li, X., Allen, N., Calhoun, D., Carson, A. P., Gidding, S., Lewis, C. E., Shikany, J. M., Shimbo, D., Sidney, S., & Muntner, P. (2018). Cumulative Incidence of Hypertension by 55 Years of Age in Blacks and Whites: The CARDIA Study. *J Am Heart Assoc*, *7*(14). https://doi.org/10.1161/JAHA.117.007988

Tomlinson, D. J., Erskine, R. M., Morse, C. I., Winwood, K., & Onambélé-Pearson, G. (2016). The impact of obesity on skeletal muscle strength and structure through adolescence to old age. *Biogerontology*, *17*(3), 467-483. https://doi.org/10.1007/s10522-015-9626-4

Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Alonso, A., Beaton, A. Z., Bittencourt, M. S., Boehme, A. K., Buxton, A. E., Carson, A. P., Commodore-Mensah, Y., Elkind, M. S. V., Evenson, K. R., Eze-Nliam, C., Ferguson, J. F., Generoso, G., Ho, J. E., Kalani, R., Khan, S. S., Kissela, B. M., . . . Martin, S. S. (2022). Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. *Circulation*, *145*(8), e153-e639. https://doi.org/10.1161/CIR.0000000000001052

Vogel, B., Acevedo, M., Appelman, Y., Bairey Merz, C. N., Chieffo, A., Figtree, G. A., Guerrero, M., Kunadian, V., Lam, C. S. P., Maas, A. H. E. M., Mihailidou, A. S., Olszanecka, A., Poole, J. E., Saldarriaga, C., Saw, J., Zühlke, L., & Mehran, R. (2021). The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030. *The Lancet*, *397*(10292), 2385-2438. https://doi.org/https://doi.org/10.1016/S0140-6736(21)00684-X

Wenger, N. K., Arnold, A., Bairey Merz, C. N., Cooper-DeHoff, R. M., Ferdinand, K. C., Fleg, J. L., Gulati, M., Isiadinso, I., Itchhaporia, D., Light-McGroary, K., Lindley, K. J., Mieres, J. H., Rosser, M. L., Saade, G. R., Walsh, M. N., & Pepine, C. J. (2018). Hypertension Across a

Woman's Life Cycle. *J Am Coll Cardiol*, *71*(16), 1797-1813. https://doi.org/10.1016/j.jacc.2018.02.033

Wind, A. E., Takken, T., Helders, P. J., & Engelbert, R. H. (2010). Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? *Eur J Pediatr*, *169*(3), 281-287. https://doi.org/10.1007/s00431-009-1010-4

Yi, D. W., Khang, A. R., Lee, H. W., Son, S. M., & Kang, Y. H. (2018). Relative handgrip strength as a marker of metabolic syndrome: the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014-2015). *Diabetes Metab Syndr Obes*, *11*, 227-240. https://doi.org/10.2147/dmso.S166875

Article 2: The longitudinal association between relative handgrip strength and hypertension risk in middle aged and older women: Midlife in the United States

Introduction

Hypertension is a common modifiable risk factor for cardiovascular disease (CVD) morbidity and mortality in women. It is well established that women have a higher prevalence of hypertension after the age of 65 compared to men (Ahmad & Oparil, 2017). This elevation in blood pressure begins decades earlier, with women experiencing a steeper rise in blood pressure with age compared to men starting around the age of 30 (Ji et al., 2020). Along a woman's lifespan, there are events and conditions unique to women that can influence blood pressure and increase the risk of HTN and CVD in women later in life, which include menarche, menstruation, pregnancy, menopause, oral contraceptive use, polycystic ovarian syndrome (PCOS), and hormone replacement therapy (Hage et al., 2013; Wenger, 2020; Wenger et al., 2018). Additionally, lifestyle factors such as diet, physical activity, smoking status, and alcohol consumption can also contribute to the increased hypertension burden among U.S. women (Appel, 2003). As the population of middle-aged and older women increases in the U.S., more attention is needed on ways to identify HTN risk early and effectively and implement prevention and management strategies to reduce the burden of HTN and CVD in women.

Disparities in HTN prevalence between Black and white women have been well established (Hicks et al., 2005; Lackland, 2014; Muntner et al., 2017; Taylor et al., 2005) . These differences in Black women disproportionally with elevated blood pressure beginning in childhood (Chen et al., 2015). In the Coronary Artery Risk Development in Young Adults Study (CARDIA), it was found that Black women regardless of baseline blood pressure in young adulthood, had a greater cumulative incidence of HTN by age 55 compared to white women with approximately 75.7% of Black women as opposed to only 40.0% of white women (Thomas et al., 2018). Additionally, Black women have higher prevalence, earlier onset, faster progression of hypertension-related end-organ damage, and higher morbidity and mortality from HTN compared to women of other racial/ethnic backgrounds (Fongwa, 2008; Gillum, 1996). Despite Black women having the highest awareness of HTN status among women and men of all racial/ethnic groups, Black women still experience suboptimal blood pressure control (Fongwa, 2008; Mozaffarian et al., 2016). Hence, further attention is needed to identify HTN risk factors in Black women and implement HTN management strategies to prevent future HTN-related CVD morbidity and mortality.

The aging process is characterized by the progressive loss of muscle mass and strength leading to reduced muscle function, called sarcopenia (McGrath et al., 2018). Handgrip strength, is an easy and inexpensive method for assessing overall muscular strength in the diagnosis of sarcopenia and predicting healthy and chronic disease outcomes in older adults (Beyer et al., 2018; Brooks et al., 2018; Peterson et al., 2016; Prasitsiriphon & Pothisiri, 2018; Sousa-Santos & Amaral, 2017; Wu et al., 2019), with conflicting results (Chong et al., 2020; Taekema et al., 2011). Lower muscular strength has been associated with increased risk for fragility, osteoporosis, diabetes, lower quality of life, metabolic syndrome, hypertension, and all-cause and CVD mortality in women (Ahn et al., 2020; Karvonen-Gutierrez et al., 2018; Mainous et al., 2015; Souza Saraiva et al., 2019; Zhang et al., 2020). Relative grip strength, which is absolute grip strength adjusted by a body composition measure (e.g., body mass index (BMI)) has been suggested to account for the difference in strength with increased body mass (Fowles et al., 2014). The relationship between handgrip strength and hypertension risk has been investigated across different age groups in numerous studies. Several studies have found significant associations between higher handgrip strength and lower hypertension risk or blood pressure in women (Feng et al., 2021; Lawman et al., 2015; Yi et al., 2018; Zhang et al., 2020) while other studies report a positive relationship or no relationship (Ji et al., 2018; Mallah et al., 2019). For example, a study conducted by Ji et al concluded that stronger HGS was associated with higher risk of hypertension in men, but no relationship was found in women after adjusting for age, BMI, smoking status, and alcohol consumption (2018). The study also found that higher handgrip strength was related to higher DBP in women (Ji et al., 2018). In a community-based, cross-sectional study of the Chinese Han population indicated that higher handgrip strength was associated with increased risk of hypertension in female subjects (Mallah et al., 2019).

The conflicting results may be due the differing definitions for handgrip strength (with or without body mass) and hypertension risk used in the studies (Gao et al., 2022). To our knowledge, there are no previous studies that investigate the relationship between relative grip strength and hypertension risk exclusively among women using longitudinal data. Longitudinal data analysis would provide more detailed information on the relationship between relative grip strength and hypertension risk. In addition, none of these studies focused specifically on this relationship in Black and white women. Leveraging HGS measurements to identify women at greater risk for HTN could potentially help with earlier HTN diagnosis and assist with implementation of management strategies in Black women.

The primary goals of this study were to 1) determine the cross-sectional relationship between relative grip strength and hypertension in age-matched middle age and older Black and white women in the U.S. and 2) examine the longitudinal association between baseline relative grip strength and future diagnosis of hypertension using the Midlife in the United States (MIDUS) survey and biomarker data. We hypothesized that lower relative handgrip strength was associated with higher risk of HTN in both Black and white women and that lower relative handgrip strength at baseline would predict hypertension risk in Black and white women at wave 2.

Method

Survey description

This study utilized data from the Midlife Development in the United States (MIDUS), a longitudinal study that began data collection in 1995 to investigate the behavioral, psychological and social predictors of health and well-being in a national sample of aging U.S. adults. Additional information about the MIDUS study can be found elsewhere (*Midlife in the United States: A National Longitudinal Study of Health & Well-Being* 2022). To summarize, the original phase of data collection, MIDUS I (M1), collected survey data from 7,108 participants that were sampled using random-digit-dialing (RDD) along with oversampling in five cities. Additionally, the original phase recruited twin pairs and siblings of the RDD respondents. Inclusion criteria for M1 were English speaking, non-institutionalized adults living in the contiguous United States ages 25-74 years old. The MIDUS study was approved by the University of Wisconsin Institutional Review Board (IRB). Participants were given a written informed consent and compensated for their participation.

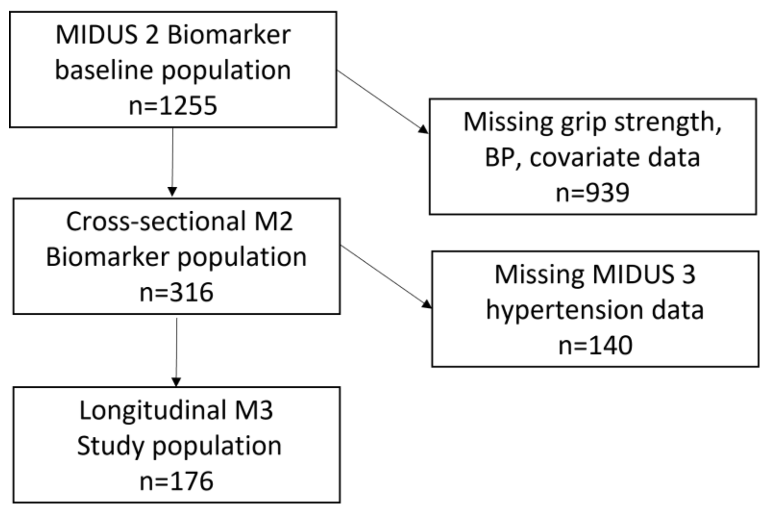
Ten years after baseline interviews, MIDUS conducted its first follow-up MIDUS II (M2) in 2004-2005 which included 4,963 participants from the first cohort. Reasons for attrition included refusal, inability to contact former participants, illness, and death. MIDUS II included an additional subsample of African Americans located in Milwaukee, WI, for a total of 5,555 participants. MIDUS II collected the same information as M1 but also introduced the biomarker, neuroscience, and cognitive projects. The current research used data from the biomarker project, a subsample of 1,255 participants ages 35-86 years old from the M2 data collection. The biomarker study consisted of a series of comprehensive biological assessments, collected in 2004-2009 during an overnight stay at one of the three General Clinical Research Centers across the U.S. Eligibility for the biomarker study required completion of both the M2 phone interview and set of two self-administered questionnaires (SAQ). MIDUS III (M3), the second follow-up wave of the MIDUS study, was collected between 2013 and 2014. Living participants who completed the phone interview for MIDUS II (M2) were eligible for the M3 survey (n=3,294). This study did not require further IRB approval due to the use of a publicly available dataset that excluded any identifiable information.

Study participants

The present research studies consist of a cross-sectional study using M2 biomarker data and a longitudinal study of the M2 biomarker participants who completed the M3 survey. Non-pregnant female participants aged $\geq$ 40 years that identified as Black or White were eligible for the studies. Participants who were missing any data related to the study objectives or had surgery on their hands or wrist due to arthritis or carpal tunnel syndrome were excluded from the study.

Due to the small representation of Black female participants in the MIDUS 2 biomarker cohort, Black female participants were age-matched to White female participants who had complete data. The final sample from the M2 biomarker study included a total of 316 female participants (Figure 3.1, n=158 Black, n=158 White).

Figure 3 Diagram of sample inclusion and exclusion criteria



Abbreviations: M2-MIDUS 2, M3-MIDUS 3

Measures

Handgrip Strength:

Handgrip strength was measured during the M2 biomarker study. MIDUS project staff collected handgrip strength data from participants using a hand dynamometer. Participants were instructed to begin the grip strength test using their right hand and to use a table, arm of chair or knee for elbow support. Handgrip strength was recorded for three trials per hand (six total attempts). The average of the six handgrip measurements was the value used for mean absolute handgrip strength and recorded in kg. Relative grip strength was measured using the equation: absolute grip strength (kg) divided by body mass index (BMI) (kg/m2).

Blood Pressure:

Nurses at the General Clinical Research Center (GCRC) collected blood pressure data using a standard protocol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were assessed in a seated position three times with a maximum of 30 seconds in between each reading. Prior to the first blood pressure measurement, participants rested for 5 minutes. The average of the two most similar SBP and DBP measurements were used for the analysis.

Hypertension Diagnosis Definition:

Self-reported health history was gathered from patients during the M2 biomarker study. For this analysis, a person was coded as having hypertension if they answered “Yes” to the question “Ever had high blood pressure” and answer “Yes” to the follow up question “Physician diagnosed high blood pressure”. Only participants who answered “yes” to the first question answered the follow up question. Self-reported hypertension status was also assessed at M3 using the item “Has a doctor ever told you that you have or had high blood pressure?”.

Anthropometry:

Participants’ height and weight were measured by GCRC clinic staff during the biologic assessment. Body mass index (BMI) was calculated by dividing weight (kg) by height^2 (m^2).

Covariates

Age, education level, health insurance status, and race/ethnicity were included as sociodemographic covariates in this study. Self-reported questionnaires were used to collect lifestyle behavior data including alcohol consumption, smoking status, and current physical activity level. Participants were asked whether they engage in moderate and/or vigorous physical activity for 20 minutes or more at least 3 times/week. Alcohol consumption was evaluated as the average number of alcoholic beverages consumed within the past month. Smoking status was assessed as whether participants currently smoked cigarettes. Number of chronic health conditions present were assessed using the item "Have you ever had any of the following conditions or illnesses diagnosed by a physician". Cardiovascular health conditions (transient ischemic attack (TIA) or stroke, heart disease, circulation problems) were coded into a composite score (none,1, 2, ≥3). Non-cardiovascular health conditions (diabetes, asthma, emphysema/COPD, cancer, cholesterol issues) present were coded into a composite score (none,1, 2, ≥3).

Statistical analyses:

The analysis will be conducted using SAS Version 9.4 (SAS Institute, Cary, North Carolina). Study participant characteristics were summarized using mean and standard error of the mean for continuous variables and frequency and percentages for categorical variables. Differences in these characteristics were calculated using one-way analysis of variance (ANOVA) for continuous variables and chi-squared tests for categorical variables. An unconditional logistic regression will be done to examine the associations between relative grip strength and blood pressure and examine racial/ethnic differences. The analysis controlled for sociodemographic variables, lifestyle behaviors, and number of chronic conditions.

Results

A total of 316 age-matched Black and white women were included at baseline for this study. Demographic characteristics for the total sample are shown in Table 2.1. Overall, the mean age of participants was 54.0 ± 11.2 years at baseline. The mean absolute handgrip strength for the study cohort was 26.4 ± 7.5 kg and the mean relative handgrip strength was 0.88 ± 0.31 kg/BMI. There was not a significant difference in absolute grip strength between groups (p=0.16). When normalizing absolute grip strength with BMI, relative grip strength was lower in Black women than white women (0.80 ± 0.3 and 0.96 ± 0.3 kg/BMI, respectively). Black women had higher BMI, SBP, DBP, non-CV-related conditions. More Black women were current smokers and participated in regular physical activity. Black women had lower relative grip strength and less education and fewer consumed alcohol compared to white women. In the subgroup analyses, both Black and white women participants with hypertension were older, had higher BMI, lower absolute and relative handgrip strength, and had more CVD and non-CVD comorbidities. Black women with hypertension consumed alcohol less than non-hypertensive Black women while this relationship was reversed in white women.

Table 2.1 Descriptive statistics for MIDUS 2 Biomarker baseline sample

	Total Population	Black	White	
n	**316**	**158**	**158**	**p-value**
Age	54.0 ± 11.2	54.7 ± 10.8	56.2 ± 11.6	0.1416
Age Categories				
35-49	110 (33.8%)	60 (38.0%)	50 (31.7%)	0.3908
50-64	138 (43.7%)	68 (43.0%)	70 (44.3%)	
65+	68 (21.5%)	30 (19.0%)	38 (24.0%)	
BMI (kg/m2)	30.4 ± 8.3	34.2 ± 9.0	29.0 ± 6.7	<.0001
Mean Handgrip strength (kg)	26.4 ± 7.5	25.8± 7.6	27.0± 7.3	0.1651
Relative grip strength	0.88 ± 0.31	0.80 ± 0.3	0.96 ± 0.3	<.0001
Blood Pressure (mmHg)				
Mean Systolic Blood Pressure	131.6 ±20.7	135.2 ± 22.4	127.9 ± 18.2	0.0016
Mean Diastolic Blood Pressure	75.6 ±11.7	78.6 ± 12.5	72.7 ± 10.1	<.0001
Education level				
Less than High School	31(9.8%)	27 (17.1%)	4 (2.5%)	<.0001
High School/ GED	81 (25.7%)	42(26.6%)	39 (24.8%)	
Some College	78(24.8%)	43 (27.2%)	35 (22.3%)	
2- year or 4-year college grad	71 (22.5%)	28 (17.7%)	43 (27.4%)	
Some Graduate school or higher	54 (17.1%)	18 (11.4%)	36 (22.9%)	
Smoker				
Yes	53 (16.8%)	37 (23.4%)	16 (10.1%)	0.0024
Hypertension				
Yes	138(44.0%)	88 (56.0%)	50 (31.9%)	<.0001
Alcohol consumption				
Yes	177 (56.0%)	76 (48.1%)	101 (63.9%)	0.0064
Cardiovascular-Related Comorbidities				
0	175 (55.4%)	82 (51.9%)	93 (58.9%)	0.1384
1	100 (31.7%)	51 (32.3%)	49 (31.0%)	
2	33 (10.4%)	18 (11.4%)	15 (9.5%)	
3+	8 (2.5%)	7 (4.4%)	1 (0.6%)	
Non-Cardiovascular-Related Comorbidities				
0	133 (42.1%)	51 (32.3%)	82 (51.9%)	0.002
1	114 (36.1%)	62 (39.2%)	52 (32.9%)	
2	49(15.5%)	31 (19.6%)	18 (11.4%)	
3+	20 (6.3%)	14 (8.9%)	6 (3.8%)	
Regular physical activity				
Yes	92 (29.1%)	67 (42.4%)	25 (15.8%)	<.0001

Table 2.2 Descriptive statistics for MIDUS 3 follow-up

	Total	Black	White	p-value
n	**176**	**69**	**107**	**group differences**
Age	52.2 ± 10.4	49.5 ± 9.3	54.0 ± 10.8	0.005
Age Categories				
35-49	77 (43.8%)	38 (55.1%)	39 (36.5%)	0.03
50-64	80 (45.4%)	27 (39.1%)	53 (49.5%)	
65+	19 (10.8%)	4 (5.8%)	15 (14.0%)	
BMI (kg/m2)	30.0 ± 8.3	33.5 ± 9.5	27.7 ± 5.7	<.0001
Mean Handgrip strength (kg)	27.6 ± 6.8	28.4± 7.4	27.1± 6.4	0.22
Relative grip strength	0.97 ± 0.3	0.90 ± 0.3	1.01 ± 0.3	0.02
Blood Pressure (mmHg)				
Mean Systolic Blood Pressure	125.7 ±18.0	128.2 ± 20.6	124.1 ± 16.0	0.14
Mean Diastolic Blood Pressure	73.1 ±10.7	76.3 ± 11.0	72.7 ± 9.9	0.0014
Education level				
Less than High School	11(6.5%)	8 (11.6%)	3 (2.8%)	0.001
High School/ GED	51 (29.0%)	25 (36.2%)	26 (24.3%)	
Some College	38(21.7 %)	19(27.5%)	19 (17.8%)	
2- year or 4-year college grad	40 (22.7%)	8 (11.6%)	32 (29.9%)	
Some Graduate school or higher	36 (20.5%)	9 (13.0%)	27 (25.2%)	
Smoker				
Yes	28 (15.9%)	18 (26.1%)	10 (9.4%)	0.003
Hypertension				
Yes	44 (25.0%)	25 (36.2%)	19 (17.8%)	0.006
Alcohol consumption				
Yes	113 (64.2%)	41 (59.4%)	72 (67.3%)	0.29
Cardiovascular-Related Comorbidities				
0	122 (69.3%)	45 (65.2%)	77 (72.0%)	0.57
1	44 (25.0%)	19 (27.5%)	25 (23.4%)	
2+	10 (6.0%)	5 (7.3%)	5 (4.7%)	
Non-Cardiovascular-Related Comorbidities				
0	97(55.1%)	32 (46.4%)	65 (60.8%)	0.15
1	62 (35.2%)	30 (43.5%)	32 (29.9%)	
2+	17 (10.0%)	4 (10.1%)	10 (9.3%)	
Regular physical activity				
Yes	43 (24.4%)	28 (40.6%)	15 (14.0%)	<.0001

Table 2.3: Odds Ratio and 95% CI for hypertension and relative grip strength cross-sectional analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.18	0.07	0.45	<0.0001
Model 2	0.28	0.11	0.72	<0.0001
Model 3	0.27	0.10	0.72	0.009

Model 1: Race and age-adjusted, Model 2: age, race, education, and comorbidiy-adjusted,
Model 3: Age, race, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

Table 2.4: Odds Ratio and 95% CI for hypertension and relative grip strength longitudinal analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.54	0.16	1.83	0.32
Model 2	0.55	0.16	1.95	0.36
Model 3	0.46	0.13	1.69	0.24

Model 1: Race and age-adjusted only, Model 2: age, race, education, and comorbidiy-adjusted,
Model 3: Age, race, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

Study participants who did not have a HTN diagnosis at baseline were included in the longitudinal analysis, which was a total of 176 women (69 Black women, 107 white women). The descriptive characteristics of longitudinal study-eligible participants are shown in Table 2.2. Forty-four women were diagnosed with hypertension by the M3 follow up. Black women in this cohort were younger, lower relative handgrip strength, had higher BMIs and DBP, more were current smokers, and higher participation in regular physical activity. More Black women were diagnosed with hypertension by M3 compared to white women (p=0.006).

A cross-sectional logistic regression was performed to analyze the effects of sociodemographic and health variables on the relationship between hypertension diagnosis and relative grip strength found a significant inverse relationship (Table 2.3, p=0.009). After controlling for covariates, individuals with higher grip strength were at a lower risk of being diagnosed with hypertension (OR=0.27. 95% CI, 0.10, 0.72). Black women in this cohort had more than 2 times higher odds of being diagnosed with hypertension compared to white women, after controlling for sociodemographic and health covariates

(OR=2.1, 95% CI, 1.18-3.93). Smoking status, alcohol consumption, education, and exercise were not associated with a hypertension diagnosis. An increased number of CVD-related and non-CVD-related conditions were associated with a higher risk of HTN diagnosis.

Table 2.5: Odds Ratio and 95% CI for hypertension and absolute grip strength cross-sectional analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.96	0.92	0.99	0.03
Model 2	0.97	0.94	1.01	0.12
Model 3	0.97	0.93	1.01	0.11

Model 1: race, BMI,age-adjusted, Model 2: age, race, BMI,education, and comorbidiy-adjusted,
Model 3: Age, race, BMI, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

Table 2.6: Odds Ratio and 95% CI for hypertension and absolute grip strength longitudinal analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	1.00	0.95	1.05	0.97
Model 2	1.00	0.95	1.06	0.89
Model 3	1	0.93	1.06	0.96

Model 1: race, BMI,age-adjusted, Model 2: age, race, BMI,education, and comorbidiy-adjusted,
Model 3: Age, race, BMI, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

When analyzing absolute handgrip strength and controlling for BMI, age and race, we found a negative relationship between absolute grip strength and hypertension (OR=0.96, 95% CI, 0.92, 0.99, p=0.03) (Table 5). After controlling for the other variables in Model 2 and 3 the relationship was no longer significant (p=0.12). For the longitudinal analysis, neither relative grip strength nor absolute grip strength at baseline predicted future hypertension diagnosis at M3 (Table 4 and Table 6).

Discussion:

The present study primarily examined the associations between relative handgrip strength and hypertension risk using data from MIDUS 2 Biomarker Project and MIDUS 3. We analyzed the association between relative handgrip strength and hypertension risk at baseline and at follow up with individuals without physician-diagnosed hypertension at baseline. This study demonstrated that lower relative handgrip strength was significantly associated with higher hypertension risk at baseline (M2B4) but did not predict hypertension risk at follow up among middle-aged and older Black and white women. The cross-sectional relationship between relative handgrip strength and hypertension risk was independent of age, race, education level, smoking behavior, alcohol consumption, and number of existing non-CVD-related and non-CVD related medical conditions. The cross-sectional analysis did not find a difference in this relationship between Black and white women. When comparing relative grip strength to absolute grip strength, we found that relative handgrip strength was a better indicator of hypertension risk than absolute grip strength.

The association between grip strength, blood pressure, and hypertension risk has been previously studied in several age groups of women. The results of these studies have been controversial, with most studies reporting inverse associations between handgrip strength and hypertension risk and/or blood pressure (Gubelmann et al., 2017; Kim et al., 2021; Lawman et al., 2015; Sayer et al., 2007; Sola-Rodríguez et al., 2021) while others either revealed no relationship (Hao et al., 2020) or a positive relationship between grip strength and hypertension risk and/or BP (Demmer et al., 2016; Ji et al., 2018; Mallah et al., 2019). The results of the cross-sectional study were in line with the findings of aim 1, which used a general sample of Black women 20 years and older. In a study of elderly community-dwelling people, it was found that increasing quartile of relative handgrip strength adjusted by body weight was associated with lower risk of cardiometabolic disorders, including hypertension in women (Kawamoto et al., 2016) . A large cross-sectional observational study of adults within the Chinese Han population found that diastolic was positively associated with absolute grip strength in women, but not systolic blood pressure (Mallah et al., 2019). The findings our cross-sectional study align with other studies in older adults, although this study is the first study to specifically analyze this relationship in middle-aged and older Black women.

Many studies in the literature on handgrip strength and have been cross-sectional design, which limits the ability to determine whether there is a causal relationship between grip strength and hypertension risk. In the current study, we did not find a longitudinal association between either absolute or relative handgrip strength in both Black and white women. A study by Hao et al. (2020) demonstrated that low relative handgrip strength predicted increased hypertension risk in males, but there was no relationship found in females. The findings of the Hao et al. study are similar to our results, where we observed no association between baseline relative grip strength and hypertension in both Black and white women. In contrast, A study by Laddu et al. (2022) found that grip strength was positively associated with both SBP and DBP in post-menopausal women. Another recent study reported that an increase in 5kg of grip strength was associated a reduction in overall cardiovascular disease risk and CVD-related conditions including heart attack and stroke in men and women (López-Bueno et al., 2022). The differences in study design used by studies to quantify handgrip strength (absolute vs relative, continuous variable vs categorical variable) may explain the conflicting study results among the longitudinal studies. The variation found in both cross-sectional and longitudinal grip strength studies makes it difficult to compare the findings and make a generalization of the relationship between handgrip strength and hypertension risk. Additional research is needed to fully determine the association between handgrip strength and hypertension risk in middle-aged and older adults.

The importance of considering body size when evaluating the relationship between grip strength and risk of hypertension other CVD-related conditions is an open question (Fowles et al., 2014; Lawman et al., 2015). It is especially important to consider the influence of body size on handgrip strength and health outcomes in Black women. Black women have the highest rates of obesity in the US, with approximately 55% of Black women fitting the clinical characteristics of obesity (Agyemang & Powell-Wiley, 2013; NCHS, 2019). Based on many of the studies in the literature, controlling for body size measures may describe the interactions between handgrip strength and poor health outcomes more accurately. A cross-sectional study reported that muscle strength was positively associated with BMI in older men and women (Keevil et al., 2015). On the other hand, another study reported an inverse relationship between grip strength and BMI. Although BMI is commonly used in clinical care and in research to assess health, current BMI categories may be discriminatory of women from different ethnic backgrounds who have varying body compositions (Stanford et al., 2019). Utilizing other body size measures, such as lean muscle mass or central adiposity in the future may provide better insight on the relationship between adiposity and negative health outcomes especially during the aging process (Hiol et al., 2021). Overall, results of the current study suggest that relative grip strength was a better indicator for evaluating hypertension risk in both Black and white women compared to absolute grip strength. After controlling for the sociodemographic and health covariates, we did not find a cross-sectional association between absolute grip strength and hypertension risk. The mechanism responsible for the link between increased hypertension risk and lower relative grip strength is currently unknown. Additional research is needed to understand the predictive value of relative grip strength in identifying potential future risk of developing hypertension.

Racial differences in muscular strength have been explored in the literature, with conflicting results. A study of disabled women ≥65 years reported that Black women had higher muscle strength and hip flexion strength than white women, possibly due to differences in muscle mass (Rantanen et al., 1998).. Another study found a similar relationship among African American and white women (Thorpe et al., 2016). Trudelle-Jackson et al. (2011) conducted a cross-sectional study to investigate the racial differences in several muscle strength measures such as handgrip strength and lower extremity strength between African American and white women 20-83 years old and found that while unadjusted handgrip strength was higher in African American women however, when handgrip strength was adjusted by body weight, white women had higher body weight-adjusted grip strength (Trudelle-Jackson et al., 2011). In our study, we found a similar relationship with older age-matched Black and white women. The differences in study designs across the various studies highlighted makes it harder to determine the actual relationship between handgrip strength and hypertension risk. Despite the conflicting findings in the literature, most of the literature supports that grip strength is a potentially beneficial tool to identify individuals at risk for hypertension and CVD risk.

A strength of the current study is the use of a prospective cohort of older Black and white women. This is important because older women, especially Black women are the most susceptible negative CVD outcomes in this demographic. There were also some limitations to this study design. First, although the MIDUS study is a nationally representative cohort of middle-aged and older adults, the representation of Black women in the study was small, which may limit the ability to truly compare the relationship to white women. Secondly, body mass index may not be the best measure to adjust for grip strength especially in a cohort of older women. Future longitudinal studies with larger cohorts of Black women may provide additional information on the predictive value of relative handgrip strength in Black women. In conclusion, the findings of this study suggest that higher relative grip strength was associated with lower odds of a hypertension diagnosis at baseline for US Black and white middle-aged and older women.

References

Agyemang, P., & Powell-Wiley, T. M. (2013). Obesity and Black Women: Special Considerations Related to Genesis and Therapeutic Approaches. *Curr Cardiovasc Risk Rep*, *7*(5), 378-386. https://doi.org/10.1007/s12170-013-0328-7

Ahmad, A., & Oparil, S. (2017). Hypertension in Women: Recent Advances and Lingering Questions. *Hypertension*, *70*(1), 19-26. https://doi.org/10.1161/HYPERTENSIONAHA.117.08317

Ahn, K. H., Lee, Y., Sohn, T. Y., Kim, D. Y., Ryu, M., Gym, H., & Lee, S. (2020). Association between Relative Handgrip Strength and Osteoporosis in Older Women: The Korea National Health and Nutrition Examination Survey 2014-2018. *Ann Geriatr Med Res*, *24*(4), 243-251. https://doi.org/10.4235/agmr.20.0076

Appel, L. J. (2003). Lifestyle modification as a means to prevent and treat high blood pressure. *J Am Soc Nephrol*, *14*(7 Suppl 2), S99-s102. https://doi.org/10.1097/01.asn.0000070141.69483.5a

Beyer, S. E., Sanghvi, M. M., Aung, N., Hosking, A., Cooper, J. A., Paiva, J. M., Lee, A. M., Fung, K., Lukaschuk, E., Carapella, V., Mittleman, M. A., Brage, S., Piechnik, S. K., Neubauer, S., & Petersen, S. E. (2018). Prospective association between handgrip strength and cardiac structure and function in UK adults. *PLoS One*, *13*(3), e0193124. https://doi.org/10.1371/journal.pone.0193124

Brooks, J. M., Titus, A. J., Bruce, M. L., Orzechowski, N. M., Mackenzie, T. A., Bartels, S. J., & Batsis, J. A. (2018). Depression and Handgrip Strength Among U.S. Adults Aged 60 Years and Older from NHANES 2011-2014. *The journal of nutrition, health & aging*, *22*(8), 938-943. https://doi.org/10.1007/s12603-018-1041-5

Chen, L., Simonsen, N., & Liu, L. (2015). Racial Differences of Pediatric Hypertension in Relation to Birth Weight and Body Size in the United States. *PLoS One*, *10*(7), e0132606. https://doi.org/10.1371/journal.pone.0132606

Chong, H., Choi, Y. E., Kong, J. Y., Park, J. H., Yoo, H. J., Byeon, J. H., Lee, H. J., & Lee, S. H. (2020). Association of Hand Grip Strength and Cardiometabolic Markers in Korean Adult Population: The Korea National Health and Nutrition Examination Survey 2015-2016. *Korean J Fam Med*, *41*(5), 291-298. https://doi.org/10.4082/kjfm.18.0129

Demmer, D. L., Beilin, L. J., Hands, B., Burrows, S., Cox, K. L., Straker, L. M., & Mori, T. A. (2016). Effects of muscle strength and endurance on blood pressure and related cardiometabolic risk factors from childhood to adolescence. *Journal of hypertension*, *34*(12), 2365-2375. https://doi.org/10.1097/hjh.0000000000001116

Feng, Q., Jiang, C., Wang, M., Cai, R., Wang, H., Wu, D., Wang, F., Lin, L., & Nassis, G. P. (2021). Association between relative handgrip strength and hypertension in Chinese adults: An analysis of four successive national surveys with 712,442 individuals (2000-2014). *PLoS One*, *16*(10), e0258763. https://doi.org/10.1371/journal.pone.0258763

Fongwa, M. N., Evangelista, Lorraines S., Hays, Ron D., Martins, David S. , Elashoff, David, Cowan, Marie J. , Morisky, Donald E. . (2008). Adherence treatment factors in hypertensive African American women. *Vascular Healht and Risk Management*, *4*(1), 157-166.

Fowles, J., Roy, J., Clarke, J., & Dogra, S. (2014). Are the fittest Canadian adults the healthiest? *Health Rep*, *25*(5), 13-18. https://www.ncbi.nlm.nih.gov/pubmed/24850392

Gao, Y., Huang, H., Ni, C., Feng, Y., Yu, J., Huang, Y., Luo, L., Jiang, Y., & Wang, A. (2022). Comparison of Five Expressions of Handgrip Strength for Predicting Cardiovascular Disease Risk Factors in Chinese Middle-Aged Community Residents. *Front Public Health*, *10*, 903036. https://doi.org/10.3389/fpubh.2022.903036

Gillum, R. F. (1996). Epidemiology of hypertension in African American women. *American Heart Journal*, *131*(2), 385-395. https://doi.org/https://doi.org/10.1016/S0002-8703(96)90371-3

Gubelmann, C., Vollenweider, P., & Marques-Vidal, P. (2017). Association of grip strength with cardiovascular risk markers. *Eur J Prev Cardiol*, *24*(5), 514-521. https://doi.org/10.1177/2047487316680695

Hage, F. G., Mansur, S. J., Xing, D., & Oparil, S. (2013). Hypertension in women. *Kidney Int Suppl (2011)*, *3*(4), 352-356. https://doi.org/10.1038/kisup.2013.76

Hao, G., Chen, H., Ying, Y., Wu, M., Yang, G., & Jing, C. (2020). The Relative Handgrip Strength and Risk of Cardiometabolic Disorders: A Prospective Study. *Frontiers in physiology*, *11*, 719. Retrieved 2020, from http://europepmc.org/abstract/MED/32714207

Hicks, L. S., Shaykevich, S., Bates, D. W., & Ayanian, J. Z. (2005). Determinants of racial/ethnic differences in blood pressure management among hypertensive patients. *BMC Cardiovasc Disord*, *5*(1), 16. https://doi.org/10.1186/1471-2261-5-16

Hiol, A. N., von Hurst, P. R., Conlon, C. A., Mugridge, O., & Beck, K. L. (2021). Body composition associations with muscle strength in older adults living in Auckland, New Zealand. *PLoS One*, *16*(5), e0250439. https://doi.org/10.1371/journal.pone.0250439

Ji, C., Zheng, L., Zhang, R., Wu, Q., & Zhao, Y. (2018). Handgrip strength is positively related to blood pressure and hypertension risk: results from the National Health and nutrition examination survey. *Lipids in health and disease*, *17*(1), 86-86. https://doi.org/10.1186/s12944-018-0734-4

Ji, H., Kim, A., Ebinger, J. E., Niiranen, T. J., Claggett, B. L., Bairey Merz, C. N., & Cheng, S. (2020). Sex Differences in Blood Pressure Trajectories Over the Life Course. *JAMA Cardiol*. https://doi.org/10.1001/jamacardio.2019.5306

Karvonen-Gutierrez, C. A., Peng, Q., Peterson, M., Duchowny, K., Nan, B., & Harlow, S. (2018). Low grip strength predicts incident diabetes among mid-life women: the Michigan Study of Women's Health Across the Nation. *Age Ageing*, *47*(5), 685-691. https://doi.org/10.1093/ageing/afy067

Kawamoto, R., Ninomiya, D., Kasai, Y., Kusunoki, T., Ohtsuka, N., Kumagi, T., & Abe, M. (2016). Handgrip strength is associated with metabolic syndrome among middle-aged and elderly community-dwelling persons. *Clin Exp Hypertens*, *38*(2), 245-251. https://doi.org/10.3109/10641963.2015.1081232

Keevil, V. L., Luben, R., Dalzell, N., Hayat, S., Sayer, A. A., Wareham, N. J., & Khaw, K. T. (2015). Cross-sectional associations between different measures of obesity and muscle strength in men and women in a British cohort study. *J Nutr Health Aging*, *19*(1), 3-11. https://doi.org/10.1007/s12603-014-0492-6

Kim, J. Y., Park, H. Y., Kim, J., & Lim, K. (2021). Body mass index and relative handgrip strength are associated with the prevalence of hypertension in Korean elderly: Korean national fitness assessment in 2019. *Phys Act Nutr*, *25*(2), 26-32. https://doi.org/10.20463/pan.2021.0012

Lackland, D. T. (2014). Racial differences in hypertension: implications for high blood pressure management. *Am J Med Sci*, *348*(2), 135-138. https://doi.org/10.1097/MAJ.0000000000000308

Lawman, H. G. P., Troiano, R. P. P., Perna, F. M. P., Wang, C.-Y. P., Fryar, C. D. M., & Ogden, C. L. P. (2015). Associations of Relative Handgrip Strength and Cardiovascular Disease Biomarkers in U.S. Adults, 2011–2012. *American journal of preventive medicine*, *50*(6), 677-683. https://doi.org/10.1016/j.amepre.2015.10.022

Mainous, A. G., 3rd, Tanner, R. J., Anton, S. D., & Jo, A. (2015). Grip Strength as a Marker of Hypertension and Diabetes in Healthy Weight Adults. *Am J Prev Med*, *49*(6), 850-858. https://doi.org/10.1016/j.amepre.2015.05.025

Mallah, M. A., Liu, M., Liu, Y., Xu, H.-F., Wu, X.-J., Chen, X.-T., Wang, H., Liu, C.-L., Tian, Y.-R., Li, M.-X., Li, Q., Fu, J., & Shen, C. (2019). Association of handgrip strength with the prevalence of hypertension in a Chinese Han population. *Chronic Diseases and Translational Medicine*, *5*(2), 113-121. https://doi.org/https://doi.org/10.1016/j.cdtm.2019.05.004

McGrath, R. P., Kraemer, W. J., Snih, S. A., & Peterson, M. D. (2018). Handgrip Strength and Health in Aging Adults. *Sports medicine (Auckland, N.Z.)*, *48*(9), 1993-2000. https://doi.org/10.1007/s40279-018-0952-y

Midlife in the United States: A National Longitudinal Study of Health & Well-Being (2022). University of Wisconsin-Madison, Institute of Aging Retrieved 10/26/21 from https://www.midus.wisc.edu/

Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., Das, S. R., de Ferranti, S., Després, J. P., Fullerton, H. J., Howard, V. J., Huffman, M. D., Isasi, C. R., Jiménez, M. C., Judd, S. E., Kissela, B. M., Lichtman, J. H., Lisabeth, L. D., Liu, S., . . . Turner, M. B. (2016). Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation*, *133*(4), e38-360. https://doi.org/10.1161/cir.0000000000000350

Muntner, P., Abdalla, M., Correa, A., Griswold, M., Hall, J. E., Jones, D. W., Mensah, G. A., Sims, M., Shimbo, D., Spruill, T. M., Tucker, K. L., & Appel, L. J. (2017). Hypertension in Blacks: Unanswered Questions and Future Directions for the JHS (Jackson Heart Study). *Hypertension*, *69*(5), 761-769. https://doi.org/10.1161/HYPERTENSIONAHA.117.09061

Peterson, M. D., Zhang, P., Choksi, P., Markides, K. S., & Al Snih, S. (2016). Muscle Weakness Thresholds for Prediction of Diabetes in Adults. *Sports Med*, *46*(5), 619-628. https://doi.org/10.1007/s40279-015-0463-z

Prasitsiriphon, O., & Pothisiri, W. (2018). Associations of Grip Strength and Change in Grip Strength With All-Cause and Cardiovascular Mortality in a European Older Population. *Clinical Medicine Insights. Cardiology*, *12*, 1179546818771894. Retrieved 2018, from http://europepmc.org/abstract/MED/29881318

Rantanen, T., Guralnik, J. M., Leveille, S., Izmirlian, G., Hirsch, R., Simonsick, E., Ling, S., & Fried, L. P. (1998). Racial differences in muscle strength in disabled older women. *J Gerontol A Biol Sci Med Sci*, *53*(5), B355-361. https://doi.org/10.1093/gerona/53a.5.b355

Sayer, A. A., Syddall, H. E., Dennison, E. M., Martin, H. J., Phillips, D. I. W., Cooper, C., Byrne, C. D., & Hertfordshire, C. (2007). Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. *QJM : monthly journal of the Association of Physicians*, *100*(11), 707-713. https://doi.org/10.1093/qjmed/hcm095

Sola-Rodríguez, S., Vargas-Hitos, J. A., Gavilán-Carrera, B., Rosales-Castillo, A., Sabio, J. M., Hernández-Martínez, A., Martínez-Rosales, E., Ortego-Centeno, N., & Soriano-Maldonado, A. (2021). Relative Handgrip Strength as Marker of Cardiometabolic Risk in Women with Systemic Lupus Erythematosus. *Int J Environ Res Public Health*, *18*(9). https://doi.org/10.3390/ijerph18094630

Sousa-Santos, A. R., & Amaral, T. F. (2017). Differences in handgrip strength protocols to identify sarcopenia and frailty - a systematic review. *BMC geriatrics*, *17*(1), 238. https://doi.org/10.1186/s12877-017-0625-y

Souza Saraiva, W., Prestes, J., Schwerz Funghetto, S., Navalta, J. W., Tibana, R. A., & da Cunha Nascimento, D. (2019). Relation Between Relative Handgrip Strength, Chronological Age and Physiological Age with Lower Functional Capacity in Older Women. *Open Access J Sports Med*, *10*, 185-190. https://doi.org/10.2147/oajsm.S227720

Stanford, F. C., Lee, M., & Hur, C. (2019). Race, Ethnicity, Sex, and Obesity: Is It Time to Personalize the Scale? *Mayo Clin Proc*, *94*(2), 362-363. https://doi.org/10.1016/j.mayocp.2018.10.014

Taekema, D. G., Maier, A. B., Westendorp, R. G., & de Craen, A. J. (2011). Higher blood pressure is associated with higher handgrip strength in the oldest old. *Am J Hypertens*, *24*(1), 83-89. https://doi.org/10.1038/ajh.2010.185

Taylor, H. A., Jr., Wilson, J. G., Jones, D. W., Sarpong, D. F., Srinivasan, A., Garrison, R. J., Nelson, C., & Wyatt, S. B. (2005). Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis*, *15*(4 Suppl 6), S6-4-17.

Thomas, S. J., Booth, J. N., 3rd, Dai, C., Li, X., Allen, N., Calhoun, D., Carson, A. P., Gidding, S., Lewis, C. E., Shikany, J. M., Shimbo, D., Sidney, S., & Muntner, P. (2018). Cumulative Incidence of Hypertension by 55 Years of Age in Blacks and Whites: The CARDIA Study. *J Am Heart Assoc*, *7*(14). https://doi.org/10.1161/JAHA.117.007988

Thorpe, R. J., Simonsick, E., Zonderman, A., & Evans, M. K. (2016). Association between Race, Household Income and Grip Strength in Middle- and Older-Aged Adults. *Ethn Dis*, *26*(4), 493-500. https://doi.org/10.18865/ed.26.4.493

Trudelle-Jackson, E., Ferro, E., & Morrow, J. R., Jr. (2011). Clinical Implications for Muscle Strength Differences in Women of Different Age and Racial Groups: The WIN Study. *J Womens Health Phys Therap*, *35*(1), 11-18. https://doi.org/10.1097/JWH.0b013e318212570c

Wenger, N. K. (2020). Adverse Cardiovascular Outcomes for Women-Biology, Bias, or Both? [Editorial Material]. *Jama Cardiology*, *5*(3), 253-254. https://doi.org/10.1001/jamacardio.2019.5576

Wenger, N. K., Arnold, A., Bairey Merz, C. N., Cooper-DeHoff, R. M., Ferdinand, K. C., Fleg, J. L., Gulati, M., Isiadinso, I., Itchhaporia, D., Light-McGroary, K., Lindley, K. J., Mieres, J. H., Rosser, M. L., Saade, G. R., Walsh, M. N., & Pepine, C. J. (2018). Hypertension Across a Woman's Life Cycle. *J Am Coll Cardiol*, *71*(16), 1797-1813. https://doi.org/10.1016/j.jacc.2018.02.033

Wu, H., Liu, M., Chi, V. T. Q., Wang, J., Zhang, Q., Liu, L., Meng, G., Yao, Z., Bao, X., Gu, Y., Zhang, S., Sun, S., Zhou, M., Jia, Q., Song, K., Huang, J., Huo, J., Zhang, B., Ding, G., & Niu, K. (2019). Handgrip strength is inversely associated with metabolic syndrome and its separate components in middle aged and older adults: a large-scale population-based study. *Metabolism*, *93*, 61-67. https://doi.org/10.1016/j.metabol.2019.01.011

Yi, D. W., Khang, A. R., Lee, H. W., Son, S. M., & Kang, Y. H. (2018). Relative handgrip strength as a marker of metabolic syndrome: the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014-2015). *Diabetes Metab Syndr Obes*, *11*, 227-240. https://doi.org/10.2147/dmso.S166875

Zhang, X., Huang, L., Peng, X., Xie, Y., Bao, X., Huang, J., & Wang, P. (2020). Association of handgrip strength with hypertension among middle-aged and elderly people in Southern China: A cross-sectional study. *Clin Exp Hypertens*, *42*(2), 190-196. https://doi.org/10.1080/10641963.2019.1601206

Article 3: Longitudinal association of relative handgrip strength and hypertension in Black South African women: Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa 2015-2019

Introduction

Hypertension, a major modifiable risk factor for cardiovascular disease (CVD) and renal diseases, impacts over 1 billion people globally and is responsible for 8.5 million deaths worldwide (NCD Risk Factor Collaboration, 2021). Nearly 80% of the hypertension-related mortality occurs in low- and middle-income countries (LMICs), therefore making hypertension a crucial health problem in these countries. Improvements in public health practices, antibiotic use, and vaccination development following World War II assisted the shift from communicable to non-communicable conditions decades ago in high-income countries (Boutayeb, 2006). Only recently, LMICs are facing a demographic and epidemiological transition from communicable to non-communicable diseases (Bawah et al., 2016). Medical advancement and increased accessibility of medications to treat communicable conditions such as HIV/AIDS and tuberculosis, have contributed to the overall increase in life expectancy and therefore a rapidly growing aging population in LMICs (Gaziano et al., 2017) . This has led to the rise in NCDs in LMICs while they continue to be burdened by communicable diseases like HIV (Houle et al., 2022). This global expansion of middle-aged and older adults combined with the challenge of managing both communicable and NCDs on already compromised health systems will further exacerbate NCDs such as hypertension in LMICs (Maimela et al., 2016).

Sub-Saharan Africa (SSA) has experienced the greatest increase in hypertension prevalence compared to other regions of the world (Bosu et al., 2017). Changes to lifestyle and income attributed to recent development, alterations in diet and health behaviors, and urbanization in SSA has led to the increase in hypertension prevalence and CVD burden (Alberts et al., 2005; Kaze et al., 2017). Hypertension epidemiology in many SSA is characterized by low awareness of hypertension status and hypertension risk factors, low detection and suboptimal control, earlier onset of hypertension-related complications, and higher prevalence of target organ damage (Bosu et al., 2017). These conditions will only exacerbate the ongoing health and economic burden of hypertension in this region (Gnugesser et al., 2022). South Africa is an upper middle-income country in SSA with an overall hypertension prevalence of more than 40% (Kandala et al., 2021). Approximately 53 percent of adults aged 40 and over have hypertension in South Africa (Kohli-Lynch et al., 2022). In a population-based cross-sectional study of six rural and urban sites in SSA, prevalence of HTN varied across the 6 sites with the South African sites reporting the highest prevalence in both men and women (Gómez-Olivé et al., 2017). Urban centers and rural areas in alike are experiencing the impact of hypertension in South Africa. Gomez-Olive et al. did not find an urban-rural difference in hypertension prevalence for women in the Agincourt, Soweto, and Dikgale regions of South Africa (Gómez-Olivé et al., 2017). Unlike the extensive research available on trends, sex differences, and prevalence of hypertension for U.S. born Black women, there is limited research available for Black South African women (Sliwa et al., 2014). Many women in South Africa are dealing with the consequences of hypertension. As Black South African women are living longer lives, there is a greater importance for implementing affordable and effective hypertension prevention and management strategies to prevent serious cardiovascular diseases and premature death.

Handgrip strength (HGS) is a simple, inexpensive and practical tool for measuring muscle strength and has been considered as a predictor of general health. Handgrip strength is influenced by several factors including age, sex, body mass, nutritional status, and physical activity level (Koopman et al., 2014). Previous studies have found that HGS is associated with both healthy aging and chronic health conditions in middle aged and older adults. In women, lower muscular strength has been associated with increased risk for fragility, osteoporosis, diabetes, lower quality of life, metabolic syndrome, hypertension, and all-cause and CVD mortality (Ahn et al., 2020; Karvonen-Gutierrez et al., 2018; Mainous et al., 2015; Souza Saraiva et al., 2019; Zhang et al., 2020). Most studies that have analyzed the relationship between grip strength and health indicators have primarily included cohorts from the western and Asian countries with limited data representing these relationships in Black women across the diaspora (Koopman et al., 2014). Therefore, it is not well understood whether handgrip strength is associated with hypertension risk among Black South African women.

HGS adjusted for body mass index (BMI) (absolute grip strength/BMI) has been recommended to account for the covariance between body mass and muscular strength (Fowles et al., 2014; Lawman et al., 2015). Shozi et al. (2021) reported that absolute grip strength was positively related to BMI in a population located in the Northwest province, South Africa. Several studies have noted that relative grip strength had a stronger association to CVD risk factors compared to absolute grip strength (Lawman et al., 2015; Lee et al., 2016). A study of middle-aged and older U.S. and Chinese adults reported that for every 0.05 decrease in the normalized grip strength (defined as grip strength divided by body mass), the odds of developing hypertension in the US and China was 1.19 and 1.10, respectively (Peterson et al., 2017). Accounting for the influence of BMI on handgrip strength may be of particular importance when analyzing this relationship for women, who have a higher proportion of individuals that are overweight or obese compared to men (Manafe et al., 2022). Obesity studies in Black women in both the U.S. and South Africa have found that Black women are in higher BMI categories compared women of other racial/ethnic categories.

This study aimed to investigate the association of handgrip strength and hypertension in a population of Black South African women aged 40 year and older. Additionally, we assessed whether there was a longitudinal relationship between baseline handgrip strength at wave 1 and future hypertension diagnosis at wave 2. The previous study discussed in article 2 found an inverse relationship between relative handgrip strength and hypertension risk in middle-aged and older US Black women but found no relationship for relative handgrip strength or absolute handgrip strength during the follow up. A limitation of the previous study was the small sample size, which may have impacted the strength of the longitudinal relationship. Considering the previous findings, in this study we hypothesized that there would find similar cross-sectional associations between relative grip strength and hypertension risk in the cohort of middle-aged and older Black South African women. We also hypothesized that high relative handgrip strength would be associated with lower hypertension risk at follow up. Furthermore, selected a cohort of middle-aged and older Black South African women for this study to explore whether the cultural and societal differences exhibited between the US and South Africa influenced the relationship between grip strength and hypertension in Black women. Understanding the relationship between hypertension risk and relative grip strength in Black South African women and the factors that influence this relationship could help create better community-based early hypertension detection interventions to ultimately decrease the global burden of hypertension and CVD among Black women worldwide.

Method

Survey description

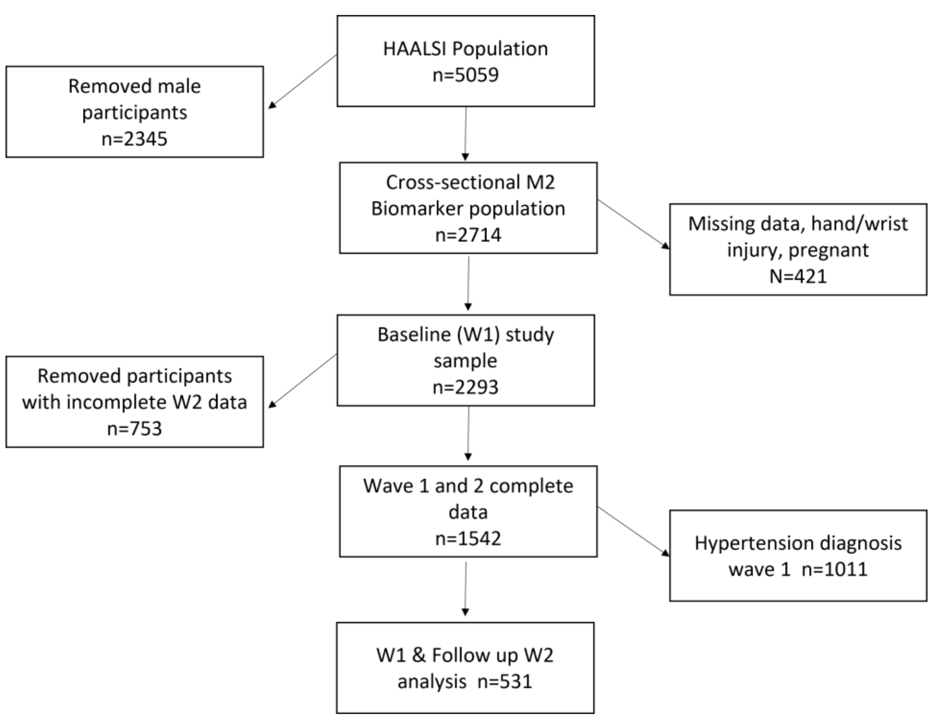
Longitudinal data from the Health and Ageing in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI) was used for this study. Detailed information regarding the HAALSI study design has been described elsewhere (Gómez-Olivé et al., 2018). In summary, the HAALSI cohort comprises a random sample of adults ≥40 years residing within the Agincourt Health and Socio-demographic Surveillance System (HDSS), a rural site in the Mpumalanga province in northeast South Africa. The area had a population of approximately 116,000 people living in 21,000 households across 31 villages covering 450 km^2. A total of 6,281 men and women were selected for the baseline main household survey with a response rate of 85.9% after excluding sampled individuals who had either died, were unable to participate, refused, were not found, or permanently migrated outside the study site area.

Baseline data collection occurred between November 2014 and November 2015 and included a total of 5059 people (n=2345 men and 2714 women). Survey data was collected electronically using Computer Assisted Personal Interviews (CAPI) during home visits by trained fieldworkers along with laboratory data including blood samples for HIV status and selected biomarkers. The second wave data collection began in 2018. Data collected included self-reported demographic, social and behavioral conditions, health and economic information as well as healthcare service utilization for diabetes, HIV and hypertension. Study materials were provided in the local language, Xitsonga, with instruments translated from English and back translated to ensure reliability. Participants could provide written informed consent in Xitsonga or English. If participants were unable to read, they were provided a witness and confirmed inform consent using an inked fingerprint. Approval for the study was provided by the University of Witwatersrad Human Research Ethics Committee, the Harvard T.H. Chan School of Public Health Institutional Research Ethics Board, and the Mpumalanga Provincial Research and Ethics Committee.

Study Population

Out of the 5089 enrolled participants, individuals who self-identified as female (n=2714) were eligible for this study. The inclusion criteria for the study were non-pregnant participants, aged 40 years and older, participated in a physical exam and who were physically able to perform a grip strength test without extreme discomfort (Table 1). Four-hundred and twenty-one participants were excluded from the baseline analysis due several factors: pregnant (n=8), missing data on grip strength, anthropometry measures or demographics (n=297), or had hand and/or wrist surgery in the past 3 months (n=116). Figure 1 provides additional details on sample inclusion. The cross-sectional analysis included a total of 2293 participants with complete data. For the longitudinal analysis, 1011 participants were excluded due to incomplete wave 2 (W2) data. In total, 531 female participants had complete W1 and W2 data.

Figure 4. Diagram of inclusion and exclusion criteria for cross-sectional and longitudinal study.



Measures

Handgrip Strength:

The predictor of interest for this study was handgrip strength. Staff collected handgrip strength data from participants using Smedley Digital Hand Dynamometer (Model 12–0286, Fabrication Enterprises, Washington, DC, United States). Participants were given the handgrip strength test in a seated position with the elbow at a 90-degree angle. The handgrip strength test was repeated twice for each hand. The average of the four handgrip measurements (two for each hand) was the value used for mean absolute handgrip strength and reported in kg. Handgrip strength measurements above 75 kg were determined out-of-range and were set to missing. Relative grip strength was calculated by the equation: absolute grip strength (kg) divided by body mass index (BMI) (kg/m2). Respondents who had surgery on their arm, hand or wrist in the previous 3 months or had experienced pain or arthritis in either hand or wrist were excluded from the sample. Handgrip strength measurements were collected at both wave 1 and wave 2.

Blood Pressure measurement:

Three blood pressure measurements were taken for systolic and diastolic blood pressure with 2 min between each measurement using the Omron M6W automated cuff (Omron, Kyoto, Japan) following a 5-min rest period. The average of the second and third blood pressure measurements were used to define systolic blood pressure (SBP) and diastolic blood pressure (DBP). Participants who had blood pressures within the hypertensive crisis range (>180 mmHg systolic blood pressure (SBP) and/or >120 mmHg diastolic blood pressure (DBP) were categorized as having extremely high blood pressures (HBP).

Hypertension diagnosis:

The outcome variable of interest for this study is hypertension diagnosis. Hypertension was defined at W1 as a participant answering “Yes” to the question “Have you ever been told by a doctor, nurse, or other healthcare worker that you have high blood pressure or hypertension” or answer “Yes” to “Are you currently on treatment for high blood pressure prescribed by a doctor, nurse, or other healthcare worker?”. At wave 2, a participant was described as having hypertension if they answered “Yes” to the question "Have you ever been told by a doctor, nurse, or other healthcare worker that you have high blood pressure or hypertension?" or answer "Yes" to the question "Are you currently on treatment for high blood pressure prescribed by a doctor, nurse, or other healthcare worker?".

Covariates

Confounding variables known to be associated with hypertension and/or cardiovascular disease were included as covariates in analyses. Covariates include age, level of education completed, smoking status, physical activity level, health insurance status and number of chronic diseases score.

Sociodemographic and Health Behavior covariates:

Age was reported as a continuous variable. Education level of completion was grouped into four categories: no formal education, some primary education (1-7 years), some secondary education (8-11 years), and completed secondary education or more (12+ years). Marital status was categorized into 4 groups: never married, separated/divorced, widowed and currently married. Smoking status was assessed by self-reported response to whether the participant is a user of smoke or smokeless tobacco. Alcohol consumption was evaluated as a dichotomous variable and defined as whether a participant consumed alcohol in the last 30 days (yes/no). The International Physical Activity Questionnaire (IPAQ) was administered to participants to collect data on physical activity level. Physical activity was assessed by whether participant engaged in moderate and/or vigorous physical activities ≥150 min/week.

Health conditions covariates:

Cardiovascular-related conditions that were considered for this study included stroke, heart failure, heart attack, HIV, angina. A composite score from 0 to 3 was created (none,1, 2, ≥3) to analyze the impact of concomitant conditions on the association between grip strength and hypertension diagnosis. Non-Cardiovascular health conditions included as covariates were high cholesterol, diabetes, cancer and HIV status. Similarly, a composite score was created that summed up the number of non-cardiovascular related health conditions the participants were diagnosed with by a physician or health care provider.

Statistical Analysis:

All analyses were conducted using SAS Version 9.4 (SAS Institute, Cary, North Carolina). Study participant characteristics were expressed using mean and standard error of the mean for continuous variables and frequency and percentages for categorical variables. Logistic regression models were used to examine the association between relative grip strength and hypertension diagnosis. The models were adjusted for age, education level, chronic illnesses, and lifestyle indicators (smoking status, physical activity, alcohol consumption). Two analyses were completed, one including the entire sample population and the second excluding participants with a SBP of ≥180 mmHg or DBP of ≥ 120 mmHg. Post-hoc analyses were performed to study within group differences between participants diagnosed with hypertension (medicated vs unmedicated, pharmaceutical therapy vs herbal remedies).

Results

The cross-sectional study included 2,293 women from the HAALSI wave 1 dataset and 531 women met the requirements for inclusion in the prospective study. Characteristics of the study participants for both wave 1 and wave 2 are presented in Table 3.1. The mean age of the total sample was 61.3 ±12.7 years. The mean absolute grip strength was 21.2 ± 6.7 kg and the mean relative grip strength was 0.76 ± 0.3 kg/m2. There were 992 women (47.8%) from the baseline analysis that self-reported a physician diagnosis of hypertension. Participant characteristics by hypertension status is provided in Table 2. In summary, hypertensive participants in the total sample were older, had lower absolute and relative grip strength, higher BMIs, less formal education, higher systolic and diastolic blood pressure, more comorbidities, and exercised less. Participants were lost to follow up for several reasons during the time between wave 1 and wave 2 collection. Before wave 2 collection, 162 died (7.0%), 98 refused to participate (4.3%), and 13 participants were not found due to relocation or loss of contact (0.6%). Over the follow-up period, 121 participants (22.8%) developed hypertension.

Table 3.1 HAALSI cohort characteristics by hypertension diagnosis

	Total Population	Hypertensive	Non-Hypertensive	p-value
n	**2293**	1098 (47.9%)	1195 (52.1%)	
Age	61.3 ±12.7	63.9 ± 12.5	58.9± 12.5	<0.0001
Age Categories				
40-59	1111 (48.5%)	436 (39.7%)	675 (56.5%)	<0.0001
60-79	934 (40.7%)	515 (46.9%)	419 (35.1%)	
80+	248 (10.8%)	147(8.4%)	101 (13.4%)	
W1 BMI (kg/m2)	29.3 ± 7.4	30.4 ± 7.0	28.2 ± 7.6	<0.0001
W1 Mean Handgrip strength (kg)	21.2 ± 6.7	20.6 ± 6.2	21.7± 7.1	<0.0001
W1 Relative grip strength	0.76 ± 0.3	0.70± 0.7	0.80 ± 0.8	<0.0001
Blood Pressure				
W1 Mean SBP	137.6 ± 7.4	143.2 ± 23.0	132.5 ± 21.5	<0.0001
W1 Mean DBP	82.4 ± 12.1	84.3 ± 12.5	80.7 ± 11.6	<0.0001
Education level				
No formal education	1108 (48.3%)	549 (50.0%)	559 (46.8%)	0.0002
Some primary education (1-7 years)	776 (33.8%)	393 (35.8%)	383 (32.1%)	
Some secondary education (8-11 years)	224 (9.8%)	87 (7.9%)	137 (11.5%)	
Secondary or more (12+ years)	185 (8.1%)	69 (6.3%)	116 (9.7%)	
Ever Smoked				
No	2260 (98.6%)	1081 (98.4%)	1179 (98.7%)	0.67
Ever Consumed Alcohol				
No	1741 (75.9%)	827 (47.5%)	914(52.5%)	0.52
# Cardiovascular-Related Comorbidities				
0	2164 (94.4%)	1011 (92.1%)	1153 (96.5%)	<0.0001
1+	117 (5.1%)	87 (7.9%)	42 (3.5%)	
# Non-Cardiovascular-Related Comorbidities				
0	2023 (88.2%)	908 (82.7%)	1115 (93.3%)	<0.0001
1+	270 (11.8%)	190 (17.3%)	80(6.7%)	
Moderate or Vigorous activity				
Yes	1691 (73.8%)	810 (73.8%)	881 (73.8%)	<0.0001

Table 3.4 and 3.5 show the results of the logistic regression analyses for relative grip strength and absolute grip strength. The cross-sectional analysis found that lower relative handgrip strength was associated with higher risk of a hypertension diagnosis after adjusting for age, education, comorbidities, physical activity, smoking behavior, and alcohol consumption variables. When analyzing the relationship between hypertension and absolute grip strength, there was an association found in the Model 1, adjusted by BMI only but failed to reach significance for Models 2 and 3 after adjusting for demographic, behavioral, and health variables. Tables 5 and 6 highlight the results of the logistic regression for the longitudinal analysis on relative and absolute grip strength, respectively. No association between relative or absolute grip strength at wave 1 and diagnosis of hypertension at follow up was found. Only age

(p<0.0001) and participation in regular physical activity (p=0.02) were significantly associated hypertension risk in the separate analyses for absolute grip strength and relative grip strength.

Table 3.2: Odds Ratio and 95% CI for hypertension and relative grip strength cross-sectional analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.25	0.18	0.35	<0.0001
Model 2	0.40	0.28	0.56	<0.0001
Model 3	0.41	0.3	0.59	<0.0001

Model 1: unadjusted, Model 2: age, education, and comorbidity-adjusted,
Model 3: Age, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted.

Table 3.3: Odds Ratio and 95% CI for hypertension and absolute grip strength cross-sectional analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.97	0.96	0.99	0.0004
Model 2	1.00	0.98	1.01	0.42
Model 3	1.00	0.98	1.01	0.53

Model 1: BMI-adjusted, Model 2: age, BMI-adjusted, education, and comorbidity-adjusted,
Model 3: Age, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

Table 3.4: Odds Ratio and 95% CI for hypertension and relative grip strength longitudinal analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.56	0.24	1.31	0.18
Model 2	0.56	0.24	1.31	0.18
Model 3	0.51	0.22	1.2	0.12

Model 1: age-adjusted, Model 2: age, education, and comorbidiy-adjusted,

Model 3: Age, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

Table 3.5: Odds Ratio and 95% CI for hypertension and absolute grip strength longitudinal analysis

	Odds Ratio	Lower limit	Upper limit	p-value
Model 1	0.99	0.95	1.02	0.47
Model 2	0.98	0.95	1.02	0.38
Model 3	0.98	0.94	1.02	0.32

Model 1: age and BMI-adjusted, Model 2: age,BMI, education, and comorbidiy-adjusted,

Model 3: Age,BMI, smoking, alcohol consumption, education, physical activity, and comorbidity adjusted

Discussion

In the current population based prospective study, the main finding was that lower relative grip strength, but not absolute grip strength, was associated with higher hypertension risk in Black South African women aged 50 years and older after adjusting for sociodemographic and health-related variables. Additionally, we did not find a longitudinal relationship between relative grip strength nor absolute grip strength and hypertension risk at follow up. To our knowledge, this is the first study to examine the longitudinal association between grip strength and hypertension status in a cohort of Black South African women aged 50 years and older. These findings could have future implications for further understanding of how muscle strength and function are linked with hypertension risk and overall CVD health and identifying populations at higher risk of hypertension earlier to decrease overall disease burden.

The results of this cross-sectional study are supported by findings of several previous studies across different age groups and disease profiles (Lawman et al., 2015; Leong et al., 2015; Mainous et al., 2015; Peterson et al., 2017). There is not a consensus in the literature on the directional relationship between hypertension risk and blood pressure and handgrip strength (Ji et al., 2018; Lee et al., 2016) in women. A study by Lee et al. (2016) did not find an association between relative handgrip strength and hypertension in women but found a significant inverse relationship in men (Lee et al. 2016). In a cohort of women with systemic lupus erythematosus found that higher relative handgrip strength was associated with more favorable cardiometabolic profile, including lower systolic blood pressure (Sola-Rodríguez et al., 2021). Similarly, Lawman et al. (2015) demonstrated that higher relative grip strength was significantly associated with lower cardiometabolic risk for several variables including lower systolic blood pressure and triglycerides. The results of the current study are like the findings of previous studies that have used relative grip strength. In the first aim of this dissertation, we found that relative grip strength has a stronger association with hypertension risk than absolute grip strength in both Black and white women, which was also found in this cohort. More studies need to be designed to clarify the relationship between relative grip strength in women of different racial and ethnic backgrounds worldwide to determine the efficiency and the practicality of using relative grip strength as an indicator for hypertension risk. Longitudinal studies examining the associations between hypertension risk and grip strength are limited in the literature and have reported conflicting results. A study that examined the cross-sectional and longitudinal associations between changes in physical performance measures including grip strength and blood pressure in postmenopausal women found that grip strength was positively associated with diastolic blood pressure at baseline. During the follow-up, incremental increases in grip strength were associated with higher systolic blood pressure and diastolic blood pressure over time (Laddu et al., 2022). The prospective study of middle-aged and older adults conducted by Taekema et al. (2011) reported a positive associated between blood pressure and grip strength in older participants, but no association was found in middle-aged participants in the cross-sectional analysis. They also found that for each 10-mmHg decline in systolic blood pressure during the follow-up period, grip strength as reduced by 0.04 kg in the oldest participants. A study of older Chinese adults concluded that participants within the higher relative handgrip strength tertiles were at lower risk for hypertension than individuals with lower relative handgrip strengths (Hao et al., 2020). The results of the current study do not agree with the findings of the longitudinal studies outlined because we found no significant association between hypertension risk and grip strength. This could be due to several factors, most notably the difference in how grip strength is quantified and represented in the studies. Studies have utilized dominant handgrip strength, combined handgrip strength, absolute handgrip strength and relative grip strength when studying its relationship to general health. These values are presented as either evaluated as a continuous variable or grip strength quartiles. The difference in how these studies were designed and analyzed limits the applicability of findings across various groups. Researchers in this area should standardize protocols and procedures in the future and determine the most effective approaches to implement best practices in clinical and community data collection.

Interestingly, in the longitudinal study, the adjusted model for BMI was not associated with hypertension diagnosis. This finding is contrary to the extensive research on the relationship between hypertension risk and obesity. Obesity is a common modifiable risk factor for hypertension. Excess weight in the form of abdominal adiposity, measured by waist circumference, has been shown to increase risk of HTN development (Rhee et al 2018; Jayedi et al. 2018). Black women have the highest rates of obesity compared to other racial/ethnic groups (Flack et al., 2010; Mensah et al., 2005). In a cohort of South African adults, a significant positive association was found between grip strength and BMI. Body mass index (BMI) is a commonly used measure to estimate adiposity and serves as a marker of disease risk (Heymsfield et al. 2016). Researchers have challenged the applicability of generalized BMI thresholds for different racial and ethnic backgrounds due to variations in body composition and fat distribution found across populations (Consultation, 2004; Stanford et al., 2019). Using a measure such as BMI that uses cut off points for overweight and obese categories that are not representative of groups with historically differing body compositions than the common reference group (white males) could inaccurately represent the true burden of obesity and other health conditions in a population, impact the meaning of handgrip strength as it relates to body size, and furthermore distort the relationship found between grip strength and hypertension. Measures such as waist-to-hip ratio that better measure central adiposity and visceral fat may be more appropriate for this group of women, but these measures may be hard to collect in large study populations or often missing in studies. Using BMI as a measure to adjust for body size when calculating relative grip strength possibly impacts the generalizability of these findings to other groups of Black women. Despite this critique, using BMI to adjust for handgrip strength provided a more significant association to hypertension risk than absolute grip strength alone. Overall, the findings of this study were like the results reported in our cohort of middle-aged and older US Black women. Therefore, this provides evidence that relative handgrip strength as a method to detect potential declines in cardiovascular health in both Black US and South African women.

In contrast to our hypothesis, our results suggest there is no significant relationship between hypertension risk and relative handgrip strength nor absolute grip strength in middle-aged and older South African women. The results of this study were like the findings of aim two, which assessed the relationship between hypertension risk and handgrip strength in a small cohort of age match middle age and older Black and white women. In both studies, we found that higher hand grip strength was associated with lower risk of hypertension at baseline but there was no association found at follow up. A possible explanation for the lack of association between hypertension risk and hand grip strength is the length of the follow up period. Our follow up period of 3-4 years may not have been enough time to detect changes in both relative grip strength and factors related to hypertension risk among this population.

In the literature, there is evidence to support the idea that lower relative grip strength is an indicator of poor health outcomes, including frailty, disability, CVD-mortality, all-cause mortality, and cognitive decline (Sola-Rodríguez et al., 2021). According to literature based on US and European cohorts, grip strength peaks around the 3rd decade of life in both men and women (Dodds et al., 2014; Perna et al., 2016). Therefore, changes in grip strength are likely to happen earlier in the aging process compared to hypertension diagnosis. The use of relative handgrip strength as an index for changes to general health in earlier ages may provide the opportunity for us to identify individuals at most risk of developing adverse health outcomes related to hypertension and allow prevention and management of these conditions to occur at earlier ages. Cardiovascular risk factors are becoming increasingly more prevalent in South Africa but there is a lack of research that focuses on characterizing the factors related to hypertension epidemiology within this region (Jardim et al., 2017). Although HIV was included in the composite score for non-cardiovascular related comorbidities, this study did not independently study how the relationship between hypertension and grip strength could be impacted by HIV diagnosis. Limited research is available to understand fully how HIV impacts muscle function and furthermore how this relationship influences how useful handgrip strength is as an indicator of CVD health in SSA countries. A systematic review of research conducted in six African countries found that people living with HIV had lower grip strength, physical function, and were frailer than individuals without HIV (Bernard et al., 2017). Due to many people living with HIV for longer than before, there is a newer group of individuals who are dealing with managing HIV and hypertension risk factors (Houle et al., 2022). Therefore, it is important for future research in SSA populations determine how HIV status affects the relationship between hypertension status and relative grip strength.

One study limitation is the reliance on only self-reported physician diagnosis of hypertension to calculate the prevalence of hypertension in this population. Ideally in clinical practice, a hypertension diagnosis is confirmed by measuring blood pressure multiple times on several occasions. During the data collection process for HAALSI, multiple blood pressure measurements were recorded on just one occasion at baseline and during follow up. Blood pressure can be impacted by numerous factors and values can vary based on improper techniques by study personnel (Ogedegbe & Pickering, 2010; Pickering et al., 2005), which could inaccurately overrepresent the prevalence of hypertension in our sample. Therefore, we decided to only include individuals with a physician diagnosis of hypertension, which could lead to an underrepresentation of the true hypertension burden within this population. Another limitation of the current study is recall bias. The reliability of study participants recollection of health history or accurately providing information on lifestyle behaviors is less than documentation from a medical center or health professional. Despite these limitations, this study adds to the literature by identifying relative handgrip strength as a potential index of hypertension risk for Black South African women, a population that has been historically underrepresented in hypertension and muscular strength research.

References

Ahn, K. H., Lee, Y., Sohn, T. Y., Kim, D. Y., Ryu, M., Gym, H., & Lee, S. (2020). Association between Relative Handgrip Strength and Osteoporosis in Older Women: The Korea National Health and Nutrition Examination Survey 2014-2018. *Ann Geriatr Med Res*, *24*(4), 243-251. https://doi.org/10.4235/agmr.20.0076

Alberts, M., Urdal, P., Steyn, K., Stensvold, I., Tverdal, A., Nel, J. H., & Steyn, N. P. (2005). Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa. *Eur J Cardiovasc Prev Rehabil*, *12*(4), 347-354. https://doi.org/10.1097/01.hjr.0000174792.24188.8e

Bawah, A., Houle, B., Alam, N., Razzaque, A., Streatfield, P. K., Debpuur, C., Welaga, P., Oduro, A., Hodgson, A., Tollman, S., Collinson, M., Kahn, K., Toan, T. K., Phuc, H. D., Chuc, N. T. K., Sankoh, O., & Clark, S. J. (2016). The Evolving Demographic and Health Transition in Four Low- and Middle-Income Countries: Evidence from Four Sites in the INDEPTH Network of Longitudinal Health and Demographic Surveillance Systems. *PLoS One*, *11*(6), e0157281. https://doi.org/10.1371/journal.pone.0157281

Bernard, C., Dabis, F., & de Rekeneire, N. (2017). Physical function, grip strength and frailty in people living with HIV in sub-Saharan Africa: systematic review. *Trop Med Int Health*, *22*(5), 516-525. https://doi.org/10.1111/tmi.12852

Bosu, W. K., Aheto, J. M. K., Zucchelli, E., & Reilly, S. (2017). Prevalence, awareness, and associated risk factors of hypertension in older adults in Africa: a systematic review and meta-analysis protocol. *Systematic Reviews, 6*. https://doi.org/https://doi.org/10.1186/s13643-017-0585-5

Boutayeb, A. (2006). The double burden of communicable and non-communicable diseases in developing countries. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *100*(3), 191-199. https://doi.org/10.1016/j.trstmh.2005.07.021

Consultation, W. E. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*, *363*(9403), 157-163. https://doi.org/10.1016/s0140-6736(03)15268-3

Dodds, R. M., Syddall, H. E., Cooper, R., Benzeval, M., Deary, I. J., Dennison, E. M., Der, G., Gale, C. R., Inskip, H. M., Jagger, C., Kirkwood, T. B., Lawlor, D. A., Robinson, S. M., Starr, J. M., Steptoe, A., Tilling, K., Kuh, D., Cooper, C., & Sayer, A. A. (2014). Grip strength across the life course: normative data from twelve British studies. *PLoS One*, *9*(12), e113637. https://doi.org/10.1371/journal.pone.0113637

Flack, J. M., Sica, D. A., Bakris, G., Brown, A. L., Ferdinand, K. C., Grimm, R. H., Jr., Hall, W. D., Jones, W. E., Kountz, D. S., Lea, J. P., Nasser, S., Nesbitt, S. D., Saunders, E., Scisney-Matlock, M., & Jamerson, K. A. (2010). Management of high blood pressure in Blacks: an update of the International Society on Hypertension in Blacks consensus statement. *Hypertension*, *56*(5), 780-800. https://doi.org/10.1161/hypertensionaha.110.152892

Fowles, J., Roy, J., Clarke, J., & Dogra, S. (2014). Are the fittest Canadian adults the healthiest? *Health Rep*, *25*(5), 13-18. https://www.ncbi.nlm.nih.gov/pubmed/24850392

Gaziano, T. A., Abrahams-Gessel, S., Gomez-Olive, F. X., Wade, A., Crowther, N. J., Alam, S., Manne-Goehler, J., Kabudula, C. W., Wagner, R., Rohr, J., Montana, L., Kahn, K., Bärnighausen, T. W., Berkman, L. F., & Tollman, S. (2017). Cardiometabolic risk in a population of older adults with multiple co-morbidities in rural south africa: the HAALSI (Health and Aging in Africa: longitudinal studies of INDEPTH communities) study. *BMC Public Health*, *17*(1), 206. https://doi.org/10.1186/s12889-017-4117-y

Gnugesser, E., Chwila, C., Brenner, S., Deckert, A., Dambach, P., Steinert, J. I., Bärnighausen, T., Horstick, O., Antia, K., & Louis, V. R. (2022). The economic burden of treating uncomplicated hypertension in Sub-Saharan Africa: a systematic literature review. *BMC Public Health*, *22*(1), 1507. https://doi.org/10.1186/s12889-022-13877-4

Gómez-Olivé, F. X., Ali, S. A., Made, F., Kyobutungi, C., Nonterah, E., Micklesfield, L., Alberts, M., Boua, R., Hazelhurst, S., Debpuur, C., Mashinya, F., Dikotope, S., Sorgho, H., Cook, I., Muthuri, S., Soo, C., Mukomana, F., Agongo, G., Wandabwa, C., . . . Ramsay, M. (2017). Regional and Sex Differences in the Prevalence and Awareness of Hypertension: An H3Africa AWI-Gen Study Across 6 Sites in Sub-Saharan Africa. *Glob Heart*, *12*(2), 81-90. https://doi.org/10.1016/j.gheart.2017.01.007

Gómez-Olivé, F. X., Montana, L., Wagner, R. G., Kabudula, C. W., Rohr, J. K., Kahn, K., Bärnighausen, T., Collinson, M., Canning, D., Gaziano, T., Salomon, J. A., Payne, C. F., Wade, A., Tollman, S. M., & Berkman, L. (2018). Cohort Profile: Health and Ageing in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI). *Int J Epidemiol*, *47*(3), 689-690j. https://doi.org/10.1093/ije/dyx247

Hao, G., Chen, H., Ying, Y., Wu, M., Yang, G., & Jing, C. (2020). The Relative Handgrip Strength and Risk of Cardiometabolic Disorders: A Prospective Study. *Frontiers in physiology*, *11*, 719. Retrieved 2020, from http://europepmc.org/abstract/MED/32714207

Houle, B., Kabudula, C. W., Tilstra, A. M., Mojola, S. A., Schatz, E., Clark, S. J., Angotti, N., Gómez-Olivé, F. X., & Menken, J. (2022). Twin epidemics: the effects of HIV and systolic blood pressure on mortality risk in rural South Africa, 2010-2019. *BMC Public Health*, *22*(1), 387. https://doi.org/10.1186/s12889-022-12791-z

Jardim, T. V., Reiger, S., Abrahams-Gessel, S., Crowther, N. J., Wade, A., Gómez-Olivé, F. X., Salomon, J., Tollman, S., & Gaziano, T. A. (2017). Disparities in Management of Cardiovascular Disease in Rural South Africa: Data From the HAALSI Study (Health and Aging in Africa: Longitudinal Studies of International Network for the Demographic Evaluation of Populations and Their Health Communities). *Circ Cardiovasc Qual Outcomes*, *10*(11). https://doi.org/10.1161/circoutcomes.117.004094

Ji, C., Zheng, L., Zhang, R., Wu, Q., & Zhao, Y. (2018). Handgrip strength is positively related to blood pressure and hypertension risk: results from the National Health and nutrition examination survey. *Lipids in health and disease*, *17*(1), 86-86. https://doi.org/10.1186/s12944-018-0734-4

Kandala, N. B., Nnanatu, C. C., Dukhi, N., Sewpaul, R., Davids, A., & Reddy, S. P. (2021). Mapping the Burden of Hypertension in South Africa: A Comparative Analysis of the National 2012 SANHANES and the 2016 Demographic and Health Survey. *Int J Environ Res Public Health*, *18*(10). https://doi.org/10.3390/ijerph18105445

Karvonen-Gutierrez, C. A., Peng, Q., Peterson, M., Duchowny, K., Nan, B., & Harlow, S. (2018). Low grip strength predicts incident diabetes among mid-life women: the Michigan Study of Women's Health Across the Nation. *Age Ageing*, *47*(5), 685-691. https://doi.org/10.1093/ageing/afy067

Kaze, A. D., Schutte, A. E., Erqou, S., Kengne, A. P., & Echouffo-Tcheugui, J. B. (2017). Prevalence of hypertension in older people in Africa: a systematic review and meta-analysis. *J Hypertens*, *35*(7), 1345-1352. https://doi.org/10.1097/hjh.0000000000001345

Kohli-Lynch, C. N., Erzse, A., Rayner, B., & Hofman, K. J. (2022). Hypertension in the South African public healthcare system: a cost-of-illness and burden of disease study. *BMJ Open*, *12*(2), e055621. https://doi.org/10.1136/bmjopen-2021-055621

Koopman, J. J. E., van Bodegom, D., van Heemst, D., & Westendorp, R. G. J. (2014). Handgrip strength, ageing and mortality in rural Africa. *Age and Ageing*, *44*(3), 465-470. https://doi.org/10.1093/ageing/afu165

Laddu, D. R., LaMonte, M. J., Haring, B., Kim, H., Cawthon, P., Bea, J. W., Banack, H., Cauley, J. A., Allison, M. A., Martin, L. W., LeBoff, M. S., Stefanick, M. L., Phillips, S. A., & Ma, J. (2022). Longitudinal physical performance and blood pressure changes in older women: Findings form the women's health initiative. *Arch Gerontol Geriatr*, *98*, 104576. https://doi.org/10.1016/j.archger.2021.104576

Lawman, H. G. P., Troiano, R. P. P., Perna, F. M. P., Wang, C.-Y. P., Fryar, C. D. M., & Ogden, C. L. P. (2015). Associations of Relative Handgrip Strength and Cardiovascular Disease Biomarkers in U.S. Adults, 2011–2012. *American journal of preventive medicine*, *50*(6), 677-683. https://doi.org/10.1016/j.amepre.2015.10.022

Lee, W. J., Peng, L. N., Chiou, S. T., & Chen, L. K. (2016). Relative Handgrip Strength Is a Simple Indicator of Cardiometabolic Risk among Middle-Aged and Older People: A Nationwide Population-Based Study in Taiwan. *PLoS One*, *11*(8), e0160876. https://doi.org/10.1371/journal.pone.0160876

Leong, D. P., Teo, K. K., Rangarajan, S., Lopez-Jaramillo, P., Avezum, A., Jr., Orlandini, A., Seron, P., Ahmed, S. H., Rosengren, A., Kelishadi, R., Rahman, O., Swaminathan, S., Iqbal, R., Gupta, R., Lear, S. A., Oguz, A., Yusoff, K., Zatonska, K., Chifamba, J., . . . Yusuf, S. (2015). Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*, *386*(9990), 266-273. https://doi.org/10.1016/s0140-6736(14)62000-6

Maimela, E., Alberts, M., Modjadji, S. E., Choma, S. S., Dikotope, S. A., Ntuli, T. S., & Van Geertruyden, J. P. (2016). The Prevalence and Determinants of Chronic Non-Communicable Disease Risk Factors amongst Adults in the Dikgale Health Demographic and Surveillance System (HDSS) Site, Limpopo Province of South Africa. *PLoS One*, *11*(2), e0147926. https://doi.org/10.1371/journal.pone.0147926

Mainous, A. G., 3rd, Tanner, R. J., Anton, S. D., & Jo, A. (2015). Grip Strength as a Marker of Hypertension and Diabetes in Healthy Weight Adults. *Am J Prev Med*, *49*(6), 850-858. https://doi.org/10.1016/j.amepre.2015.05.025

Manafe, M., Chelule, P. K., & Madiba, S. (2022). The Perception of Overweight and Obesity among South African Adults: Implications for Intervention Strategies. *Int J Environ Res Public Health*, *19*(19). https://doi.org/10.3390/ijerph191912335

Mensah, G. A., Mokdad, A. H., Ford, E. S., Greenlund, K. J., & Croft, J. B. (2005). State of disparities in cardiovascular health in the United States. *Circulation*, *111*(10), 1233-1241. https://doi.org/10.1161/01.CIR.0000158136.76824.04

Ogedegbe, G., & Pickering, T. (2010). Principles and techniques of blood pressure measurement. *Cardiol Clin*, *28*(4), 571-586. https://doi.org/10.1016/j.ccl.2010.07.006

Perna, F. M., Coa, K., Troiano, R. P., Lawman, H. G., Wang, C. Y., Li, Y., Moser, R. P., Ciccolo, J. T., Comstock, B. A., & Kraemer, W. J. (2016). Muscular Grip Strength Estimates of the U.S. Population from the National Health and Nutrition Examination Survey 2011-2012. *J Strength Cond Res*, *30*(3), 867-874. https://doi.org/10.1519/jsc.0000000000001104

Peterson, M. D., Duchowny, K., Meng, Q., Wang, Y., Chen, X., & Zhao, Y. (2017). Low Normalized Grip Strength is a Biomarker for Cardiometabolic Disease and Physical Disabilities Among U.S. and Chinese Adults. *J Gerontol A Biol Sci Med Sci*, *72*(11), 1525-1531. https://doi.org/10.1093/gerona/glx031

Pickering, T. G., Hall, J. E., Appel, L. J., Falkner, B. E., Graves, J., Hill, M. N., Jones, D. W., Kurtz, T., Sheps, S. G., & Roccella, E. J. (2005). Recommendations for Blood Pressure Measurement in Humans and Experimental Animals. *Circulation*, *111*(5), 697-716. https://doi.org/doi:10.1161/01.CIR.0000154900.76284.F6

Sliwa, K., Ojji, D., Bachelier, K., Bohm, M., Damasceno, A., & Stewart, S. (2014). Hypertension and hypertensive heart disease in African women. *Clin Res Cardiol*, *103*(7), 515-523. https://doi.org/10.1007/s00392-014-0660-z

Sola-Rodríguez, S., Vargas-Hitos, J. A., Gavilán-Carrera, B., Rosales-Castillo, A., Sabio, J. M., Hernández-Martínez, A., Martínez-Rosales, E., Ortego-Centeno, N., & Soriano-Maldonado, A. (2021). Relative Handgrip Strength as Marker of Cardiometabolic Risk in Women with Systemic Lupus Erythematosus. *Int J Environ Res Public Health*, *18*(9). https://doi.org/10.3390/ijerph18094630

Souza Saraiva, W., Prestes, J., Schwerz Funghetto, S., Navalta, J. W., Tibana, R. A., & da Cunha Nascimento, D. (2019). Relation Between Relative Handgrip Strength, Chronological Age and Physiological Age with Lower Functional Capacity in Older Women. *Open Access J Sports Med*, *10*, 185-190. https://doi.org/10.2147/oajsm.S227720

Stanford, F. C., Lee, M., & Hur, C. (2019). Race, Ethnicity, Sex, and Obesity: Is It Time to Personalize the Scale? *Mayo Clin Proc*, *94*(2), 362-363. https://doi.org/10.1016/j.mayocp.2018.10.014

Zhang, X., Huang, L., Peng, X., Xie, Y., Bao, X., Huang, J., & Wang, P. (2020). Association of handgrip strength with hypertension among middle-aged and elderly people in Southern China: A cross-sectional study. *Clin Exp Hypertens*, *42*(2), 190-196. https://doi.org/10.1080/10641963.2019.1601206

GENERAL DISCUSSION AND OVERALL CONCLUSION

Discussion

Hypertension is a global public health concern responsible for approximately 8.5 million deaths annually (Collaboration, 2021). Hypertension is a major modifiable risk factor for cardiovascular disease and is the leading cause of cardiovascular-related deaths and premature death (Brook et al., 2013; Mills et al., 2020). It is estimated that more than 1.3 billion adults have hypertension, with approximately 80% of hypertensive adults located in low-and middle-income countries (LMICs) (Hendriks et al., 2012). Reducing the health burden of hypertension is of great importance for preventing poor health outcomes. Despite the growing awareness of hypertension status and the availability of pharmacological and non-pharmacological interventions, treatment and control remain suboptimal (Butler et al., 2017; Muntner et al., 2020). This phenomenon is especially apparent in Black women, a population at higher risk for developing hypertension, earlier onset, and more severe increases in blood pressure. Over the past several decades, a large body of research has outlined the epidemiology of hypertension and cardiovascular risk factors in US Black women (Aggarwal et al., 2021; Carnethon et al., 2017; Nesbitt, 2008). However, the epidemiology of hypertension is not well characterized among Black women in rural South Africa, a region experiencing a rise in hypertension and cardiovascular diseases in recent years. The disparity in hypertension prevalence in Black women compared to their counterparts indicates the importance of identifying effective strategies that promote early detection and management of hypertension in this population.

Many studies have established the utility of handgrip strength as an index for general health across the lifespan (Fanelli Kuczmarski et al., 2018; Leong et al., 2015; McGrath et al., 2018; Ntuk et al., 2017; Sayer & Kirkwood, 2015). Specifically, several studies have reported low hand grip strength was associated with a higher risk of poor health outcomes such as cardiometabolic diseases and hypertension (Lawman et al., 2015; Peterson et al., 2017). However, research on the capacity of handgrip strength as a tool to identify hypertension risk in Black women is lacking. Currently, it is unknown whether a significant association between grip strength and hypertension risk is present in US Black women and whether this relationship was unique to US Black women only.   Therefore, the main goal of this dissertation was to assess the relationship between grip strength and hypertension diagnosis in Black women residing in the US (Studies 1 and 2). The final study (Study 3) was designed to determine whether handgrip strength was related to hypertension in Black South African women, a population more recently dealing with the consequences of increased hypertension prevalence due to advancements in medical care that have prolonged lifespans.

This dissertation produced the following findings: 1) Relative handgrip strength (absolute grip lisectional study design, after controlling for demographic and sociodemographic covariates. A similar relationship was observed in white women. When compared to absolute grip strength, relative handgrip strength was a better indicator of hypertension risk (Chapter 2). 2) Relative handgrip strength measured at baseline did not predict a future diagnosis of hypertension at follow-up in both middle-aged and older US Black and white women (Chapter 3). 3) Low relative handgrip strength was associated with hypertension diagnosis in middle-aged and older Black South African women in the cross-sectional analysis, but results of the prospective study suggested relative handgrip strength did not predict future hypertension diagnosis at follow-up (chapter 4).

The findings of this dissertation align with several cross-sectional studies that suggest relative handgrip strength better indicates hypertension risk than absolute grip strength. In our studies, we did not find a significant association between absolute handgrip strength and hypertension risk after controlling for demographic, lifestyle, and health factors in both Black and white women. In contrast to the present study, Mainous et. al (2015) reported that absolute grip strength was associated with hypertension among individuals with undiagnosed and diagnosed hypertension.   Zhang et al. (2018) found that absolute handgrip strength was associated with hypertension in elderly female participants. Ji et al. reported no significant associations between absolute grip strength and hypertension, systolic, and diastolic blood pressure in female participants but found significant associations in males. The variation in study results between these studies can be explained by differences in study population and design. In this dissertation, we examined the relationship between absolute grip strength, relative grip strength, and BMI across studies similar to Lawman et al. (Figures 1 and 2) and stratified by race/ethnic category. We found that relative grip strength declined with increasing body mass categories for all groups while absolute grip strength increased with higher body mass in all groups except for Black women in the MIDUS study. The reduction of relative grip strength with each increasing BMI category highlights the impact BMI has on grip strength with individuals with higher BMIs having lower relative grip strength. Relative grip strength was found to have a stronger cross-sectional association to hypertension than absolute grip strength. This provides further support for the argument that body size measures should be accounted for in the grip strength measure when examining its influence on health outcomes. As highlighted in papers 1-3, BMI has some limitations in its application to varying ethnic groups. Despite these limitations, BMI is a practical measure to use when evaluating the relationship between grip strength and hypertension risk in Black women.

Handgrip strength is influenced by multiple factors including age, sex, hand dominance, and anthropometric measures. Normative data on handgrip strength is available in many countries with thresholds for muscular weakness and these reference values are typically stratified by age and sex. In a study of adults from a Chinese Han population, increasing tertile of handgrip strength was associated with higher diastolic blood pressure. Additionally, the high handgrip strength tertile was significantly associated with higher odds of developing hypertension (Mallah et al., 2019). We chose to represent absolute and relative as continuous variables in our analyses which can reduce the ease of application to a generalized population. An advantage of using reference ranges for grip strength instead of representing it as a continuous variable is that reference ranges provide a standard to compare individual handgrip strength values to values from a representative population stratified by factors such as age, gender, and ethnicity. This can serve valuable in clinical settings, where indexes and cut-off points are already used to diagnose conditions such as hypertension, obesity, and sarcopenia. One disadvantage of using reference values for handgrip strength when trying to understand the relationship between grip strength and hypertension risk is that these reference values are largely based on healthy, homogeneous populations derived from participants located in high-income western and Asian-Pacific countries (Leong et al., 2016). For individualized hypertension management, reference values would need to be adapted to individual populations of interest because each population may have different characteristics influencing their handgrip strength based on genetics, location, environmental exposures, occupation, and health behaviors. A large study of individuals 35-70 years old found that handgrip strength values ranged based on geographic location, with handgrip strength being higher in the US and Europe and the lowest in South and Southeast Asian countries and Africa (Leong et al., 2016). Additionally, the variation between study protocols defining cut-off grip strength values makes it challenging to draw a consensus in the literature. Although there are limitations in the use of handgrip strength as a continuous variable in our analysis, we believed that was a better measure for the population used in our 3 studies.

The second article of the dissertation built on the findings from study 1 by performing a longitudinal analysis to investigate the effectiveness of using baseline relative handgrip strength to predict hypertension diagnosis in middle-aged and older Black women. Although this dissertation was not focused on the influence of age on our outcome variable, we chose the MIDUS dataset based on literature that observed steep increases in BP in women approaching midlife and older age who would be at greater risk of developing hypertension. We found that relative handgrip strength did not predict future hypertension risk at follow-up among Black women or white women in our study. This finding was contrary to Laddu et al. who reported that incremental increases in grip strength were associated with higher systolic blood pressure and diastolic blood pressure over time (Laddu et al., 2022). Another conflicting study of older Chinese adults by Hao et al. concluded that participants within the higher relative handgrip strength tertiles were at a lower risk for hypertension than individuals with a lower relative handgrip strength (Hao et al., 2020). The lack of association found in our study may be due to our small sample size (n=176). We decided to do an age-matched cohort of Black and white women because of the difference in study population between the two groups. In the original MIDUS cohort, white women represented over 80% of the population and were more likely to have complete study data. We also found that fewer Black women participated in the follow-up because of hypertension diagnosis at wave 1, death before wave 2, or a lack of complete information. Therefore, we may have found a difference with a larger sample. Secondly, the differences in findings may also be attributed to the use of grip strength tertiles by Hao et al. and Laddu et al, which potentially helped elucidate the relationship between grip strength and hypertension status by determining which grip strength tertile was most influenced by the relationship between grip strength and hypertension risk factors.

The third article of this dissertation assessed the effectiveness of relative handgrip strength as a tool to predict hypertension risk in a cohort of middle-aged and older Black South African women. The rationale for this study is that we wanted to determine whether the relationship between relative grip strength and hypertension we found in studies 1 and 2 among nationally representative samples of US Black women was also detected in other populations of Black women. Hypertension in Black women is characterized by earlier onset, is more severe, and they are at higher risk of blood pressure-induced target organ damage and mortality than women from other groups (Brown et al., 2017; Williams et al., 2016). The differences in hypertension prevalence among Black women are not fully explained by factors such as obesity, history of cardiovascular disease, physical activity level, socioeconomic status, and access to healthcare (Fuchs, 2011). In recent years, researchers have emphasized the impact of stress on blood pressure, and extended periods of stress can have detrimental consequences for cardiovascular health (Black et al., 2015; Panza et al., 2019). Black people in the US and South Africa share a history of experiencing pervasive forms of racism through institutionalized systems that promoted segregation and discrimination, which have brought long-lasting stressors that have outlived the institutions created (Zinkel, 2019). To better characterize the relationship between relative handgrip strength and hypertension among different groups of Black women, we studied middle-aged and older South African women. Data used in the HAALSI study was collected from Agincourt, a rural town in the Mpumalanga province of South Africa, while the US samples from NHANES and MIDUS were a nationally representative sample encompassing both rural and urban communities. Differences in study design and sample characteristics prevented a direct comparison between the two populations, but the study was a valuable exploration into whether cultural and societal differences influenced the relationship between handgrip strength and hypertension risk. We found that relative handgrip strength was inversely associated with hypertension risk in the cross-sectional study while no relationship was found in the longitudinal study. These findings aligned with the results of study 2, which comprised a small sample of middle-aged and older adults. The results of aim 3 provide further support for grip strength as an indicator of cardiovascular health in populations outside of the western and Asian countries that are commonly represented in the literature.

The mechanisms responsible for the relationship between hypertension risk and handgrip strength are not fully understood. One possible explanation is that hypertension is related to age-associated loss of muscle mass, called sarcopenia. Sarcopenia is a major risk factor for age-related chronic conditions such as hypertension. Low grip strength is a marker of poor muscle fitness and function, and a lack of muscle fitness in less physically active adults could ultimately increase the risk of hypertension in this population (Bai et al., 2020; Hao et al., 2020). Another potential mechanism that could explain the association between grip strength and hypertension risk is a changing vascular structure that contributes to reduced muscle mass and function in individuals with low grip strength (König et al., 2021). The aging process is characterized by the stiffening of the vasculature. Particularly stiffness of the aortic artery is associated with increased risk of hypertension and cardiovascular diseases such as coronary artery disease, heart failure, stroke, and heart failure (Shirwany & Zou, 2010). Several studies have showed that pulse wave velocity (PWV), a measurement for arterial stiffness), was associated with poor muscle function and reductions in muscular strength (Aminuddin et al., 2021). The mechanism responsible for vascular changes, grip strength, and their relationship to hypertension risk may possibly be connected which could explain the relationship found in the literature.

Declining grip strength is an index for poor health outcomes, which can increase overall risk for hypertension. Currently, it is unknown whether there is a cause-and-effect relationship between relative handgrips strength and hypertension risk. An important note to keep in mind is that increasing handgrip strength through physical activity may not be directly linked to improvements in hypertension and cardiovascular disease profile. Alternatively, engaging in isometric exercise training (IET) through handgrip strength training over time will build grip strength while also lowering blood pressure (Cornelissen & Smart, 2013; Inder et al., 2016; Smart et al., 2019). Reductions in RBP after isometric exercise training interventions have been observed in individuals of various age groups and hypertension status (normotensive, elevated/pre-hypertensive, and hypertensive) (Smart et al., 2019). Isometric Handgrip training is practical for implementation in clinical, community, and home settings and equipment is inexpensive and easy to transport. More research is needed to understand the mechanisms influencing the relationship between grip strength and hypertension in women before full implementation into clinical practice.

In chapter 1, the diagnosis of hypertension in Black women based on current US hypertension guidelines was challenged based on disparities found in the 2017 ACC/AHA guidelines for hypertension management in Black women (Whelton et al., 2018). Race-based prescription of antihypertensive medications has not reduced the prevalence of hypertension among Black women overall (Reddick, 2021; Roberts, 2008). The differences in recommendations for hypertension management in current US guidelines are reminiscent of the 2005 U.S. Food and Drug Administration’s approval of the heart failure medication BiDil based on race, approved for patients with African ancestry (Roberts, 2011). Differentiating medical care based on racial groups can be problematic by creating further distrust in healthcare providers and potentially delaying treatment for hypertension that is better suited to reduce blood pressure long-term. Creating guidelines with attainable blood pressure for pharmacological and non-pharmacological intervention instead of low arbitrary blood pressure cut-offs may improve blood pressure management. Developing realistic blood pressure guidelines may also increase the efficacy of grip strength as an index for hypertension risk. Furthermore, targeted and individualized management strategies should be implemented to provide better blood pressure control. Future blood pressure management interventions should account for the influence of genetics, environment, social, behavioral, and stress-related factors on the effectiveness of interventions for Black women.

There were a few limitations to our work. First, in studies 1-3 we defined hypertension by participant recall of a hypertension diagnosis by a physician or health care provider. This definition assumes that participants will accurately recall a diagnosis or that the participant has interacted with a health care professional often enough to obtain a hypertension diagnosis. Also, the stigma of hypertension diagnosis may inhibit some participants from disclosing it or they may be unaware. In defining hypertension this way, we excluded individuals with a blood pressure measurement equal to or above 130/80 mmHg and 140/90 mmHg based on US and South African hypertension guidelines, respectively (Seedat et al., 2014; Whelton et al., 2018). This potentially underestimated the total number of individuals with hypertension in our sample which could have impacted our results. Secondly, the use of secondary data invites the possibility of missing information in data collection and errors in coding or data entry. In all of our studies, many individuals were excluded because of missing handgrip strength, anthropometric, blood pressure, and sociodemographic variables. We were limited in selecting datasets by the availability of handgrip strength data and datasets with an adequate sample of Black women. This resulted in a small study sample for study 2 which may have influenced the results of our longitudinal analysis. Therefore, future longitudinal studies with larger samples and repeated grip strength measures may come to alternative conclusions.

Conclusion

Overall, the purpose of this dissertation was to explore the use of handgrip strength as an index for hypertension risk in Black women. We aimed to provide additional evidence on alternative methods for blood pressure management and increase the representation of Black women in CVD-related research. Handgrip strength is a promising tool that has the potential for wide applications in clinical and community settings. Measuring handgrip strength alongside blood pressure in clinical settings and monitoring overtime could provide more insight into changes in health profile and alert medical professionals of future health concerns that are asymptomatic at present or aid in tracking the success of exercise interventions for improvement of muscular strength and general health. To our knowledge, the studies described within this dissertation were the first investigations into handgrip strength and hypertension risk in US and South African Black women. While the results of the longitudinal studies did not align with our hypotheses, this was a first step in identifying simple, non-invasive strategies to manage hypertension risk and CVD risk in Black women. This dissertation also provided a critique of current guidelines for hypertension diagnosis and treatment and how they disproportionately impact Black women. Future studies should be designed to account for differences in body size and management strategies to better determine the relationship between relative handgrip strength and hypertension. If we evaluated the prevalence and risk of hypertension based on indices and guidelines that were equitable, the true burden of hypertension could be discovered, and effective management strategies could be created to reduce the prevalence of hypertension in Black women and women of other racial/ethnic groups.

References

Abel, W. M., & Efird, J. T. (2013). The Association between Trust in Health Care Providers and Medication Adherence among Black Women with Hypertension. *Front Public Health*, *1*, 66. https://doi.org/10.3389/fpubh.2013.00066

Aggarwal, R., Chiu, N., Wadhera, R. K., Moran, A. E., Raber, I., Shen, C., Yeh, R. W., & Kazi, D. S. (2021). Racial/Ethnic Disparities in Hypertension Prevalence, Awareness, Treatment, and Control in the United States, 2013 to 2018. *Hypertension*, *78*(6), 1719-1726. https://doi.org/10.1161/hypertensionaha.121.17570

Agyemang, P., & Powell-Wiley, T. M. (2013). Obesity and Black Women: Special Considerations Related to Genesis and Therapeutic Approaches. *Curr Cardiovasc Risk Rep*, *7*(5), 378-386. https://doi.org/10.1007/s12170-013-0328-7

Ahmad, A., & Oparil, S. (2017). Hypertension in Women: Recent Advances and Lingering Questions. *Hypertension*, *70*(1), 19-26. https://doi.org/10.1161/HYPERTENSIONAHA.117.08317

Ahn, K. H., Lee, Y., Sohn, T. Y., Kim, D. Y., Ryu, M., Gym, H., & Lee, S. (2020). Association between Relative Handgrip Strength and Osteoporosis in Older Women: The Korea National Health and Nutrition Examination Survey 2014-2018. *Ann Geriatr Med Res*, *24*(4), 243-251. https://doi.org/10.4235/agmr.20.0076

Ahuja, K. D., Robertson, I. K., & Ball, M. J. (2009). Acute effects of food on postprandial blood pressure and measures of arterial stiffness in healthy humans. *The American Journal of Clinical Nutrition*, *90*(2), 298-303. https://doi.org/10.3945/ajcn.2009.27771

Alberts, M., Urdal, P., Steyn, K., Stensvold, I., Tverdal, A., Nel, J. H., & Steyn, N. P. (2005). Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa. *Eur J Cardiovasc Prev Rehabil*, *12*(4), 347-354. https://doi.org/10.1097/01.hjr.0000174792.24188.8e

Aminuddin, A., Noor Hashim, M. F., Mohd Zaberi, N. A. S., Zheng Wei, L., Ching Chu, B., Jamaludin, N. A., Salamt, N., Che Roos, N. A., & Ugusman, A. (2021). The Association Between Arterial Stiffness and Muscle Indices Among Healthy Subjects and Subjects With Cardiovascular Risk Factors: An Evidence-Based Review. *Front Physiol*, *12*, 742338. https://doi.org/10.3389/fphys.2021.742338

Appel, L. J. (2003). Lifestyle modification as a means to prevent and treat high blood pressure. *J Am Soc Nephrol*, *14*(7 Suppl 2), S99-s102. https://doi.org/10.1097/01.asn.0000070141.69483.5a

Armstrong, M., Kerndt, C. C., & Moore, R. A. (2022). Physiology, Baroreceptors. In *StatPearls*. StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC.

Bai, T., Fang, F., Li, F., Ren, Y., Hu, J., & Cao, J. (2020). Sarcopenia is associated with hypertension in older adults: a systematic review and meta-analysis. *BMC geriatrics*, *20*(1), 279. https://doi.org/10.1186/s12877-020-01672-y

Barba, G., Casullo, C., Dello Russo, M., Russo, P., Nappo, A., Lauria, F., & Siani, A. (2008). Gender-Related Differences in the Relationships Between Blood Pressure, Age, and Body Size in Prepubertal Children. *Am J Hypertens*, *21*(9), 1007-1010. https://doi.org/10.1038/ajh.2008.228

Baross, A. W., Wiles, J. D., & Swaine, I. L. (2012). Effects of the intensity of leg isometric training on the vasculature of trained and untrained limbs and resting blood pressure in middle-aged men. *Int J Vasc Med*, *2012*, 964697. https://doi.org/10.1155/2012/964697

Bawah, A., Houle, B., Alam, N., Razzaque, A., Streatfield, P. K., Debpuur, C., Welaga, P., Oduro, A., Hodgson, A., Tollman, S., Collinson, M., Kahn, K., Toan, T. K., Phuc, H. D., Chuc, N. T. K., Sankoh, O., & Clark, S. J. (2016). The Evolving Demographic and Health Transition in Four Low- and Middle-Income Countries: Evidence from Four Sites in the INDEPTH Network of Longitudinal Health and Demographic Surveillance Systems. *PLoS One*, *11*(6), e0157281. https://doi.org/10.1371/journal.pone.0157281

Benjamin, E. J., Muntner, P., Alonso, A., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Chang, A. R., Cheng, S., Das, S. R., Delling, F. N., Djousse, L., Elkind, M. S. V., Ferguson, J. F., Fornage, M., Jordan, L. C., Khan, S. S., Kissela, B. M., Knutson, K. L., . . . Stroke Statistics, S. (2019). Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation*, *139*(10), e56-e528. https://doi.org/10.1161/CIR.0000000000000659

Beyer, S. E., Sanghvi, M. M., Aung, N., Hosking, A., Cooper, J. A., Paiva, J. M., Lee, A. M., Fung, K., Lukaschuk, E., Carapella, V., Mittleman, M. A., Brage, S., Piechnik, S. K., Neubauer, S., & Petersen, S. E. (2018). Prospective association between handgrip strength and cardiac structure and function in UK adults. *PLoS One*, *13*(3), e0193124. https://doi.org/10.1371/journal.pone.0193124

Black, L. L., Johnson, R., & VanHoose, L. (2015). The Relationship Between Perceived Racism/Discrimination and Health Among Black American Women: a Review of the Literature from 2003 to 2013. *J Racial Ethn Health Disparities*, *2*(1), 11-20. https://doi.org/10.1007/s40615-014-0043-1

Bohannon, R. W. (2019). Grip Strength: An Indispensable Biomarker For Older Adults. *Clin Interv Aging*, *14*, 1681-1691. https://doi.org/10.2147/cia.S194543

Bosu, W. K., Aheto, J. M. K., Zucchelli, E., & Reilly, S. (2017). Prevalence, awareness, and associated risk factors of hypertension in older adults in Africa: a systematic review and meta-analysis protocol. *Systematic Reviews*, *6*. https://doi.org/https://doi.org/10.1186/s13643-017-0585-5

Bosworth, H. B., Powers, B., Grubber, J. M., Thorpe, C. T., Olsen, M. K., Orr, M., & Oddone, E. Z. (2008). Racial differences in blood pressure control: potential explanatory factors. *J Gen Intern Med*, *23*(5), 692-698. https://doi.org/10.1007/s11606-008-0547-7

Boutayeb, A. (2006). The double burden of communicable and non-communicable diseases in developing countries. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *100*(3), 191-199. https://doi.org/10.1016/j.trstmh.2005.07.021

Brahmbhatt, Y., Gupta, M., & Hamrahian, S. (2019). Hypertension in Premenopausal and Postmenopausal Women. *Curr Hypertens Rep*, *21*(10), 74. https://doi.org/10.1007/s11906-019-0979-y

Brook, R. D., Appel, L. J., Rubenfire, M., Ogedegbe, G., Bisognano, J. D., Elliott, W. J., Fuchs, F. D., Hughes, J. W., Lackland, D. T., Staffileno, B. A., Townsend, R. R., Rajagopalan, S., American Heart Association Professional Education Committee of the Council for High Blood Pressure

Research, C. o. C., Stroke Nursing, C. o. E., Prevention, & Council on Nutrition, P. A. (2013). Beyond medications and diet: alternative approaches to lowering blood pressure: a scientific statement from the american heart association. *Hypertension*, *61*(6), 1360-1383. https://doi.org/10.1161/HYP.0b013e318293645f

Brooks, J. M., Titus, A. J., Bruce, M. L., Orzechowski, N. M., Mackenzie, T. A., Bartels, S. J., & Batsis, J. A. (2018). Depression and Handgrip Strength Among U.S. Adults Aged 60 Years and Older from NHANES 2011-2014. *The journal of nutrition, health & aging*, *22*(8), 938-943. https://doi.org/10.1007/s12603-018-1041-5

Brown, A. G. M., Houser, R. F., Mattei, J., Mozaffarian, D., Lichtenstein, A. H., & Folta, S. C. (2017). Hypertension among US-born and foreign-born non-Hispanic Blacks: National Health and Nutrition Examination Survey 2003-2014 data. *J Hypertens*, *35*(12), 2380-2387. https://doi.org/10.1097/hjh.0000000000001489

Brown, E. C., Buchan, D. S., Madi, S. A., Gordon, B. N., & Drignei, D. (2020). Grip Strength Cut Points for Diabetes Risk Among Apparently Healthy U.S. Adults. *Am J Prev Med*, *58*(6), 757-765. https://doi.org/10.1016/j.amepre.2020.01.016

Bushman, B. A. (2018). Lifestyle Modifications to Promote Healthy Blood Pressure. *ACSM's Health & Fitness Journal*, *22*(5). https://journals.lww.com/acsm-healthfitness/Fulltext/2018/09000/Lifestyle_Modifications_to_Promote_Healthy_Blood.4.aspx

Butler, M. J., Tanner, R. M., Muntner, P., Shimbo, D., Bress, A. P., Shallcross, A. J., Sims, M., Ogedegbe, G., & Spruill, T. M. (2017). Adherence to antihypertensive medications and associations with blood pressure among African Americans with hypertension in the Jackson Heart Study. *J Am Soc Hypertens*, *11*(9), 581-588.e585. https://doi.org/10.1016/j.jash.2017.06.011

Calhoun, D. A., & Harding, S. M. (2010). Sleep and hypertension. *Chest*, *138*(2), 434-443. https://doi.org/10.1378/chest.09-2954

Carey, R. M., Muntner, P., Bosworth, H. B., & Whelton, P. K. (2018). Prevention and Control of Hypertension: JACC Health Promotion Series. *J Am Coll Cardiol*, *72*(11), 1278-1293. https://doi.org/10.1016/j.jacc.2018.07.008

Carlson, D. J., Dieberg, G., Hess, N. C., Millar, P. J., & Smart, N. A. (2014). Isometric exercise training for blood pressure management: a systematic review and meta-analysis. *Mayo Clin Proc*, *89*(3), 327-334. https://doi.org/10.1016/j.mayocp.2013.10.030

Carnethon, M. R., Pu, J., Howard, G., Albert, M. A., Anderson, C. A. M., Bertoni, A. G., Mujahid, M. S., Palaniappan, L., Taylor, H. A., Jr., Willis, M., Yancy, C. W., American Heart Association Council on, E., Prevention, Council on Cardiovascular Disease in the, Y., Council on, C., Stroke, N., Council on Clinical, C., Council on Functional, G., Translational, B., & Stroke, C. (2017). Cardiovascular Health in African Americans: A Scientific Statement From the American Heart Association. *Circulation*, *136*(21), e393-e423. https://doi.org/10.1161/CIR.0000000000000534

Carretero, O. A., & Oparil, S. (2000). Essential hypertension. Part I: definition and etiology. *Circulation*, *101*(3), 329-335. https://doi.org/10.1161/01.cir.101.3.329

Carson, A. P., Howard, G., Burke, G. L., Shea, S., Levitan, E. B., & Muntner, P. (2011). Ethnic differences in hypertension incidence among middle-aged and older adults: the multi-ethnic study of atherosclerosis. *Hypertension*, *57*(6), 1101-1107. https://doi.org/10.1161/hypertensionaha.110.168005

Cazabon, D., Farrell, M., Gupta, R., Joseph, L., Pathni, A. K., Sahoo, S., Kunwar, A., Elliott, K., Cohn, J., Frieden, T. R., & Moran, A. E. (2022). A simple six-step guide to National-Scale Hypertension Control Program implementation. *Journal of Human Hypertension*, *36*(7), 591-603. https://doi.org/10.1038/s41371-021-00612-6

Chainani, V., Shaharyar, S., Dave, K., Choksi, V., Ravindranathan, S., Hanno, R., Jamal, O., Abdo, A., & Abi Rafeh, N. (2016). Objective measures of the frailty syndrome (hand grip strength and gait speed) and cardiovascular mortality: A systematic review. *International Journal of Cardiology*, *215*, 487-493. https://doi.org/https://doi.org/10.1016/j.ijcard.2016.04.068

Chang, C. Y., Chu, N. F., Lin, M. H., Wang, S. C., Wu, D. M., Tsai, M. K., & Lu, C. H. (2022). Association between Grip Strength, Obesity, and Cardiometabolic Risk Factors among the Community-Dwelling Elderly Population in Taiwan. *Int J Environ Res Public Health*, *19*(18). https://doi.org/10.3390/ijerph191811359

Charles, L., Triscott, J., & Dobbs, B. (2017). Secondary Hypertension: Discovering the Underlying Cause. *Am Fam Physician*, *96*(7), 453-461.

Chen, C. Y., & Bonham, A. C. (2010). Postexercise hypotension: central mechanisms. *Exerc Sport Sci Rev*, *38*(3), 122-127. https://doi.org/10.1097/JES.0b013e3181e372b5

Chen, L., Simonsen, N., & Liu, L. (2015). Racial Differences of Pediatric Hypertension in Relation to Birth Weight and Body Size in the United States. *PLoS One*, *10*(7), e0132606. https://doi.org/10.1371/journal.pone.0132606

Chen, V., Ning, H., Allen, N., Kershaw, K., Khan, S., Lloyd-Jones, D. M., & Wilkins, J. T. (2019). Lifetime Risks for Hypertension by Contemporary Guidelines in African American and White Men and Women. *JAMA Cardiol*, *4*(5), 455-459. https://doi.org/10.1001/jamacardio.2019.0529

Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo, J. L., Jr., Jones, D. W., Materson, B. J., Oparil, S., Wright, J. T., Jr., & Roccella, E. J. (2003). Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*, *42*(6), 1206-1252. https://doi.org/10.1161/01.HYP.0000107251.49515.c2

Choi, H. Y., Park, H. C., & Ha, S. K. (2015). Salt Sensitivity and Hypertension: A Paradigm Shift from Kidney Malfunction to Vascular Endothelial Dysfunction. *Electrolyte Blood Press*, *13*(1), 7-16. https://doi.org/10.5049/ebp.2015.13.1.7

Chon, D., Shin, J., & Kim, J. H. (2020). Consideration of body mass index (BMI) in the association between hand grip strength and hypertension: Korean Longitudinal Study of Ageing (KLoSA). *PLoS One*, *15*(10), e0241360. https://doi.org/10.1371/journal.pone.0241360

Chong, H., Choi, Y. E., Kong, J. Y., Park, J. H., Yoo, H. J., Byeon, J. H., Lee, H. J., & Lee, S. H. (2020). Association of Hand Grip Strength and Cardiometabolic Markers in Korean Adult Population: The Korea National Health and Nutrition Examination Survey 2015-2016. *Korean J Fam Med*, *41*(5), 291-298. https://doi.org/10.4082/kjfm.18.0129

Churilla, J. R., Summerlin, M., Richardson, M. R., & Boltz, A. J. (2020). Mean Combined Relative Grip Strength and Metabolic Syndrome: 2011-2014 National Health and Nutrition Examination Survey. *J Strength Cond Res*, *34*(4), 995-1000. https://doi.org/10.1519/jsc.0000000000003515

Cífková, R., & Strilchuk, L. (2022). Sex differences in hypertension. Do we need a sex-specific guideline? *Front Cardiovasc Med*, *9*, 960336. https://doi.org/10.3389/fcvm.2022.960336

Clifford, P. S. (2011). Local control of blood flow. *Adv Physiol Educ*, *35*(1), 5-15. https://doi.org/10.1152/advan.00074.2010

Coffman, T. M., & Crowley, S. D. (2008). Kidney in hypertension: guyton redux. *Hypertension*, *51*(4), 811-816. https://doi.org/10.1161/hypertensionaha.105.063636

Cohen, J. B., & Cohen, D. L. (2016). Integrating Out-of-Office Blood Pressure in the Diagnosis and Management of Hypertension. *Curr Cardiol Rep*, *18*(11), 112. https://doi.org/10.1007/s11886-016-0780-3

Collaboration, N. R. F. (2021). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*, *398*(10304), 957-980. https://doi.org/10.1016/s0140-6736(21)01330-1

Cooper, R., Tomlinson, D., Hamer, M., & Pinto Pereira, S. M. (2022). Lifetime body mass index and grip strength at age 46 years: the 1970 British Cohort Study. *J Cachexia Sarcopenia Muscle*, *13*(4), 1995-2004. https://doi.org/10.1002/jcsm.12992

Cornelissen, V. A., & Smart, N. A. (2013). Exercise training for blood pressure: a systematic review and meta-analysis. *Journal of the American Heart Association*, *2*(1), e004473-e004473. https://doi.org/10.1161/JAHA.112.004473

Crimmins, E. M., Shim, H., Zhang, Y. S., & Kim, J. K. (2019). Differences between Men and Women in Mortality and the Health Dimensions of the Morbidity Process. *Clin Chem*, *65*(1), 135-145. https://doi.org/10.1373/clinchem.2018.288332

Curry, F. R. (2005). Atrial natriuretic peptide: an essential physiological regulator of transvascular fluid, protein transport, and plasma volume. *J Clin Invest*, *115*(6), 1458-1461. https://doi.org/10.1172/jci25417

Degaute, J. P., van de Borne, P., Linkowski, P., & Van Cauter, E. (1991). Quantitative analysis of the 24-hour blood pressure and heart rate patterns in young men. *Hypertension*, *18*(2), 199-210. https://doi.org/10.1161/01.hyp.18.2.199

Demmer, D. L., Beilin, L. J., Hands, B., Burrows, S., Cox, K. L., Straker, L. M., & Mori, T. A. (2016). Effects of muscle strength and endurance on blood pressure and related cardiometabolic risk factors from childhood to adolescence. *Journal of hypertension*, *34*(12), 2365-2375. https://doi.org/10.1097/hjh.0000000000001116

Desai, A. N. (2020). High Blood Pressure. *Jama*, *324*(12), 1254-1255. https://doi.org/10.1001/jama.2020.11289

Ehret, G. B., Ferreira, T., Chasman, D. I., Jackson, A. U., Schmidt, E. M., Johnson, T., Thorleifsson, G., Luan, J., Donnelly, L. A., Kanoni, S., Petersen, A. K., Pihur, V., Strawbridge, R. J., Shungin, D., Hughes, M. F., Meirelles, O., Kaakinen, M., Bouatia-Naji, N., Kristiansson, K., . . . Munroe, P. B. (2016). The genetics of blood pressure regulation and its target organs from association studies in 342,415 individuals. *Nat Genet*, *48*(10), 1171-1184. https://doi.org/10.1038/ng.3667

Fahim, M. (1998). Role of arterial baroreceptor reflex in controlling circulation. *Current Science*, *75*(5), 443-450. http://www.jstor.org/stable/24101189

Fanelli Kuczmarski, M., Pohlig, R. T., Stave Shupe, E., Zonderman, A. B., & Evans, M. K. (2018). Dietary Protein Intake and Overall Diet Quality Are Associated with Handgrip Strength in African American and White Adults. *J Nutr Health Aging*, *22*(6), 700-709. https://doi.org/10.1007/s12603-018-1006-8

Feng, Q., Jiang, C., Wang, M., Cai, R., Wang, H., Wu, D., Wang, F., Lin, L., & Nassis, G. P. (2021). Association between relative handgrip strength and hypertension in Chinese adults: An analysis of four successive national surveys with 712,442 individuals (2000-2014). *PLoS One*, *16*(10), e0258763. https://doi.org/10.1371/journal.pone.0258763

Flack, J. M., Calhoun, D. A., Satlin, L., Barbier, M., Hilkert, R., & Brunel, P. (2009). Efficacy and safety of initial combination therapy with amlodipine/valsartan compared with amlodipine monotherapy in black patients with stage 2 hypertension: the EX-STAND study. *J Hum Hypertens*, *23*(7), 479-489. https://doi.org/10.1038/jhh.2008.153

Flack, J. M., Sica, D. A., Bakris, G., Brown, A. L., Ferdinand, K. C., Grimm, R. H., Jr., Hall, W. D., Jones, W. E., Kountz, D. S., Lea, J. P., Nasser, S., Nesbitt, S. D., Saunders, E., Scisney-Matlock, M., & Jamerson, K. A. (2010). Management of high blood pressure in Blacks: an update of the International Society on Hypertension in Blacks consensus statement. *Hypertension*, *56*(5), 780-800. https://doi.org/10.1161/hypertensionaha.110.152892

Flood, A., Chung, A., Parker, H., Kearns, V., & O'Sullivan, T. A. (2014). The use of hand grip strength as a predictor of nutrition status in hospital patients. *Clinical Nutrition*, *33*(1), 106-114. https://doi.org/https://doi.org/10.1016/j.clnu.2013.03.003

Fongwa, M. N., Evangelista, Lorraines S., Hays, Ron D., Martins, David S. , Elashoff, David, Cowan, Marie J. , Morisky, Donald E. . (2008). Adherence treatment factors in hypertensive African American women. *Vascular Healht and Risk Management*, *4*(1), 157-166.

Fountain, J. H., & Lappin, S. L. (2022). Physiology, Renin Angiotensin System. In *StatPearls*. StatPearls Publishing

Copyright © 2022, StatPearls Publishing LLC.

Fowles, J., Roy, J., Clarke, J., & Dogra, S. (2014). Are the fittest Canadian adults the healthiest? *Health Rep*, *25*(5), 13-18. https://www.ncbi.nlm.nih.gov/pubmed/24850392

Freeman, R., Abuzinadah, A. R., Gibbons, C., Jones, P., Miglis, M. G., & Sinn, D. I. (2018). Orthostatic Hypotension. *Journal of the American College of Cardiology*, *72*(11), 1294-1309. https://doi.org/doi:10.1016/j.jacc.2018.05.079

Fryar, C. D., Ostchega, Y., Hales, C. M., Zhang, G., & Kruszon-Moran, D. (2017). Hypertension Prevalence and Control Among Adults: United States, 2015-2016. *NCHS Data Brief*(289), 1-8.

Fuchs, F. D. (2011). Why do black Americans have higher prevalence of hypertension?: an enigma still unsolved. *Hypertension*, *57*(3), 379-380. https://doi.org/10.1161/HYPERTENSIONAHA.110.163196

Fuchs, F. D., & Whelton, P. K. (2020). High Blood Pressure and Cardiovascular Disease. *Hypertension*, *75*(2), 285-292. https://doi.org/10.1161/hypertensionaha.119.14240

Fuller-Rowell, T. E., Curtis, D. S., Klebanov, P. K., Brooks-Gunn, J., & Evans, G. W. (2017). Racial Disparities in Blood Pressure Trajectories of Preterm Children: The Role of Family and Neighborhood Socioeconomic Status. *Am J Epidemiol*, *185*(10), 888-897. https://doi.org/10.1093/aje/kww198

Gao, Y., Huang, H., Ni, C., Feng, Y., Yu, J., Huang, Y., Luo, L., Jiang, Y., & Wang, A. (2022). Comparison of Five Expressions of Handgrip Strength for Predicting Cardiovascular Disease Risk Factors in Chinese Middle-Aged Community Residents. *Front Public Health*, *10*, 903036. https://doi.org/10.3389/fpubh.2022.903036

Gauci, S., Cartledge, S., Redfern, J., Gallagher, R., Huxley, R., Lee, C. M. Y., Vassallo, A., & O'Neil, A. (2022). Biology, Bias, or Both? The Contribution of Sex and Gender to the Disparity in Cardiovascular Outcomes Between Women and Men. *Curr Atheroscler Rep*, *24*(9), 701-708. https://doi.org/10.1007/s11883-022-01046-2

Gaziano, T. A., Abrahams-Gessel, S., Gomez-Olive, F. X., Wade, A., Crowther, N. J., Alam, S., Manne-Goehler, J., Kabudula, C. W., Wagner, R., Rohr, J., Montana, L., Kahn, K., Bärnighausen, T. W., Berkman, L. F., & Tollman, S. (2017). Cardiometabolic risk in a population of older adults with multiple co-morbidities in rural south africa: the HAALSI (Health and Aging in Africa: longitudinal studies of INDEPTH communities) study. *BMC Public Health*, *17*(1), 206. https://doi.org/10.1186/s12889-017-4117-y

Ghazi, L., & Bello, N. A. (2021). Hypertension in Women Across the Lifespan [Review]. *Current Atherosclerosis Reports*, *23*(8), 11, Article 43. https://doi.org/10.1007/s11883-021-00941-4

Gillum, R. F. (1996). Epidemiology of hypertension in African American women. *American Heart Journal*, *131*(2), 385-395. https://doi.org/https://doi.org/10.1016/S0002-8703(96)90371-3

Gnugesser, E., Chwila, C., Brenner, S., Deckert, A., Dambach, P., Steinert, J. I., Bärnighausen, T., Horstick, O., Antia, K., & Louis, V. R. (2022). The economic burden of treating uncomplicated hypertension in Sub-Saharan Africa: a systematic literature review. *BMC Public Health*, *22*(1), 1507. https://doi.org/10.1186/s12889-022-13877-4

Gómez-Olivé, F. X., Ali, S. A., Made, F., Kyobutungi, C., Nonterah, E., Micklesfield, L., Alberts, M., Boua, R., Hazelhurst, S., Debpuur, C., Mashinya, F., Dikotope, S., Sorgho, H., Cook, I., Muthuri, S., Soo, C., Mukomana, F., Agongo, G., Wandabwa, C., . . . Ramsay, M. (2017). Regional and Sex Differences in the Prevalence and Awareness of Hypertension: An H3Africa AWI-Gen Study Across 6 Sites in Sub-Saharan Africa. *Glob Heart*, *12*(2), 81-90. https://doi.org/10.1016/j.gheart.2017.01.007

Gómez-Olivé, F. X., Montana, L., Wagner, R. G., Kabudula, C. W., Rohr, J. K., Kahn, K., Bärnighausen, T., Collinson, M., Canning, D., Gaziano, T., Salomon, J. A., Payne, C. F., Wade, A., Tollman, S. M., & Berkman, L. (2018). Cohort Profile: Health and Ageing in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI). *Int J Epidemiol*, *47*(3), 689-690j. https://doi.org/10.1093/ije/dyx247

Green, B. B., Anderson, M. L., Ehrlich, K., Hall, Y. N., Hansell, L. D., Hsu, C., Joseph, D., Margolis, K. L., McClure, J. B., Munson, S. A., & Thompson, M. J. (2022). Blood Pressure Checks for Diagnosing Hypertension: Health Professionals' Knowledge, Beliefs, and Practices. *J Am Board Fam Med*, *35*(2), 310-319. https://doi.org/10.3122/jabfm.2022.02.210318

Gubelmann, C., Vollenweider, P., & Marques-Vidal, P. (2017). Association of grip strength with cardiovascular risk markers. *Eur J Prev Cardiol*, *24*(5), 514-521. https://doi.org/10.1177/2047487316680695

Guerrero-García, C., & Rubio-Guerra, A. F. (2018). Combination therapy in the treatment of hypertension. *Drugs Context*, *7*, 212531. https://doi.org/10.7573/dic.212531

Guyton, A. C. (1991). Blood pressure control--special role of the kidneys and body fluids. *Science*, *252*(5014), 1813-1816. https://doi.org/10.1126/science.2063193

Hage, F. G., Mansur, S. J., Xing, D., & Oparil, S. (2013). Hypertension in women. *Kidney Int Suppl (2011)*, *3*(4), 352-356. https://doi.org/10.1038/kisup.2013.76

Hairi, N. N., Cumming, R. G., Naganathan, V., Handelsman, D. J., Le Couteur, D. G., Creasey, H., Waite, L. M., Seibel, M. J., & Sambrook, P. N. (2010). Loss of muscle strength, mass (sarcopenia), and quality (specific force) and its relationship with functional limitation and physical disability: the Concord Health and Ageing in Men Project. *J Am Geriatr Soc*, *58*(11), 2055-2062. https://doi.org/10.1111/j.1532-5415.2010.03145.x

Hall, W. J., Chapman, M. V., Lee, K. M., Merino, Y. M., Thomas, T. W., Payne, B. K., Eng, E., Day, S. H., & Coyne-Beasley, T. (2015). Implicit Racial/Ethnic Bias Among Health Care Professionals and Its Influence on Health Care Outcomes: A Systematic Review. *Am J Public Health*, *105*(12), e60-76. https://doi.org/10.2105/ajph.2015.302903

Hao, G., Chen, H., Ying, Y., Wu, M., Yang, G., & Jing, C. (2020). The Relative Handgrip Strength and Risk of Cardiometabolic Disorders: A Prospective Study. *Frontiers in physiology*, *11*, 719. Retrieved 2020, from http://europepmc.org/abstract/MED/32714207

Hardy, S. T., Sakhuja, S., Jaeger, B. C., Urbina, E. M., Suglia, S. F., Feig, D. I., & Muntner, P. (2021). Trends in Blood Pressure and Hypertension Among US Children and Adolescents, 1999-2018. *JAMA Netw Open*, *4*(4), e213917. https://doi.org/10.1001/jamanetworkopen.2021.3917

Hendriks, M. E., Wit, F. W., Roos, M. T., Brewster, L. M., Akande, T. M., de Beer, I. H., Mfinanga, S. G., Kahwa, A. M., Gatongi, P., Van Rooy, G., Janssens, W., Lammers, J., Kramer, B., Bonfrer, I., Gaeb, E., van der Gaag, J., Rinke de Wit, T. F., Lange, J. M., & Schultsz, C. (2012). Hypertension in sub-Saharan Africa: cross-sectional surveys in four rural and urban communities. *PLoS One*, *7*(3), e32638. https://doi.org/10.1371/journal.pone.0032638

Hicken, M. T., Lee, H., Morenoff, J., House, J. S., & Williams, D. R. (2014). Racial/ethnic disparities in hypertension prevalence: reconsidering the role of chronic stress. *Am J Public Health*, *104*(1), 117-123. https://doi.org/10.2105/AJPH.2013.301395

Hicks, L. S., Shaykevich, S., Bates, D. W., & Ayanian, J. Z. (2005). Determinants of racial/ethnic differences in blood pressure management among hypertensive patients. *BMC Cardiovasc Disord*, *5*(1), 16. https://doi.org/10.1186/1471-2261-5-16

Hiol, A. N., von Hurst, P. R., Conlon, C. A., Mugridge, O., & Beck, K. L. (2021). Body composition associations with muscle strength in older adults living in Auckland, New Zealand. *PLoS One*, *16*(5), e0250439. https://doi.org/10.1371/journal.pone.0250439

Houle, B., Kabudula, C. W., Tilstra, A. M., Mojola, S. A., Schatz, E., Clark, S. J., Angotti, N., Gómez-Olivé, F. X., & Menken, J. (2022). Twin epidemics: the effects of HIV and systolic blood pressure on mortality risk in rural South Africa, 2010-2019. *BMC Public Health*, *22*(1), 387. https://doi.org/10.1186/s12889-022-12791-z

Inder, J. D., Carlson, D. J., Dieberg, G., McFarlane, J. R., Hess, N. C., & Smart, N. A. (2016). Isometric exercise training for blood pressure management: a systematic review and meta-analysis to optimize benefit. *Hypertens Res*, *39*(2), 88-94. https://doi.org/10.1038/hr.2015.111

Inoue, T., Nonoguchi, H., & Tomita, K. (2001). Physiological effects of vasopressin and atrial natriuretic peptide in the collecting duct. *Cardiovascular Research*, *51*(3), 470-480. https://doi.org/10.1016/s0008-6363(01)00248-6

Ivy, J. R., & Bailey, M. A. (2014). Pressure natriuresis and the renal control of arterial blood pressure. *J Physiol*, *592*(18), 3955-3967. https://doi.org/10.1113/jphysiol.2014.271676

James, P. A., Oparil, S., Carter, B. L., Cushman, W. C., Dennison-Himmelfarb, C., Handler, J., Lackland, D. T., LeFevre, M. L., MacKenzie, T. D., Ogedegbe, O., Smith, S. C., Jr., Svetkey, L. P., Taler, S. J., Townsend, R. R., Wright, J. T., Jr., Narva, A. S., & Ortiz, E. (2014). 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*, *311*(5), 507-520. https://doi.org/10.1001/jama.2013.284427

Ji, C., Zheng, L., Zhang, R., Wu, Q., & Zhao, Y. (2018). Handgrip strength is positively related to blood pressure and hypertension risk: results from the National Health and nutrition examination survey. *Lipids in health and disease*, *17*(1), 86-86. https://doi.org/10.1186/s12944-018-0734-4

Ji, H., Kim, A., Ebinger, J. E., Niiranen, T. J., Claggett, B. L., Bairey Merz, C. N., & Cheng, S. (2020). Sex Differences in Blood Pressure Trajectories Over the Life Course. *JAMA Cardiol*. https://doi.org/10.1001/jamacardio.2019.5306

Joyner, M. J., Barnes, J. N., Hart, E. C., Wallin, B. G., & Charkoudian, N. (2015). Neural control of the circulation: how sex and age differences interact in humans. *Compr Physiol*, *5*(1), 193-215. https://doi.org/10.1002/cphy.c140005

Joyner, M. J., & Limberg, J. K. (2014). Blood pressure regulation: every adaptation is an integration? *Eur J Appl Physiol*, *114*(3), 445-450. https://doi.org/10.1007/s00421-013-2636-5

Kandala, N. B., Nnanatu, C. C., Dukhi, N., Sewpaul, R., Davids, A., & Reddy, S. P. (2021). Mapping the Burden of Hypertension in South Africa: A Comparative Analysis of the National 2012 SANHANES and the 2016 Demographic and Health Survey. *Int J Environ Res Public Health*, *18*(10). https://doi.org/10.3390/ijerph18105445

Kang, S. Y., Lim, J., & Park, H. S. (2018). Relationship between low handgrip strength and quality of life in Korean men and women. *Qual Life Res*, *27*(10), 2571-2580. https://doi.org/10.1007/s11136-018-1920-6

Karvonen-Gutierrez, C. A., Peng, Q., Peterson, M., Duchowny, K., Nan, B., & Harlow, S. (2018). Low grip strength predicts incident diabetes among mid-life women: the Michigan Study of Women's Health Across the Nation. *Age Ageing*, *47*(5), 685-691. https://doi.org/10.1093/ageing/afy067

Kauko, A., Aittokallio, J., Vaura, F., Ji, H. W., Ebinger, J. E., Niiranen, T., & Cheng, S. S. (2021). Sex Differences in Genetic Risk for Hypertension [Letter]. *Hypertension*, *78*(4), 1153-1155. https://doi.org/10.1161/hypertensionaha.121.17796

Kawamoto, R., Ninomiya, D., Kasai, Y., Kusunoki, T., Ohtsuka, N., Kumagi, T., & Abe, M. (2016). Handgrip strength is associated with metabolic syndrome among middle-aged and elderly community-dwelling persons. *Clin Exp Hypertens*, *38*(2), 245-251. https://doi.org/10.3109/10641963.2015.1081232

Kaze, A. D., Schutte, A. E., Erqou, S., Kengne, A. P., & Echouffo-Tcheugui, J. B. (2017). Prevalence of hypertension in older people in Africa: a systematic review and meta-analysis. *J Hypertens*, *35*(7), 1345-1352. https://doi.org/10.1097/hjh.0000000000001345

Keevil, V. L., Luben, R., Dalzell, N., Hayat, S., Sayer, A. A., Wareham, N. J., & Khaw, K. T. (2015). Cross-sectional associations between different measures of obesity and muscle strength in men and women in a British cohort study. *J Nutr Health Aging*, *19*(1), 3-11. https://doi.org/10.1007/s12603-014-0492-6

Khatib, R., Schwalm, J. D., Yusuf, S., Haynes, R. B., McKee, M., Khan, M., & Nieuwlaat, R. (2014). Patient and healthcare provider barriers to hypertension awareness, treatment and follow up: a systematic review and meta-analysis of qualitative and quantitative studies. *PLoS One*, *9*(1), e84238. https://doi.org/10.1371/journal.pone.0084238

Kim, J. Y., Park, H. Y., Kim, J., & Lim, K. (2021). Body mass index and relative handgrip strength are associated with the prevalence of hypertension in Korean elderly: Korean national fitness assessment in 2019. *Phys Act Nutr*, *25*(2), 26-32. https://doi.org/10.20463/pan.2021.0012

Kirkland, E. B., Heincelman, M., Bishu, K. G., Schumann, S. O., Schreiner, A., Axon, R. N., Mauldin, P. D., & Moran, W. P. (2018). Trends in Healthcare Expenditures Among US Adults With Hypertension: National Estimates, 2003-2014. *J Am Heart Assoc*, *7*(11). https://doi.org/10.1161/jaha.118.008731

Kohli-Lynch, C. N., Erzse, A., Rayner, B., & Hofman, K. J. (2022). Hypertension in the South African public healthcare system: a cost-of-illness and burden of disease study. *BMJ Open*, *12*(2), e055621. https://doi.org/10.1136/bmjopen-2021-055621

König, M., Buchmann, N., Seeland, U., Spira, D., Steinhagen-Thiessen, E., & Demuth, I. (2021). Low muscle strength and increased arterial stiffness go hand in hand. *Scientific Reports*, *11*(1), 2906. https://doi.org/10.1038/s41598-021-81084-z

Koopman, J. J. E., van Bodegom, D., van Heemst, D., & Westendorp, R. G. J. (2014). Handgrip strength, ageing and mortality in rural Africa. *Age and Ageing*, *44*(3), 465-470. https://doi.org/10.1093/ageing/afu165

Kotchen, T. A. (2010). The search for strategies to control hypertension. *Circulation*, *122*(12), 1141-1143. https://doi.org/10.1161/circulationaha.110.978759

Lackland, D. T. (2014). Racial differences in hypertension: implications for high blood pressure management. *Am J Med Sci*, *348*(2), 135-138. https://doi.org/10.1097/MAJ.0000000000000308

Lad, U. P., Satyanarayana, P., Shisode-Lad, S., Siri Ch, C., & Kumari, N. R. (2013). A Study on the Correlation Between the Body Mass Index (BMI), the Body Fat Percentage, the Handgrip Strength and the Handgrip Endurance in Underweight, Normal Weight and Overweight Adolescents. *J Clin Diagn Res*, *7*(1), 51-54. https://doi.org/10.7860/jcdr/2012/5026.2668

Laddu, D. R., LaMonte, M. J., Haring, B., Kim, H., Cawthon, P., Bea, J. W., Banack, H., Cauley, J. A., Allison, M. A., Martin, L. W., LeBoff, M. S., Stefanick, M. L., Phillips, S. A., & Ma, J. (2022). Longitudinal physical performance and blood pressure changes in older women: Findings form the women's health initiative. *Arch Gerontol Geriatr*, *98*, 104576. https://doi.org/10.1016/j.archger.2021.104576

Lau, E. S., Paniagua, S. M., Guseh, J. S., Bhambhani, V., Zanni, M. V., Courchesne, P., Lyass, A., Larson, M. G., Levy, D., & Ho, J. E. (2019). Sex Differences in Circulating Biomarkers of Cardiovascular Disease. *J Am Coll Cardiol*, *74*(12), 1543-1553. https://doi.org/10.1016/j.jacc.2019.06.077

Lawman, H. G. P., Troiano, R. P. P., Perna, F. M. P., Wang, C.-Y. P., Fryar, C. D. M., & Ogden, C. L. P. (2015). Associations of Relative Handgrip Strength and Cardiovascular Disease Biomarkers in U.S. Adults, 2011–2012. *American journal of preventive medicine*, *50*(6), 677-683. https://doi.org/10.1016/j.amepre.2015.10.022

Lee, K., Lee, J. Y., & Kim, Y. H. (2021). Low Grip Strength and Muscle Mass Increase the Prevalence of Osteopenia and Osteoporosis in Elderly Women. *Healthcare (Basel)*, *9*(4). https://doi.org/10.3390/healthcare9040476

Lee, S. H., & Gong, H. S. (2020). Measurement and Interpretation of Handgrip Strength for Research on Sarcopenia and Osteoporosis. *J Bone Metab*, *27*(2), 85-96. https://doi.org/10.11005/jbm.2020.27.2.85

Lee, W. J., Peng, L. N., Chiou, S. T., & Chen, L. K. (2016). Relative Handgrip Strength Is a Simple Indicator of Cardiometabolic Risk among Middle-Aged and Older People: A Nationwide Population-Based Study in Taiwan. *PLoS One*, *11*(8), e0160876. https://doi.org/10.1371/journal.pone.0160876

Leong, D. P., Teo, K. K., Rangarajan, S., Kutty, V. R., Lanas, F., Hui, C., Quanyong, X., Zhenzhen, Q., Jinhua, T., Noorhassim, I., AlHabib, K. F., Moss, S. J., Rosengren, A., Akalin, A. A., Rahman, O., Chifamba, J., Orlandini, A., Kumar, R., Yeates, K., . . . Yusuf, S. (2016). Reference ranges of handgrip strength from 125,462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. *J Cachexia Sarcopenia Muscle*, *7*(5), 535-546. https://doi.org/10.1002/jcsm.12112

Leong, D. P., Teo, K. K., Rangarajan, S., Lopez-Jaramillo, P., Avezum, A., Jr., Orlandini, A., Seron, P., Ahmed, S. H., Rosengren, A., Kelishadi, R., Rahman, O., Swaminathan, S., Iqbal, R., Gupta, R., Lear, S. A., Oguz, A., Yusoff, K., Zatonska, K., Chifamba, J., . . . Yusuf, S. (2015). Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*, *386*(9990), 266-273. https://doi.org/10.1016/s0140-6736(14)62000-6

Leung, A. A., Daskalopoulou, S. S., Dasgupta, K., McBrien, K., Butalia, S., Zarnke, K. B., Nerenberg, K., Harris, K. C., Nakhla, M., Cloutier, L., Gelfer, M., Lamarre-Cliche, M., Milot, A., Bolli, P., Tremblay, G., McLean, D., Tran, K. C., Tobe, S. W., Ruzicka, M., . . . Rabi, D. M. (2017). Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults. *Can J Cardiol*, *33*(5), 557-576. https://doi.org/10.1016/j.cjca.2017.03.005

Lewington, S., Clarke, R., Qizilbash, N., Peto, R., & Collins, R. (2002). Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*, *360*(9349), 1903-1913. https://doi.org/10.1016/s0140-6736(02)11911-8

Liguori, G. (2021). *ACSM's Guidelines for Exercise Testing and Prescription*, *11th Edition*. Lippincott Williams & Wilkins.

Liu, G., Xue, Y., Wang, S., Zhang, Y., & Geng, Q. (2021). Association between hand grip strength and stroke in China: a prospective cohort study. *Aging*, *13*(6), 8204-8213. https://doi.org/10.18632/aging.202630

Lloyd-Sherlock, P., Beard, J., Minicuci, N., Ebrahim, S., & Chatterji, S. (2014). Hypertension among older adults in low- and middle-income countries: prevalence, awareness and control. *Int J Epidemiol*, *43*(1), 116-128. https://doi.org/10.1093/ije/dyt215

Lombardi M, S. P., Mazza A, Bendini MG, Caldarone E, Armeni M, D'Emidio, S, and Leggio, M. (2017). Sex Differences in Hypertension: A Question worth Asking? *Annals of Clinical Hypertension*(1), 001-005. https://doi.org/10.29328/journal.ach.1001001

López-Bueno, R., Andersen, L. L., Calatayud, J., Casaña, J., Smith, L., Jacob, L., Koyanagi, A., López-Gil, J. F., & del Pozo Cruz, B. (2022). Longitudinal association of handgrip strength with all-cause and cardiovascular mortality in older adults using a causal framework. *Experimental Gerontology*, *168*, 111951. https://doi.org/https://doi.org/10.1016/j.exger.2022.111951

Maas, A. H. E. M. (2019). Hypertension in women: no "silent" lady killer. *E-Journal of Cardiology Practice*, *17*(21). https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-17/hypertension-in-women-no-silent-lady-killer

Maimela, E., Alberts, M., Modjadji, S. E., Choma, S. S., Dikotope, S. A., Ntuli, T. S., & Van Geertruyden, J. P. (2016). The Prevalence and Determinants of Chronic Non-Communicable Disease Risk Factors amongst Adults in the Dikgale Health Demographic and Surveillance System (HDSS) Site, Limpopo Province of South Africa. *PLoS One*, *11*(2), e0147926. https://doi.org/10.1371/journal.pone.0147926

Mainous, A. G., 3rd, Tanner, R. J., Anton, S. D., & Jo, A. (2015). Grip Strength as a Marker of Hypertension and Diabetes in Healthy Weight Adults. *Am J Prev Med*, *49*(6), 850-858. https://doi.org/10.1016/j.amepre.2015.05.025

Mallah, M. A., Liu, M., Liu, Y., Xu, H.-F., Wu, X.-J., Chen, X.-T., Wang, H., Liu, C.-L., Tian, Y.-R., Li, M.-X., Li, Q., Fu, J., & Shen, C. (2019). Association of handgrip strength with the prevalence of hypertension in a Chinese Han population. *Chronic Diseases and Translational Medicine*, *5*(2), 113-121. https://doi.org/https://doi.org/10.1016/j.cdtm.2019.05.004

Manafe, M., Chelule, P. K., & Madiba, S. (2022). The Perception of Overweight and Obesity among South African Adults: Implications for Intervention Strategies. *Int J Environ Res Public Health*, *19*(19). https://doi.org/10.3390/ijerph191912335

Mancia, G., Fagard, R., Narkiewicz, K., Redón, J., Zanchetti, A., Böhm, M., Christiaens, T., Cifkova, R., De Backer, G., Dominiczak, A., Galderisi, M., Grobbee, D. E., Jaarsma, T., Kirchhof, P., Kjeldsen, S. E., Laurent, S., Manolis, A. J., Nilsson, P. M., Ruilope, L. M., . . . Zannad, F. (2013). 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*, *31*(7), 1281-1357. https://doi.org/10.1097/01.hjh.0000431740.32696.cc

Mannelli, M., Rossi, G. P., Vanderriele, P.-E., & Parenti, G. (2018). The Endocrine Regulation of Blood Pressure. In A. Belfiore & D. LeRoith (Eds.), *Principles of Endocrinology and Hormone Action* (pp. 611-625). Springer International Publishing. https://doi.org/10.1007/978-3-319-44675-2_23

Maranon, R., & Reckelhoff, J. F. (2013). Sex and gender differences in control of blood pressure. *Clin Sci (Lond)*, *125*(7), 311-318. https://doi.org/10.1042/CS20130140

Martinez-Quinones, P., McCarthy, C. G., Watts, S. W., Klee, N. S., Komic, A., Calmasini, F. B., Priviero, F., Warner, A., Chenghao, Y., & Wenceslau, C. F. (2018). Hypertension Induced Morphological and Physiological Changes in Cells of the Arterial Wall. *Am J Hypertens*, *31*(10), 1067-1078. https://doi.org/10.1093/ajh/hpy083

Mayfield, S. K., Foti, K., Moran, A. E., Blakeman, D. E., & Frieden, T. R. (2022). Hypertension Call to Action: Will We Respond to the Call With Action? *Am J Hypertens*, *35*(3), 214-216. https://doi.org/10.1093/ajh/hpab191

McDonald, M., Hertz, R. P., Unger, A. N., & Lustik, M. B. (2009). Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci*, *64*(2), 256-263. https://doi.org/10.1093/gerona/gln016

McGrath, R. P., Kraemer, W. J., Snih, S. A., & Peterson, M. D. (2018). Handgrip Strength and Health in Aging Adults. *Sports medicine (Auckland, N.Z.)*, *48*(9), 1993-2000. https://doi.org/10.1007/s40279-018-0952-y

Mena, L. J., Felix, V. G., Melgarejo, J. D., & Maestre, G. E. (2017). 24-Hour Blood Pressure Variability Assessed by Average Real Variability: A Systematic Review and Meta-Analysis. *J Am Heart Assoc*, *6*(10). https://doi.org/10.1161/jaha.117.006895

Mensah, G. A. (2016). Hypertension and Target Organ Damage: Don't Believe Everything You Think! *Ethn Dis*, *26*(3), 275-278. https://doi.org/10.18865/ed.26.3.275

Mensah, G. A., Mokdad, A. H., Ford, E. S., Greenlund, K. J., & Croft, J. B. (2005). State of disparities in cardiovascular health in the United States. *Circulation*, *111*(10), 1233-1241. https://doi.org/10.1161/01.CIR.0000158136.76824.04

Messerli Franz, H., Rimoldi Stefano, F., & Bangalore, S. (2017). The Transition From Hypertension to Heart Failure. *JACC: Heart Failure*, *5*(8), 543-551. https://doi.org/10.1016/j.jchf.2017.04.012

Midlife in the United States: A National Longitudinal Study of Health & Well-Being (2022). University of Wisconsin-Madison, Institute of Aging Retrieved 10/26/21

Mills, K. T., Bundy, J. D., Kelly, T. N., Reed, J. E., Kearney, P. M., Reynolds, K., Chen, J., & He, J. (2016). Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation*, *134*(6), 441-450. https://doi.org/10.1161/CIRCULATIONAHA.115.018912

Mills, K. T., Stefanescu, A., & He, J. (2020). The global epidemiology of hypertension. *Nat Rev Nephrol*, *16*(4), 223-237. https://doi.org/10.1038/s41581-019-0244-2

Modena, M. G. (2014). Hypertension in postmenopausal women: how to approach hypertension in menopause. *High Blood Press Cardiovasc Prev*, *21*(3), 201-204. https://doi.org/10.1007/s40292-014-0057-0

Mohsen Ibrahim, M. (2018). Hypertension in Developing Countries: A Major Challenge for the Future. *Curr Hypertens Rep*, *20*(5), 38. https://doi.org/10.1007/s11906-018-0839-1

Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., Das, S. R., de Ferranti, S., Després, J. P., Fullerton, H. J., Howard, V. J., Huffman, M. D., Isasi, C. R., Jiménez, M. C., Judd, S. E., Kissela, B. M., Lichtman, J. H., Lisabeth, L. D., Liu, S., . . . Turner, M. B. (2016). Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation*, *133*(4), e38-360. https://doi.org/10.1161/cir.0000000000000350

Mueller, M., Purnell, T. S., Mensah, G. A., & Cooper, L. A. (2015). Reducing racial and ethnic disparities in hypertension prevention and control: what will it take to translate research into practice and policy? *Am J Hypertens*, *28*(6), 699-716. https://doi.org/10.1093/ajh/hpu233

Muiesan, M. L., Paini, A., Aggiusti, C., Bertacchini, F., Rosei, C. A., & Salvetti, M. (2018). Hypertension and Organ Damage in Women. *High Blood Press Cardiovasc Prev*, *25*(3), 245-252. https://doi.org/10.1007/s40292-018-0265-0

Muiesan, M. L., Salvetti, M., Rizzoni, D., Paini, A., Agabiti-Rosei, C., Aggiusti, C., & Agabiti Rosei, E. (2013). Resistant hypertension and target organ damage. *Hypertension Research*, *36*(6), 485-491. https://doi.org/10.1038/hr.2013.30

Muntner, P., Abdalla, M., Correa, A., Griswold, M., Hall, J. E., Jones, D. W., Mensah, G. A., Sims, M., Shimbo, D., Spruill, T. M., Tucker, K. L., & Appel, L. J. (2017). Hypertension in Blacks: Unanswered Questions and Future Directions for the JHS (Jackson Heart Study). *Hypertension*, *69*(5), 761-769. https://doi.org/10.1161/HYPERTENSIONAHA.117.09061

Muntner, P., Carey, R. M., Gidding, S., Jones, D. W., Taler, S. J., Wright, J. T., Jr., & Whelton, P. K. (2018). Potential US Population Impact of the 2017 ACC/AHA High Blood Pressure Guideline. *Circulation*, *137*(2), 109-118. https://doi.org/10.1161/circulationaha.117.032582

Muntner, P., Hardy, S. T., Fine, L. J., Jaeger, B. C., Wozniak, G., Levitan, E. B., & Colantonio, L. D. (2020). Trends in Blood Pressure Control Among US Adults With Hypertension, 1999-2000 to 2017-2018. *Jama*, *324*(12), 1190-1200. https://doi.org/10.1001/jama.2020.14545

Muntner, P., Shimbo, D., Carey, R. M., Charleston, J. B., Gaillard, T., Misra, S., Myers, M. G., Ogedegbe, G., Schwartz, J. E., Townsend, R. R., Urbina, E. M., Viera, A. J., White, W. B., & Wright, J. T., Jr. (2019). Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association. *Hypertension*, *73*(5), e35-e66. https://doi.org/10.1161/HYP.0000000000000087

Mutz, J., & Lewis, C. M. (2021). Lifetime depression and age-related changes in body composition, cardiovascular function, grip strength and lung function: sex-specific analyses in the UK Biobank. *Aging*, *13*(13), 17038-17079. https://doi.org/10.18632/aging.203275

Myers, M. G., Godwin, M., Dawes, M., Kiss, A., Tobe, S. W., & Kaczorowski, J. (2012). Conventional versus automated measurement of blood pressure in the office (CAMBO) trial. *Fam Pract*, *29*(4), 376-382. https://doi.org/10.1093/fampra/cmr113

National Department of Health, & ICF. (2019). *South Africa Demographic and Health Survey 2016*. http://dhsprogram.com/pubs/pdf/FR337/FR337.pdf

NCHS. (2019). *Health, United States, 2018*.

Nesbitt, S. D. (2005). Hypertension in Black Patients: Special Issues and Considerations. *Curr Hypertens Rep*(7), 244-248.

Nesbitt, S. D. (2008). Environmental,Societal and Genetic Contributions to the Epidemic of Hypertension in African Americans. *Curr Hypertens Rep*(2), 181-186.

Ntuk, U. E., Celis-Morales, C. A., Mackay, D. F., Sattar, N., Pell, J. P., & Gill, J. M. R. (2017). Association between grip strength and diabetes prevalence in black, South-Asian, and white European ethnic groups: a cross-sectional analysis of 418 656 participants in the UK Biobank study. *Diabet Med*, *34*(8), 1120-1128. https://doi.org/10.1111/dme.13323

Odedosu, T., Schoenthaler, A., Vieira, D. L., Agyemang, C., & Ogedegbe, G. (2012). Overcoming barriers to hypertension control in African Americans. *Cleve Clin J Med*, *79*(1), 46-56. https://doi.org/10.3949/ccjm.79a.11068

Ogedegbe, G. (2008). Barriers to optimal hypertension control. *J Clin Hypertens (Greenwich)*, *10*(8), 644-646. https://doi.org/10.1111/j.1751-7176.2008.08329.x

Ogedegbe, G., & Pickering, T. (2010). Principles and techniques of blood pressure measurement. *Cardiol Clin*, *28*(4), 571-586. https://doi.org/10.1016/j.ccl.2010.07.006

Pagani, M., & Lucini, D. (2001). Autonomic dysregulation in essential hypertension: insight from heart rate and arterial pressure variability. *Auton Neurosci*, *90*(1-2), 76-82. https://doi.org/10.1016/s1566-0702(01)00270-3

Panza, G. A., Puhl, R. M., Taylor, B. A., Zaleski, A. L., Livingston, J., & Pescatello, L. S. (2019). Links between discrimination and cardiovascular health among socially stigmatized groups: A systematic review. *PLoS One*, *14*(6), e0217623. https://doi.org/10.1371/journal.pone.0217623

Parati, G., Torlasco, C., Pengo, M., Bilo, G., & Ochoa, J. E. (2020). Blood pressure variability: its relevance for cardiovascular homeostasis and cardiovascular diseases. *Hypertens Res*, *43*(7), 609-620. https://doi.org/10.1038/s41440-020-0421-5

Peck, R. N., Smart, L. R., Beier, R., Liwa, A. C., Grosskurth, H., Fitzgerald, D. W., & Schmidt, B. M. W. (2013). Difference in blood pressure response to ACE-Inhibitor monotherapy between black and white adults with arterial hypertension: a meta-analysis of 13 clinical trials. *BMC Nephrology*, *14*(1), 201. https://doi.org/10.1186/1471-2369-14-201

Pescatello, L. S., Franklin, B. A., Fagard, R., Farquhar, W. B., Kelley, G. A., & Ray, C. A. (2004). American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exerc*, *36*(3), 533-553. https://doi.org/10.1249/01.mss.0000115224.88514.3a

Pescatello, L. S., MacDonald, H. V., Lamberti, L., & Johnson, B. T. (2015). Exercise for Hypertension: A Prescription Update Integrating Existing Recommendations with Emerging Research. *Current Hypertension Reports*, *17*(11), 87. https://doi.org/10.1007/s11906-015-0600-y

Peters, P. G., Alessio, H. M., Hagerman, A. E., Ashton, T., Nagy, S., & Wiley, R. L. (2006). Short-term isometric exercise reduces systolic blood pressure in hypertensive adults: possible role of reactive oxygen species. *Int J Cardiol*, *110*(2), 199-205. https://doi.org/10.1016/j.ijcard.2005.07.035

Peterson, M. D., Duchowny, K., Meng, Q., Wang, Y., Chen, X., & Zhao, Y. (2017). Low Normalized Grip Strength is a Biomarker for Cardiometabolic Disease and Physical Disabilities Among U.S. and Chinese Adults. *J Gerontol A Biol Sci Med Sci*, *72*(11), 1525-1531. https://doi.org/10.1093/gerona/glx031

Peterson, M. D., Zhang, P., Choksi, P., Markides, K. S., & Al Snih, S. (2016). Muscle Weakness Thresholds for Prediction of Diabetes in Adults. *Sports Med*, *46*(5), 619-628. https://doi.org/10.1007/s40279-015-0463-z

Pickering, T. G., Hall, J. E., Appel, L. J., Falkner, B. E., Graves, J., Hill, M. N., Jones, D. W., Kurtz, T., Sheps, S. G., & Roccella, E. J. (2005). Recommendations for Blood Pressure Measurement in Humans and Experimental Animals. *Circulation*, *111*(5), 697-716. https://doi.org/doi:10.1161/01.CIR.0000154900.76284.F6

Poulter, N. R., Castillo, R., Charchar, F. J., Schlaich, M. P., Schutte, A. E., Tomaszewski, M., Touyz, R. M., & Wang, J. G. (2018). Are the American Heart Association/American College of Cardiology High Blood Pressure Guidelines Fit for Global Purpose?: Thoughts From the International Society of Hypertension. *Hypertension*, *72*(2), 260-262. https://doi.org/10.1161/hypertensionaha.118.11452

Poulter, N. R., Prabhakaran, D., & Caulfield, M. (2015). Hypertension. *Lancet*, *386*(9995), 801-812. https://doi.org/10.1016/s0140-6736(14)61468-9

Prasitsiriphon, O., & Pothisiri, W. (2018). Associations of Grip Strength and Change in Grip Strength With All-Cause and Cardiovascular Mortality in a European Older Population. *Clinical Medicine Insights. Cardiology*, *12*, 1179546818771894. Retrieved 2018, from http://europepmc.org/abstract/MED/29881318

Radler, B. T. (2014). The Midlife in the United States (MIDUS) Series: A National Longitudinal Study of Health and Well-being. *Open Health Data*, *2*(1). https://doi.org/10.5334/ohd.ai

Ramirez, L. A., & Sullivan, J. C. (2018). Sex Differences in Hypertension: Where We Have Been and Where We Are Going. *Am J Hypertens*, *31*(12), 1247-1254. https://doi.org/10.1093/ajh/hpy148

Rantanen, T., Guralnik, J. M., Leveille, S., Izmirlian, G., Hirsch, R., Simonsick, E., Ling, S., & Fried, L. P. (1998). Racial differences in muscle strength in disabled older women. *J Gerontol A Biol Sci Med Sci*, *53*(5), B355-361. https://doi.org/10.1093/gerona/53a.5.b355

Raven, P. B., & Chapleau, M. W. (2014). Blood pressure regulation XI: overview and future research directions. *Eur J Appl Physiol*, *114*(3), 579-586. https://doi.org/10.1007/s00421-014-2823-z

Rayner, B., Jones, E., Veriava, Y., & Seedat, Y. K. (2019). South African Hypertension Society commentary on the American College of Cardiology/American Heart Association hypertension guidelines. *Cardiovascular journal of Africa*, *30*(3), 184-187. https://doi.org/10.5830/cvja-2019-025

Reckelhoff, J. F. (2007). Polycystic ovary syndrome: androgens and hypertension. *Hypertension*, *49*(6), 1220-1221. https://doi.org/10.1161/hypertensionaha.107.088138

Reddick, B. (2021). Fallacies and Dangers of Practicing Race-Based Medicine. *Am Fam Physician*, *104*(2), 122-123.

Reglin, B., & Pries, A. R. (2014). Metabolic control of microvascular networks: oxygen sensing and beyond. *J Vasc Res*, *51*(5), 376-392. https://doi.org/10.1159/000369460

Rimando, M. (2015). Perceived Barriers to and Facilitators of Hypertension Management among Underserved African American Older Adults. *Ethn Dis*, *25*(3), 329-336. https://doi.org/10.18865/ed.25.3.329

Rimoldi, S. F., Scherrer, U., & Messerli, F. H. (2014). Secondary arterial hypertension: when, who, and how to screen? *Eur Heart J*, *35*(19), 1245-1254. https://doi.org/10.1093/eurheartj/eht534

Roberts, D. E. (2008, 2008 Fall). Is race-based medicine good for us? African American approaches to race, biomedicine, and equality. *Journal of Law, Medicine & Ethics*, *36*(3), 537+. https://link.gale.com/apps/doc/A186516804/AONE?u=char69915&sid=bookmark-AONE&xid=2e46c8c4

Roberts, D. E. (2011). What's Wrong with Race-Based Medicine. *Minnesota Journal of Law, Science, and Technology*, *435*. https://scholarship.law.upenn.edu/faculty_scholarship/435

Samad, Z., Wang, T. Y., Frazier, C. G., Shah, S. H., Dolor, R. J., & Newby, L. K. (2008). Closing the gap: treating hypertension in women. *Cardiol Rev*, *16*(6), 305-313. https://doi.org/10.1097/CRD.0b013e31817f9350

Sandberg, K., & Ji, H. (2012). Sex differences in primary hypertension. *Biol Sex Differ*, *3*(1), 7. https://doi.org/10.1186/2042-6410-3-7

Sanders, J. S., Mark, A. L., & Ferguson, D. W. (1989). Importance of aortic baroreflex in regulation of sympathetic responses during hypotension. Evidence from direct sympathetic nerve recordings in humans. *Circulation*, *79*(1), 83-92. https://doi.org/10.1161/01.cir.79.1.83

Saugel, B., Thiele, R. H., Hapfelmeier, A., & Cannesson, M. (2020). Technological Assessment and Objective Evaluation of Minimally Invasive and Noninvasive Cardiac Output Monitoring Systems. *Anesthesiology*, *133*(4), 921-928. https://doi.org/10.1097/aln.0000000000003483

Sayer, A. A., & Kirkwood, T. B. L. (2015). Grip strength and mortality: a biomarker of ageing? *The Lancet*, *386*(9990), 226-227. https://doi.org/https://doi.org/10.1016/S0140-6736(14)62349-7

Sayer, A. A., Syddall, H. E., Dennison, E. M., Martin, H. J., Phillips, D. I. W., Cooper, C., Byrne, C. D., & Hertfordshire, C. (2007). Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. *QJM : monthly journal of the Association of Physicians*, *100*(11), 707-713. https://doi.org/10.1093/qjmed/hcm095

Schutte, A. E., Srinivasapura Venkateshmurthy, N., Mohan, S., & Prabhakaran, D. (2021). Hypertension in Low- and Middle-Income Countries. *Circ Res*, *128*(7), 808-826. https://doi.org/10.1161/circresaha.120.318729

Seedat, Y. K., Rayner, B. L., & Veriava, Y. (2014). South African hypertension practice guideline 2014. *Cardiovascular journal of Africa*, *25*(6), 288-294. https://doi.org/10.5830/cvja-2014-062

Shahoud, J. S., Sanvictores, T., & Aeddula, N. R. (2022). Physiology, Arterial Pressure Regulation. In *StatPearls*. StatPearls Publishing

Copyright © 2022, StatPearls Publishing LLC.

Sharma, J. N. (2009). Hypertension and the bradykinin system. *Curr Hypertens Rep*, *11*(3), 178-181. https://doi.org/10.1007/s11906-009-0032-7

Shimbo, D., Abdalla, M., Falzon, L., Townsend, R. R., & Muntner, P. (2015). Role of Ambulatory and Home Blood Pressure Monitoring in Clinical Practice: A Narrative Review. *Ann Intern Med*, *163*(9), 691-700. https://doi.org/10.7326/m15-1270

Shirwany, N. A., & Zou, M. H. (2010). Arterial stiffness: a brief review. *Acta Pharmacol Sin*, *31*(10), 1267-1276. https://doi.org/10.1038/aps.2010.123

Silva, G. O., Farah, B. Q., Germano-Soares, A. H., Andrade-Lima, A., Santana, F. S., Rodrigues, S. L., & Ritti-Dias, R. M. (2018). Acute blood pressure responses after different isometric handgrip protocols in hypertensive patients. *Clinics (Sao Paulo)*, *73*, e373. https://doi.org/10.6061/clinics/2018/e373

Sliwa, K., Ojji, D., Bachelier, K., Bohm, M., Damasceno, A., & Stewart, S. (2014). Hypertension and hypertensive heart disease in African women. *Clin Res Cardiol*, *103*(7), 515-523. https://doi.org/10.1007/s00392-014-0660-z

Smart, N. A., Way, D., Carlson, D., Millar, P., McGowan, C., Swaine, I., Baross, A., Howden, R., Ritti-Dias, R., Wiles, J., Cornelissen, V., Gordon, B., Taylor, R., & Bleile, B. (2019). Effects of isometric resistance training on resting blood pressure: individual participant data meta-analysis. *J Hypertens*, *37*(10), 1927-1938. https://doi.org/10.1097/HJH.0000000000002105

Sola-Rodríguez, S., Vargas-Hitos, J. A., Gavilán-Carrera, B., Rosales-Castillo, A., Sabio, J. M., Hernández-Martínez, A., Martínez-Rosales, E., Ortego-Centeno, N., & Soriano-Maldonado, A. (2021). Relative Handgrip Strength as Marker of Cardiometabolic Risk in Women with Systemic Lupus Erythematosus. *Int J Environ Res Public Health*, *18*(9). https://doi.org/10.3390/ijerph18094630

Sousa-Santos, A. R., & Amaral, T. F. (2017). Differences in handgrip strength protocols to identify sarcopenia and frailty - a systematic review. *BMC geriatrics*, *17*(1), 238. https://doi.org/10.1186/s12877-017-0625-y

Souza Saraiva, W., Prestes, J., Schwerz Funghetto, S., Navalta, J. W., Tibana, R. A., & da Cunha Nascimento, D. (2019). Relation Between Relative Handgrip Strength, Chronological Age and Physiological Age with Lower Functional Capacity in Older Women. *Open Access J Sports Med*, *10*, 185-190. https://doi.org/10.2147/oajsm.S227720

Soysal, P., Hurst, C., Demurtas, J., Firth, J., Howden, R., Yang, L., Tully, M. A., Koyanagi, A., Ilie, P. C., López-Sánchez, G. F., Schwingshackl, L., Veronese, N., & Smith, L. (2021). Handgrip strength and health outcomes: Umbrella review of systematic reviews with meta-analyses of observational studies. *Journal of Sport and Health Science*, *10*(3), 290-295. https://doi.org/https://doi.org/10.1016/j.jshs.2020.06.009

Staessen, J. A., Thijisq, L., Fagard, R., Celis, H., Birkenhäger, W. H., Bulpitt, C. J., de Leeuw, P. W., Fletcher, A. E., Forette, F., Leonetti, G., McCormack, P., Nachev, C., O'Brien, E., Rodicio, J. L., Rosenfeld, J., Sarti, C., Tuomilehto, J., Webster, J., Yodfat, Y., & Zanchetti, A. (2004). Effects of immediate versus delayed antihypertensive therapy on outcome in the Systolic Hypertension in Europe Trial. *J Hypertens*, *22*(4), 847-857. https://doi.org/10.1097/00004872-200404000-00029

Stanford, F. C., Lee, M., & Hur, C. (2019). Race, Ethnicity, Sex, and Obesity: Is It Time to Personalize the Scale? *Mayo Clin Proc*, *94*(2), 362-363. https://doi.org/10.1016/j.mayocp.2018.10.014

Studenski, S. A., Peters, K. W., Alley, D. E., Cawthon, P. M., McLean, R. R., Harris, T. B., Ferrucci, L., Guralnik, J. M., Fragala, M. S., Kenny, A. M., Kiel, D. P., Kritchevsky, S. B., Shardell, M. D., Dam, T. T., & Vassileva, M. T. (2014). The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. *J Gerontol A Biol Sci Med Sci*, *69*(5), 547-558. https://doi.org/10.1093/gerona/glu010

Syme, C., Abrahamowicz, M., Leonard, G. T., Perron, M., Richer, L., Veillette, S., Xiao, Y., Gaudet, D., Paus, T., & Pausova, Z. (2009). Sex Differences in Blood Pressure and Its Relationship to Body Composition and Metabolism in Adolescence. *Archives of Pediatrics & Adolescent Medicine*, *163*(9), 818-825. https://doi.org/10.1001/archpediatrics.2009.92

Taekema, D. G., Maier, A. B., Westendorp, R. G., & de Craen, A. J. (2011). Higher blood pressure is associated with higher handgrip strength in the oldest old. *Am J Hypertens*, *24*(1), 83-89. https://doi.org/10.1038/ajh.2010.185

Taylor, A. C., McCartney, N., Kamath, M. V., & Wiley, R. L. (2003). Isometric training lowers resting blood pressure and modulates autonomic control. *Med Sci Sports Exerc*, *35*(2), 251-256. https://doi.org/10.1249/01.MSS.0000048725.15026.B5

Taylor, H. A., Jr., Wilson, J. G., Jones, D. W., Sarpong, D. F., Srinivasan, A., Garrison, R. J., Nelson, C., & Wyatt, S. B. (2005). Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis*, *15*(4 Suppl 6), S6-4-17.

Thomas, S. J., Booth, J. N., 3rd, Dai, C., Li, X., Allen, N., Calhoun, D., Carson, A. P., Gidding, S., Lewis, C. E., Shikany, J. M., Shimbo, D., Sidney, S., & Muntner, P. (2018). Cumulative Incidence of Hypertension by 55 Years of Age in Blacks and Whites: The CARDIA Study. *J Am Heart Assoc*, *7*(14). https://doi.org/10.1161/JAHA.117.007988

Thorpe, R. J., Simonsick, E., Zonderman, A., & Evans, M. K. (2016). Association between Race, Household Income and Grip Strength in Middle- and Older-Aged Adults. *Ethn Dis*, *26*(4), 493-500. https://doi.org/10.18865/ed.26.4.493

Tomlinson, D. J., Erskine, R. M., Morse, C. I., Winwood, K., & Onambélé-Pearson, G. (2016). The impact of obesity on skeletal muscle strength and structure through adolescence to old age. *Biogerontology*, *17*(3), 467-483. https://doi.org/10.1007/s10522-015-9626-4

Townsend, R. R. (2020). Out-of-Office Blood Pressure Monitoring: A Comparison of Ambulatory Blood Pressure Monitoring and Home (Self) Monitoring Of Blood Pressure. *Hypertension*, *76*(6), 1667-1673. https://doi.org/10.1161/hypertensionaha.120.14650

Trudelle-Jackson, E., Ferro, E., & Morrow, J. R., Jr. (2011). Clinical Implications for Muscle Strength Differences in Women of Different Age and Racial Groups: The WIN Study. *J Womens Health Phys Therap*, *35*(1), 11-18. https://doi.org/10.1097/JWH.0b013e318212570c

Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Alonso, A., Beaton, A. Z., Bittencourt, M. S., Boehme, A. K., Buxton, A. E., Carson, A. P., Commodore-Mensah, Y., Elkind, M. S. V., Evenson, K. R., Eze-Nliam, C., Ferguson, J. F., Generoso, G., Ho, J. E., Kalani, R., Khan, S. S., Kissela, B. M., . . . Martin, S. S. (2022). Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. *Circulation*, *145*(8), e153-e639. https://doi.org/10.1161/CIR.0000000000001052

Tsioufis, C., Thomopoulos, C., & Kreutz, R. (2018). Treatment Thresholds and Targets in Hypertension: Different Readings of the Same Evidence? *Hypertension*, *71*(6), 966-968. https://doi.org/10.1161/hypertensionaha.118.10815

van Oort, S., Beulens, J. W. J., van Ballegooijen, A. J., Grobbee, D. E., & Larsson, S. C. (2020). Association of Cardiovascular Risk Factors and Lifestyle Behaviors With Hypertension: A Mendelian Randomization Study. *Hypertension*, *76*(6), 1971-1979. https://doi.org/10.1161/hypertensionaha.120.15761

Viera, A. J., & Neutze, D. M. (2010). Diagnosis of secondary hypertension: an age-based approach. *Am Fam Physician*, *82*(12), 1471-1478.

Vogel, B., Acevedo, M., Appelman, Y., Bairey Merz, C. N., Chieffo, A., Figtree, G. A., Guerrero, M., Kunadian, V., Lam, C. S. P., Maas, A. H. E. M., Mihailidou, A. S., Olszanecka, A., Poole, J. E., Saldarriaga, C., Saw, J., Zühlke, L., & Mehran, R. (2021). The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030. *The Lancet*, *397*(10292), 2385-2438. https://doi.org/https://doi.org/10.1016/S0140-6736(21)00684-X

Wadei, H. M., & Textor, S. C. (2012). The role of the kidney in regulating arterial blood pressure. *Nat Rev Nephrol*, *8*(10), 602-609. https://doi.org/10.1038/nrneph.2012.191

Wajngarten, M., & Silva, G. S. (2019). Hypertension and Stroke: Update on Treatment. *Eur Cardiol*, *14*(2), 111-115. https://doi.org/10.15420/ecr.2019.11.1

Weber, M. A., Schiffrin, E. L., White, W. B., Mann, S., Lindholm, L. H., Kenerson, J. G., Flack, J. M., Carter, B. L., Materson, B. J., Ram, C. V., Cohen, D. L., Cadet, J. C., Jean-Charles, R. R., Taler, S., Kountz, D., Townsend, R. R., Chalmers, J., Ramirez, A. J., Bakris, G. L., . . . Harrap, S. B. (2014). Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens (Greenwich)*, *16*(1), 14-26. https://doi.org/10.1111/jch.12237

Wehrwein, E. A., & Joyner, M. J. (2013). Regulation of blood pressure by the arterial baroreflex and autonomic nervous system. *Handb Clin Neurol*, *117*, 89-102. https://doi.org/10.1016/b978-0-444-53491-0.00008-0

Wenger, N. K. (2020). Adverse Cardiovascular Outcomes for Women-Biology, Bias, or Both? [Editorial Material]. *Jama Cardiology*, *5*(3), 253-254. https://doi.org/10.1001/jamacardio.2019.5576

Wenger, N. K., Arnold, A., Bairey Merz, C. N., Cooper-DeHoff, R. M., Ferdinand, K. C., Fleg, J. L., Gulati, M., Isiadinso, I., Itchhaporia, D., Light-McGroary, K., Lindley, K. J., Mieres, J. H., Rosser, M. L., Saade, G. R., Walsh, M. N., & Pepine, C. J. (2018). Hypertension Across a Woman's Life Cycle. *J Am Coll Cardiol*, *71*(16), 1797-1813. https://doi.org/10.1016/j.jacc.2018.02.033

Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Jr., Collins, K. J., Dennison Himmelfarb, C., DePalma, S. M., Gidding, S., Jamerson, K. A., Jones, D. W., MacLaughlin, E. J., Muntner, P., Ovbiagele, B., Smith, S. C., Jr., Spencer, C. C., Stafford, R. S., Taler, S. J., Thomas, R. J., Williams, K. A., Sr., . . . Wright, J. T., Jr. (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*, *71*(6), e13-e115. https://doi.org/10.1161/HYP.0000000000000065

Whelton, P. K., Carey, R. M., Mancia, G., Kreutz, R., Bundy, J. D., & Williams, B. (2022). Harmonization of the American College of Cardiology/American Heart Association and European Society of Cardiology/European Society of Hypertension Blood Pressure/Hypertension Guidelines: Comparisons, Reflections, and Recommendations. *J Am Coll Cardiol*, *80*(12), 1192-1201. https://doi.org/10.1016/j.jacc.2022.07.005

WHO. (2019). *World health statistics overview 2019: monitoring health for the SDGs, sustainable development goals*.

Wiley, R. L., Dunn, C. L., Cox, R. H., Hueppchen, N. A., & Scott, M. S. (1992). Isometric exercise training lowers resting blood pressure. *Med Sci Sports Exerc*, *24*(7), 749-754.

Williams, S. K., Ravenell, J., Seyedali, S., Nayef, S., & Ogedegbe, G. (2016). Hypertension Treatment in Blacks: Discussion of the U.S. Clinical Practice Guidelines. *Prog Cardiovasc Dis*, *59*(3), 282-288. https://doi.org/10.1016/j.pcad.2016.09.004

Wind, A. E., Takken, T., Helders, P. J., & Engelbert, R. H. (2010). Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? *Eur J Pediatr*, *169*(3), 281-287. https://doi.org/10.1007/s00431-009-1010-4

Wright, J. T., Jr., Dunn, J. K., Cutler, J. A., Davis, B. R., Cushman, W. C., Ford, C. E., Haywood, L. J., Leenen, F. H., Margolis, K. L., Papademetriou, V., Probstfield, J. L., Whelton, P. K., & Habib, G. B. (2005). Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. *Jama*, *293*(13), 1595-1608. https://doi.org/10.1001/jama.293.13.1595

Wright, J. T., Jr., Williamson, J. D., Whelton, P. K., Snyder, J. K., Sink, K. M., Rocco, M. V., Reboussin, D. M., Rahman, M., Oparil, S., Lewis, C. E., Kimmel, P. L., Johnson, K. C., Goff, D. C., Jr., Fine, L. J., Cutler, J. A., Cushman, W. C., Cheung, A. K., & Ambrosius, W. T. (2015). A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med*, *373*(22), 2103-2116. https://doi.org/10.1056/NEJMoa1511939

Wu, H., Liu, M., Chi, V. T. Q., Wang, J., Zhang, Q., Liu, L., Meng, G., Yao, Z., Bao, X., Gu, Y., Zhang, S., Sun, S., Zhou, M., Jia, Q., Song, K., Huang, J., Huo, J., Zhang, B., Ding, G., & Niu, K. (2019). Handgrip strength is inversely associated with metabolic syndrome and its separate components in middle aged and older adults: a large-scale population-based study. *Metabolism*, *93*, 61-67. https://doi.org/10.1016/j.metabol.2019.01.011

Yi, D. W., Khang, A. R., Lee, H. W., Son, S. M., & Kang, Y. H. (2018). Relative handgrip strength as a marker of metabolic syndrome: the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014-2015). *Diabetes Metab Syndr Obes*, *11*, 227-240. https://doi.org/10.2147/dmso.S166875

Yoder, S. R., Thornburg, L. L., & Bisognano, J. D. (2009). Hypertension in pregnancy and women of childbearing age. *Am J Med*, *122*(10), 890-895. https://doi.org/10.1016/j.amjmed.2009.03.036

Zhang, X., Huang, L., Peng, X., Xie, Y., Bao, X., Huang, J., & Wang, P. (2020). Association of handgrip strength with hypertension among middle-aged and elderly people in Southern China: A cross-sectional study. *Clin Exp Hypertens*, *42*(2), 190-196. https://doi.org/10.1080/10641963.2019.1601206

Ziemens, B., Wallaschofski, H., Völzke, H., Rettig, R., Dörr, M., Nauck, M., Keevil, B. G., Brabant, G., & Haring, R. (2013). Positive association between testosterone, blood pressure, and hypertension in women: longitudinal findings from the Study of Health in Pomerania. *J Hypertens*, *31*(6), 1106-1113. https://doi.org/10.1097/HJH.0b013e3283603eb1

Zinkel, B. (2019). Apartheid and Jim Crow: Drawing Lessons from South Africa's Truth and Reconciliation Commission. *Journal of dispute resolution*, *2019*(1), 229.