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Chloe W. Eng Date

Influence of Socioeconomic Status and Body Composition on Young Adult Blood Pressure: The Birth to Twenty Cohort

By

Chloe W. Eng
Master of Science in Public Health

Epidemiology

_____

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Faculty Thesis Advisor

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By

Chloe W. Eng

B.S.
Northeastern University
2014

Thesis Committee Chair: Aryeh D. Stein, PhD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
in Epidemiology
2016

Abstract

Objective:
We assessed relationships between composite measures of socioeconomic status (SES) and blood pressure measures in South African young adults, and investigated the potential moderating or mediating role of body mass index (BMI).

Participants and Setting:
Participants of the Young Adult Survey of Birth to Twenty (Bt20), an urban longitudinal birth cohort from Soweto, Johannesburg, South Africa.

Methods:
Multivariate linear and logistic regression models were used to explore the influence of socioeconomic indices on two measures of the outcome of blood pressure: continuous systolic blood pressure (SBP) and the dichotomous presence of hypertension or pre-hypertension. Models controlled for height, body mass index (BMI), and potential interaction between BMI and SES. Mediation analyses were conducted using effect decomposition and assessment of potential mediation by BMI on the direct and indirect effects of SES on SBP.

Results:
Pre-hypertension prevalence was 39.8% in males and 25.8% in females, and hypertension prevalence was 7.9% in males and 5.7% in females. Caregiver's highest grade at the time of the participant's birth and internet access in males, and wealth quintile at birth, being married or cohabitating, completion of grade 12, MNet/satellite access, and internet access in females were independently associated with measures of blood pressure in bivariate analysis. However composite measures of SES showed associations with systolic blood pressure and pre-hypertension / hypertension only after consideration of interaction between SES and BMI, and a high percentage of the effect of SES on blood pressure was mediated by obesity when effect-mediator interaction was present.

Conclusions:
BMI appeared to have a stronger influence on young adult SBP and pre-hypertension / hypertension than all measures of SES, but significant moderation and mediation was observed between BMI and various measures of SES. Further research is needed into the role of BMI as a mediator or moderator on SES and young adult blood pressure, and to investigate whether individual components of SES may predict young adult blood pressure.

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Acknowledgements

I would like to extend my sincerest thanks and appreciation to:

Aryeh D. Stein,
for allowing me this learning opportunity, as well as his insight, support, and ongoing patience whenever I veer off topic.

Shane Norris, PhD, study staff and researchers at DPHRU, and University of the Witwatersrand, for their efforts towards the continuation of Birth to Twenty, for allowing me the ability to learn from them through the practicum experience, and the hospitality that has continued past the culmination of my practicum.

The Global Field Experience (GFE) Committee,
for providing me with the funding that allowed me to help clean and analyze this data in the context in which it was collected.

Sara Hanson,
for your company in South Africa, your indispensable advice, and for letting me rely on you for cell phone access and transportation while abroad.

My friends and fellow Rollins classmates,
for the laughter, levity, and late nights that made these past years immensely enjoyable.

And finally, my parents,
for being my ever present anchors and for allowing me the opportunities to learn and grow so many miles away from home for the past six years.

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Chapter I: Literature Review

Introduction

Globally, non-communicable disease (NCD) has begun to replace communicable, or infectious, disease as the major contributor to mortality.[1] One example of this epidemiologic shift seen in South Africa, a middle-income country that exhibits rates of chronic diseases such as hypertension as high as or exceeding those seen in high-income nations. Hypertension is now regarded as one of South Africa and Sub-Saharan Africa's greatest health challenges after the HIV/AIDs crisis.[2]

Nationally representative World Health Organization (WHO) data from 2007 to 2010 showed a hypertension prevalence of 77.9% [95% confidence interval (CI): 76.4 – 79.4] in South African adults over age 50, the highest rate reported in this age group of any nation in the world. After stratifying by gender, hypertension prevalence rates were reported to be as high as 74.7% [95% CI: 72.6 – 76.8] in males and 80.3% [95% CI: 78.6 – 82.0] for females.[3] However despite the similarities in hypertension prevalence with high income countries, South Africa and many other Sub-Saharan African nations report significantly lower rates of detection, treatment, and control than high-income nations.[2]

South Africa reports some of the highest rates of obesity as well, a condition that has shown consistent associations with hypertension. The WHO Study on Global Aging and Adult Health (SAGE) compiled data from the six middle-income countries of China, Ghana, India, Mexico, Russia, and South Africa, and found that age and obesity were consistently significant predictors of hypertension prevalence in all six countries (though significance in South Africa data alone was only significant in the 60 – 79 year age group,

with an odds ratio of 38.89 and 95% confidence interval of 5.55 to 272.6). Socioeconomic factors such as insurance status were also found to be significantly correlated with diagnosis of hypertension, and income was found to have a significant association with hypertension treatment status, though it showed no effect on prevalence.[4, 5]

This thesis uses data from the Birth to Twenty Cohort to investigate the effect of socioeconomic status on blood pressure in young adults from South Africa, an age group that remains underrepresented in the study of hypertension in sub-Saharan Africa. Birth to Twenty is distinctive as the longest running longitudinal birth cohort in Africa and has focused on the early expression of metabolic risk factors and conditions as one of its primary domains.[6] Because the presence of risk factors such as obesity and hypertension in childhood are strongly associated with adverse health outcomes in later years, the data from this cohort provides a unique opportunity to examine health and development from youth to early adulthood. This cohort is the first to allow for tracking of health throughout early life in South Africa, and past findings have contributed to nation-wide policies, including regulation of age for school attendance and restrictions on tobacco purchasing.[7] Therefore, this research aims to explore blood pressure in the young adult data collection wave, and to assess how the major risk factor of obesity may mediate observed associations in the unique socioeconomic context of post-Apartheid South Africa.

Background

Hypertension Definition and Pathophysiology

Blood pressure is the force with which blood circulates in the body during the active and resting phases of the heartbeat, and is measured as systolic pressure during the systole

(active) phase and diastolic pressure during the diastole (resting) phase.[8] These two phases are used in the classification of hypertension, or chronic elevation of blood pressure that results in an increased risk of morbidity and mortality.[9]

Hypertension may be classified as either essential (primary) or secondary. Essential hypertension occurs independently of other conditions in an individual, and accounts for approximately 95% of all hypertension cases. Secondary hypertension occurs as a result of an existing condition that causes an elevation in blood pressure, such as renal failure, pheochromocytoma, or aldosteronism. Though the specific causes and etiology have yet to be fully understood, it has been shown that a number of factors are associated with an increased risk of developing elevated blood pressure. These factors include genetics, obesity, insulin resistance, and lifestyle factors such as sedentary behavior, alcohol or salt intakes, and stress, along with many potential others.[10] Conversely, secondary hypertension is often characterized by early age of onset, a lack of familial risk, and a clear cause such as disease or iatrogenic trigger (e.g. birth control).[11] For the purposes of this thesis, hypertension will be used to refer to primary hypertension.

Increases in blood pressure can result from a number of different factors, including increased systemic vascular resistance, increased vascular stiffness, and increased vascular responsiveness to stimuli.[9] Peripheral vascular resistance is determined by the small arterioles rather than major arteries or capillaries, and the walls of these arterioles contain smooth muscle cells which contract in relation to intracellular calcium concentration. Structural changes such as arteriolar thickening are thought to occur after prolonged constriction of smooth muscle, and lead to a permanent increases in peripheral resistance. [12] The increased peripheral vascular resistance causes an imbalance with cardiac output

from the heart, as shown through the normal cardiac output rates often seen in hypertensive patients. However an alternative theory suggests that raised cardiac output following sympathetic over-activity is the cause of very early hypertension, before peripheral resistance is present. This theory suggests that peripheral arteriolar resistance develops as a result of the rise in output, and in turn affects cell homeostasis. The renal system is intricately involved in the regulation of blood pressure as well, through the renin-angiotensin system (RAS) which monitors fluid balance in the body and as a result, blood pressure. Though spread throughout multiple systems, RAS is dependent on the production of the protease, renin, in the kidney. The kidneys are also hypothesized to contribute to hypertension as sodium and water retention increase, through increases in intracellular calcium in response to elevated sodium via the sodium-calcium exchange pathway.[9]

The two major cardiac conditions resulting from hypertension are left ventricular hypertrophy and coronary artery disease, and the global burden of disease due to hypertension is largely mediated through the development of coronary heart disease and stroke.[11] Heart failure may arise as a result from chronic pressure overload, and strokes often result from hypertension-associated thrombotic conditions.[9] Prehypertension serves as a marker of cardiovascular risk as well, and individuals with stage 2 prehypertension have approximately twice the risk of developing diabetes mellitus, coronary heart disease, and metabolic syndrome than normotensive adults. Pre-hypertensive individuals are also more likely to have a multitude of coronary risk factors such as being overweight, showing insulin resistance, and or displaying hypertriglyceridemia.[13, 14] These associations have been shown to hold longitudinally from young adulthood over decades, emphasizing the need for interventions as early as young adulthood or before.[15]

Patterns in Blood Pressure Measurement

The methods used to assess blood pressure have evolved greatly throughout the past century, and diastolic pressure was seen as the most critical component of blood pressure throughout the early 1900's. However studies in recent decades have indicated that systolic blood pressure may serve as a better predictor of long-term risk.[8] Systolic blood pressure shows stronger associations with adverse cardiovascular outcomes than diastolic blood pressure, and elevated systolic measures have been established as a risk factor for cardiovascular conditions, with or without the presence of elevated diastolic pressure.[10, 16] The cutoff points for hypertension classifications have evolved as well, and past definitions of abnormal blood pressure have been as high as 160/100 mmHg.[17]

Hypertension guidelines

There are currently a number of major guidelines defining hypertension and indications for initial drug therapy that differ by governing body and country of origin. One set of standards from the United States comes from the Joint National Committee (JNC 7), housed within the U.S. National Heart, Lung, and Blood Institute. Others include the World Health Organization / International Society of Hypertension (WHO-ISH), the British Hypertension Society (BHS), and the European Society of Hypertension / European Society of Cardiology (ESH/ESC).[18, 19] Though many of the guidelines agree on aspects of management, there are often major differences in the types of drugs recommended and the specific indications for the use of drug treatment.[18] For example, JNC 7 uses a blood pressure of 140/90 as the threshold for hypertension in individuals under the age of 60 years as well as individuals with diabetes or chronic kidney disease, and 150/90 in

individuals over the age of 60 years. Prehypertension is defined as either a systolic blood pressure between 120 to 139 mmHg or a diastolic blood pressure over 80 mm Hg. Initial drug treatments are also specific to race, with different recommendations for black and non-black individuals.[20] The recent ESH/ESC guidelines use the same goal blood pressure cutoffs as the JNC7. However their recommendations for initial drug treatment do not separate black and non-black patients, and includes beta-blockers for the general population, which the JNC7 does not suggest as an initial drug treatment option in any population.[21]

Despite the numerous country-specific and international guidelines for the treatment and management of hypertension, many developing countries lack national guidelines for the diagnosis and treatment of high blood pressure. The few that do are based on American or European standards, which have been shown to be potentially inadequate when applied in developing countries.[22] More research is needed in ethnic populations and developing countries to determine the efficacy of these cutoffs for use in research and diagnosis in low- and middle-income countries.

Risk Factors for Hypertension

Risk factors for hypertension can be characterized as non-modifiable or modifiable. Non-modifiable risk factors include innate characteristics that cannot be changed, such as age or genetic predispositions. Modifiable risk factors include all other lifestyle or environmental exposures that can be targeted through behavioral change, such as diet quality or physical activity.[22]

Non-modifiable Risk Factors

Hypertension risk has been shown to increase with age, in both the general population and in hypertensive patients.[23] As individuals age, blood vessels lose elasticity, atherosclerosis increases, and arterial vessels hypertrophy. These factors cause blood vessels to lose their ability to cushion, amplifying each circulatory wave and leading to higher blood pressure levels.[24] The kidneys also begin to lose efficiency in salt load excretion, leading to increased blood pressure, and kidney function is further affected by increased rates of diabetes and glucose intolerance.[24] Gender differences have also been clearly established, with better rates of hypertension detection, treatment, and control seen in women of low- and middle- income countries as well as high income countries.[2] These differences include increased risk following menopause in women and higher risk of cardiovascular disease at younger ages in men than in women. Past hypotheses suggest that these differences may be related to reduction in androgen levels and other sex steroids at multiple levels, such as increases in adiposity and subsequent effects on the nervous system. However many past investigations were conducted in rodent models, and additional research is needed to determine whether these effects are consistent in humans.[25]

Genetic factors and ethnic ancestry have been identified as non-modifiable risk factors as well and individuals of African descent have been shown to report lower plasma renin levels than other ethnic groups. The resulting suppression of the renin-angiotensin-aldosterone system, which assists in the regulation of blood pressure, results in higher sensitivity to high-salt diets and decreased response to select hypertension drugs such as angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and beta blockers.[26] Other genetic studies in families have indicated hypertension heritability rates

of 30 to 50%, and a recent gene-centric meta-analysis identified 11 loci that were associated with blood pressure in individuals of European descent alone.[27, 28] Such gene studies can further the understanding of hypertension, both through the identification of new pathways for therapeutic treatment and targeted approaches to increase efficacy of medication outcomes in current patients.

Recent studies have identified intrauterine programming as an additional non-modifiable risk factor for the development of later life hypertension. Several studies have suggested preterm birth as a determinant of hypertension as individuals age, though further observations found that associations between higher birth weight and high blood pressure in childhood did not persist into later years.[29-32] Other studies have suggested that the inverse relationship between birth weight and later life hypertension exists only with systolic measurements of blood pressure.[33] Gestational age at time of birth has also been shown correlation with rates of hypertension in a cohort of men as old as the age of 49 years, but these associations were absent in individuals born at term or later.[34, 35] Proposed hypotheses for the association between low birth weight and cardiovascular risk include poor renal growth and reduced nephron endowment in utero among low birth weight infants that may lead to impaired kidney function later in life, along with other epigenetic modifications resulting from uteroplacental insufficiency.[36, 37]

Modifiable Risk Factors

Rates of hypertension are significantly higher in adult overweight and obese populations, and the Nurses' Health Study II found that body-mass index was the strongest independent predictor of hypertension, with another study indicating obesity as an

increased risk for resistance to treatment as well.[38, 39] One proposed cause for this association include the increased levels of adipocytokines, such as leptin, seen in obese individuals. Leptin has been linked to increased intima media thickness and activation of the sympathetic nervous system that results in hypertension, independent of age and obesity.[40] Other proposed mechanisms include the depression of immune and inflammatory responses or changes in the gut microbiome obese patients, based on observed associations between increased levels of C-reactive protein (CRP), a commonly used inflammatory marker, and increased risk of developing hypertension in patients both with and without coronary risk factors.[39, 40]

Other modifiable risk factors for hypertension include dietary or physical activity exposures such as salt intake, low potassium intake, chronically unhealthy diets high in calories and fat, and a sedentary lifestyle. Salt intake is often cited as the most prominent dietary influence on the pathogenesis of hypertension, and increased sodium intake may lead to vascular dysfunction and expansion of intravascular fluid volume. In most individuals, this is followed by an increase in sodium and fluid excretion in the kidneys to compensate for the increased renal perfusion pressure. However, the excretion of renal sodium is impaired in many hypertensive patients. This relationship between sodium intake and blood pressure has been confirmed through multiple randomized clinical trials, including the DASH-Sodium Trial, and supported by results of cross-sectional and observational follow-up studies such as the International Study of Salt and Blood Pressure (INTERSALT).[41] However recommendations to reduce sodium intake as a blood pressure reduction intervention has been challenged on the basis of limited evidence for long-term cardiovascular complication risk reduction, as well as reported differences in sodium

sensitivity between population subgroups of race or age.[42-44] Conversely, potassium intake has shown inverse associations with blood pressure, though urinary potassium to sodium ratio has also proven to have a more significant association with blood pressure than the individual urinary excretion measures of either electrolyte.[41]

A dose-dependent relationship between alcohol and hypertension has been reported in multiple observational cohorts and randomized control trials, as well as increased blood pressure dysregulation in individuals reporting binge or other episodic drinking in comparison to individuals with regular intake of comparable volumes.[45, 46] Acute increases in blood pressure have also been observed following both first-hand cigarette use as well as exposure to second-hand smoke, and JNC7 guidelines identify the cessation of smoking as the single most critical factor in halting the exacerbation of peripheral arterial disease in already diagnosed patients. [47, 48] Though the precise mechanistic pathway between smoking and hypertension is not yet fully understood, suggested pathways include endothelial damage in blood vessels, up-regulation of matrix metalloproteinases that weaken arterial walls, increases in low-density lipoprotein cholesterol and triglycerides coupled with decreases in high-density lipoprotein cholesterol, an elevated risk of thrombus formation and arterial damage following platelet activation, and increased oxidative stress from exposure to free radicals, all as a result of exposure to cigarette smoke.[49]

Recent investigations into childhood antecedents as life course exposures have identified the long-term effects of psychological stress in childhood as a potential risk factor for hypertension as well, with suggested links between self-reported abuse in childhood and later life cardiovascular disease and metabolic conditions.[50, 51] Other reports

highlighted associations between overall stress in childhood, including both abuse and adverse socioeconomic conditions, and increased risk of hypertension in adulthood.[52, 53]

Socioeconomic Status and Blood Pressure

Socioeconomic status (SES) is consistently associated with blood pressure in older adults from high-income nations, but high-quality data on blood pressure in younger populations, especially in LMICs, is often lacking. SES is often considered a modifiable risk factor, though this categorization can be interpreted differently depending on the measures utilized. Socioeconomic status is a multidimensional concept, and components range from education and occupation, to access to goods and services and overall household welfare.[54] The role of SES in determining health has been widely explored in academic literature, and has been linked to health disparities for a multitude of health outcomes and occurrences. However the concept of SES encompasses a wide range of exposures, preventing creation of a standardized definition or methodology to obtain this measure. Many studies consider only a single socioeconomic variable measured at a single period, not fully accounting for variation between subjects or between points in time. Even these singular measures may differ between region, and a 2005 review noted that occupational category was a common measure in European-based studies while American publications were more likely to use income or level of education. Though these differences can have minimal effects on effect estimate calculation in some instances, sensitivity analyses show that this potential misclassification in using a singular measure may make the difference in the precision of a confidence interval or even the direction of an effect estimate in the same data.[55] A similar effect was seen in a meta-analysis

investigating geographic differences in hypertension gradients in regions of Asia. No overall difference in hypertension was seen when using educational status as the measure of SES, but associations in conflicting directions were found after stratifying by geographical region. On the other hand, income showed an overall positive association with hypertension.[56]

The challenge in defining socioeconomic status increases in research based in LMICs, where little research has been done to quantify disparities and associations are rarely seen between health outcomes and the commonly used SES measures of industrialized nations of education and income.[57] One such reason for this occurrence is the inability for measures of occupation to capture the complexity of job situations common in LMIC's, such as the holding of multiple jobs or seasonal differences in farming environments that may further differ by type and size of farm.[58] Asset indexes or wealth indexes have been proposed as a means of addressing this issue, and much of the theoretical development and methodology of this measure was based around the Demographic and Health Surveys (DHS) after being adopted by the World Bank and other international institutions. Asset indexes can be calculated through other, often simpler methods as well, such as inverse probability weighting or multiple correspondence analysis.[59] Asset indexes measure the ownership of specific consumer objects such as cars and microwaves, housing characteristics, and the type of access to basic services such as electricity or utilities such as an indoor water source.[57] Other measures include consumption expenditure, a measurement of household purchases and spending distribution, or participatory wealth rankings in which community members rank other households in their community, under

the premise that those individuals are the best equipped to judge the social hierarchy in place.[57]

Asset indexes are commonly used in epidemiologic research in sub-Saharan Africa, and principal component analysis (PCA) is the commonly employed technique for the calculation of asset indexes.[60] However, there is no standardized methodology for analysis, and use of PCA ranges from the inclusion of multiple principal components that meet various eigenvalue-based inclusion criteria to the calculation of a singular weighted score. Others use only the first principal component (PC), many of which explain only 12 to 34% of the variance.[61] Furthermore, multiple studies have compared PC-based asset indexes with measures of wealth such as consumption expenditure and wealth quintiles, and found that there were poor exchangeability and high rates of misclassification.[54, 59] An additional study used simulated data to determine whether simulations would yield the same quintile rank as a PC-based asset index, and found a minimum misclassification rate of 50% when the PC-based asset index accounted for less than 30% of the total variance. The authors proposed that misclassification may arise when both positively and negatively correlated variables are included in the measure, and add to the literature that suggests a need for investigation into to the validity of PC-based asset indexes.[61]

An alternate reduction method that has been suggested in more recent years has been multiple correspondence analysis (MCA), a multivariate technique developed to quantify relationships between categorical variables. Though PCA and factor analysis are commonly used in the calculation of asset indices, these methods were designed for use with continuous or interval variables and may not always be the ideal choice for the binary or categorical measures often considered in epidemiologic data.[62] The method of MCA

first originated in France in the 1980s, but has been introduced under a number of alternative names in the Netherlands, Japan, and Canada as well.[63] Though this technique has been widely used in financial and consumer science research, its use in epidemiologic analysis is still relatively new.[64] The applicability of MCA in large scale African health surveys was introduced as recently as 2014, when researchers from University of KwaZulu-Natal applied the technique to jointly analyze socio-economic, demographic and geographic factors.[63]

Multiple correspondence analysis is similar to PCA and factor analysis in that it is also based on matrix eigenvectors and eigenvalues. MCA can be viewed as PCA applied to a complete disjunctive table, and uses similar criterion for the interpretation of results. However correspondence analysis has been shown to be a more effective analysis for large data matrixes with homogenous variables, and allows for more in-depth graphical displays of underlying relationships between variable responses.[63] Recent literature strengthening the adoption of MCA in a global and social context include a decomposition analysis of socioeconomic inequalities in adult obesity prevalence in Cape Town, which used MCA to create the asset index measure, and an analysis of socioeconomic, demographic and geographic factors related to malaria rapid diagnostic test results in Ethiopia.[63, 65]

Chapter II: Manuscript Draft

Influence of Socioeconomic Status and Body Composition on Young Adult Blood Pressure: The Birth to Twenty Cohort

Chloe W. Eng

Abstract

Objective:
We assessed relationships between composite measures of socioeconomic status (SES) and blood pressure measures in South African young adults, and investigated the potential moderating or mediating role of body mass index (BMI).

Participants and Setting:
Participants of the Young Adult Survey of Birth to Twenty (Bt20), an urban longitudinal birth cohort from Soweto, Johannesburg, South Africa.

Methods:
Multivariate linear and logistic regression models were used to explore the influence of socioeconomic indices on two measures of the outcome of blood pressure: continuous systolic blood pressure (SBP) and the dichotomous presence of hypertension or pre-hypertension. Models controlled for height, body mass index (BMI), and potential interaction between BMI and SES. Mediation analyses were conducted using effect decomposition and assessment of potential mediation by BMI on the direct and indirect effects of SES on SBP.

Results:
Pre-hypertension prevalence was 39.8% in males and 25.8% in females, and hypertension prevalence was 7.9% in males and 5.7% in females. Caregiver's highest grade at the time of the participant's birth and internet access in males, and wealth quintile at birth, being married or cohabitating, completion of grade 12, MNet/satellite access, and internet access in females were independently associated with measures of blood pressure in bivariate analysis. However composite measures of SES showed associations with systolic blood pressure and pre-hypertension / hypertension only after consideration of interaction between SES and BMI, and a high percentage of the effect of SES on blood pressure was mediated by obesity when effect-mediator interaction was present.

Conclusions:
BMI appeared to have a stronger influence on young adult SBP and pre-hypertension / hypertension than all measures of SES, but significant moderation and mediation was observed between BMI and various measures of SES. Further research is needed into the role of BMI as a mediator or moderator on SES and young adult blood pressure, and to investigate whether individual components of SES may predict young adult blood pressure.

Introduction

Hypertension, an independent modifiable risk factor for cardiovascular disease traditionally seen in high-income countries (HICs), has become increasingly prevalent in low-to-middle income countries (LMICs) as urbanization increases and lifestyles of HICs are adopted.[66-71]. The 2010 Global Burden of Disease (GBD) study ranked hypertension as the single leading risk factor based on disability-adjusted life years (DALYs), a measure of years of life lost due to morbidity and premature mortality, and hypertension has been referred to as one of South Africa and Sub-Saharan Africa's greatest health challenges after the HIV/AIDs crisis.[2, 72]

Hypertension has shown associations with lower socioeconomic status in many high-income settings, but often displays differing patterns in developing nations. As LMICs undergo increasing rates of economic development, hypertension prevalence rises fastest in the highest socioeconomic class, often mirroring or exceeding rates seen in HICs, as seen in the case in South Africa.[73] Rates then equalize across strata as development progresses and wealth increases, and until hypertension becomes most prevalent in the lowest socioeconomic classes.[2, 73]

South Africa provides a unique context for the study of socioeconomic influences on blood pressure as a center of development in sub-Saharan Africa, and a nation that continues to suffer from disparities that persist in both health and wealth distributions during this post-Apartheid era. As in many other middle-income nations, mortality from chronic conditions has increased despite improvements in economic development and advancements in health interventions with the highest burden in mortality persisting in the poorest populations.[74] The distribution of poverty in South Africa is still influenced in part

by racial overtones and unequal allocation of healthcare resources have led to constrained access to health care in the a large proportion of the South African population.[75] Furthermore, many of the policies and social grants implemented after the abolition of apartheid encouraged unequal growth rather than redistribution, affecting socioeconomic characteristics ranging from educational accessibility to the typical family structure in black South Africans.[76] South Africa also reports some of the highest rates of cardiovascular risk factors worldwide, with hypertension rates in older adults as high as 74.7% [95% CI: 72.6 – 76.8] in males and 80.3% [95% CI: 78.6 – 82.0] for females, yet continues to display significantly lower rates of detection, treatment, and control than many high-income countries.[2, 3]

Despite increasing attention directed towards understanding cardiovascular risk factors in Sub-Saharan Africa, there have been limited investigations into hypertension risk in young adults in this region. Therefore, this research aims to explore blood pressure in young adults and to assess how the major risk factor of obesity may mediate observed associations, in the unique socioeconomic context of post-Apartheid South Africa. The primary analysis will investigate socioeconomic status (SES) in relation to measures of young adult blood pressure, using data from the Birth to Twenty (Bt20) Cohort. Secondary analyses will investigate the mediating effect of body composition, using direct and indirect effect measures to determine potential causal relationships in response to previously published mediating effects of obesity on SES and hypertension in a South African population.[77]

Methods

Data Source

Birth to Twenty (BT20) is an observational longitudinal birth cohort investigating environmental, physiological, psychosocial, and genetic determinants of growth and development in Soweto, a major township of Johannesburg, South Africa. Though not a consideration in the initial stages of the study, BT20 participants comprise the first large-scale cohort to be born into a democratic South Africa and are colloquially referred to as Mandela's Children for the proximity of their births to Nelson Mandela's release from prison.[6] The original cohort consisted of a sample of 3,273 infants who were born within a 6-week window in South Africa during 1990, with original plans to follow them for only 10 years. The study was however extended first to 20 years, followed by further extension to the age of 22 to 24 for the Young Adults Study, which concluded in mid-2014. Data collection occurred at a local hospital, through numerous self-reported questionnaires and/or interviews, anthropometric measurement by trained nurses, DXA scans for bone health and adiposity, and blood/urine samples. Other measures include general health, self-reported diet and physical activity, household socioeconomic status (SES), and preparedness for independence among others. A total of 1635 participants participated in the young adult wave. The final population included in the analysis was comprised of participants with available blood pressure and gender data in the young adult wave, and included 1550 participants. All included participants were black and assumed to be of approximately the same age.

Definition of Socioeconomic Status

The exposure of interest in this analysis was SES in young adulthood. Independent household SES was assessed in the young adult wave by administering the previously used questionnaire to the Bt20 participants. The SES questionnaire was based on standard measures from the Demographic and Health Surveys (DHS) designed for use in developing countries and was initially piloted in 30 caregivers not enrolled in the Bt20 cohort to assess translation of concepts and optimal layout. Measures include education and occupation, number of persons in the household and number of sleeping rooms, private verses public medical insurance, home ownership status, type of housing, presence of an attached kitchen, refuse removal, number of adult financial contributions to child support, caregiver social support, presence of household electricity, type of water/toilet facilities, and a cumulative measure of consumer durable ownership from binary variables (e.g. TV, car, radio, etc., with additions at age 9/10 to reflect changing technology such as microwaves and video). These binary variables were coded to represent either the presence or absence of each asset in the household at each data collection point. The household SES survey was repeated in the Young Adult Survey (YAS), and was completed by the Bt20 participants to reflect changes in living status during the transition into adulthood. Participants were also asked whether they lived alone, felt safe during the day, felt safe at night, and about their perceived level of crime in their neighborhood.

Outcome of Interest

The two outcomes of interest in this analysis were continuous systolic blood pressure and prevalence of pre-hypertension in young adulthood, as rates of hypertension

were assumed to be low in this age group and population. Blood pressure classifications were based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). Normotensives were individuals with both a systolic blood pressure of less than 120 mmHg and a diastolic blood pressure of less than 80 mmHg. Pre-hypertension was defined as either a systolic blood pressure between 120 and 139 mmHg or a diastolic blood pressure over 80 mmHg. Hypertension was defined as a systolic blood pressure of 140 mmHg or greater, or a diastolic blood pressure of 90 mmHg or greater.[48] Three measurements of blood pressure and pulse were obtained at each study visit, taken in two minute intervals. Measurements were obtained using an Omron 6 automated machine (Kyoto, Japan) for all waves after the participants reached the age of 8 years. The first blood pressure and pulse readings were discarded, and the average of the second and third blood pressure and pulse measurements were included for all analyses. In the event that only one blood pressure measurement was recorded, the singular measurement was used.

Covariates of Interest

Gender has been previously shown to have confounding effects on rates of blood pressure, in both local and global populations.[78] For this reason, gender was treated as a confounding affect and analyses were stratified based on gender categorization. Anthropometric measurements have also shown clear associations with blood pressure, and were measured at all ages by trained research assistants. Weight was measured to the nearest 0.1 kg on a digital scale from childhood onward, with participants in light clothes without shoes. A wall-mounted stadiometer (Holtain, UK) was used to measure standing

height to the nearest 0.1 cm. Body mass index (BMI) was used as the measure of body composition in this analysis, and was calculated from weight and standing height using the standard formula of weight (kg) divided by height squared (m^2).

Other potential confounders considered were self-reported through the core and medical young adult questionnaires, and included pregnancy and reproductive history for females, early life stressors (measured using a cumulative scale of life events including death or imprisonment of a family member, caregiver unemployment, shortage of food, chronic illness, parental divorce, abusive or depressed caregivers, and feelings of being loved), and medical history (diagnoses of tuberculosis, diabetes mellitus, human immunodeficiency virus, and disability).[79] Measures of household SES and maternal/neonatal characteristics such as maternal age at time of the participants birth and whether the participant was born pre-term was self-reported by caregivers at the time of participants' births. Physical activity was self-reported using the Global Physical Activity Questionnaire (GPAQ). The GPAQ was designed for global physical activity surveillance, and uses hours of physical activity at varying levels and metabolic-equivalent (MET) values to calculate MET minutes per week based on WHO guidelines. Other covariates of interest identified through both past Bt20 analyses and in previously published peer-reviewed literature included birth weight, gestational age at birth, and maternal complications or comorbidities present during pregnancy.[80-84] Tobacco use was also of interest for its associations in previously published literature and the high rates of use in young South Africans.[85-87] Smoking status was self-reported during the Bt20 young adult wave using a computer-assisted survey program.

Data analysis

Descriptive Statistics

Descriptive statistics were used to characterize the distribution of variables for all participants in the most recent data collection wave. In order to stratify by sex, individuals with missing data for the gender variable or SES measures were excluded, leaving a sample size of 1520. All other missing values were assumed to be missing at random.

Socioeconomic Measures

For the purposes of this investigation, socioeconomic measures considered characteristics of the individual in young adulthood, the household in young adulthood, perceptions of neighborhood safety in young adulthood, and maternal social and household characteristics at the time of the participant's birth. Five approaches to the measurement of SES were considered: a summative measure with equal weights for each element of DHS-based household factors, a derived component measure calculated using principal component analysis (PCA) for all SES variables, derived component measures for individual level, neighborhood, and birth SES characteristics calculated using separate PCA procedures for each category, a derived component measure calculated using multiple correspondence analysis (MCA) for all SES variables and derived component measures for individual level, neighborhood, and birth SES characteristics calculated using separate MCA procedures for each category. Consumer durable ownership variables were considered as binary variables indicating ownership. Nominal categorical variables were dichotomized to allow for inclusion in the principal components analysis.[60] Water and toilet facilities were transformed into dichotomous measures to indicate presence of indoor water and toilet access compared to outdoor facilities. Home type was dichotomized as habitation

in a house, flat, or cottage in comparison to residence in a shack, zozo, garage, hostel, or other structure. Educational status was coded as 1 for the completion of grade 12, and 0 if the participant had not yet reached that grade or dropped out before the completion of grade 12. Relationship status was measured as being married or cohabitating, verses being single, in a committed relationship but not living together or married, divorced, separated, or widowed. Because SES was assumed to have a non-differential distribution in regards to gender, SES measures were calculated using all eligible participants.

SES Measure Creation

The asset index was calculated as a sum of the presence of the DHS-based household indicators, which has been previously used to investigate SES in this population.[88] These indicators included type of home, water and toilet access, and all measures of consumer durable ownership.

Due to the large number of socioeconomic factors under consideration, two separate data reduction methods were explored and compared. Principal component analysis (PCA) was the first method used, and is widely used as to derive measures such as household asset indexes for the measurement of SES. Multiple correspondence analysis (MCA) is an alternative method of data reduction developed for use with binary and categorical measures, to address measurement assumptions that PCA may ignore. To create the primary PCA and MCA measures for total SES, all SES variables in the young adult survey, which included the household measures previously listed as well as living alone as a young adult, marital status (married/cohabitating verses other), completion of grade 12, and perceptions of neighborhood safety were considered based on previous investigations in this population. Although additional measures past the consumer asset index and

water/toilet facilities have not been previously included in socioeconomic measures in this population, the young adult wave represents the first wave in which Bt20 participants are likely to begin to display independence and necessitated the consideration of potentially correlated variables. Caregiver education at birth, maternal marital status at birth, maternal self-reported use of preventative health services, toilet/water access, and caregiver wealth characterization using quintiles were also assessed for correlation and considered for inclusion, based on previous literature.[89, 90] To create individual-, birth-, and neighborhood-specific measures, only those variables falling under that categorization were included.

Multivariable Modeling

A directed acyclic graph was first drawn to assess for potential confounding (**Figure 1**). A model-based approach to confounding assessment was then performed using the five approaches to the measurement of SES. Each model was run to obtain estimates of effect for both continuous blood pressure using multivariate linear regression and a dichotomous variable representing presence of either pre-hypertension or hypertension verses normal blood pressure using logistic regression. All model approaches were stratified by gender and controlled for height and BMI *a priori*, based on previous literature establishing differences in blood pressure by height and gender. All other independently associated covariates with a p-value of less than 0.10 were considered and assessed for significance using hierarchical backwards elimination. Each model considered estimates of effect for both the presence and absence of interaction between SES and BMI to examine potential moderation.

Mediation Analysis

In order to investigate the potentially mediating role of body composition on the path between socioeconomic status and young adult blood pressure, mediation analysis was performed using the effect decomposition methods and a corresponding SAS macro developed to estimate direct and indirect effects assuming mediator interaction. This method is an extension of the Baron and Kenny product approach to mediation analysis, and allows for the consideration of binary, continuous, or count measures.[91] Although the inclusion of the mediator in the model may suffice when there is no interaction between the exposure and mediator variables, the same macro was used in order to maintain consistency in the results.[92] All variables and measures were defined *a priori* based on the results of multivariate analyses. Consistent with the multivariate regression analyses, separate mediation analyses were carried out for both men and women and body composition was considered as a continuous measure of BMI. For models where multiple categories of SES were considered, each was run as an independent outcome considering the other categories as covariates. When significant interaction between SES and BMI were found in multivariate analyses, the presence of exposure-mediator interaction was considered in the mediation analysis.

Ethical considerations

All statistical analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC), and all hypothesis tests were 2-sided at the 0.05 significance level. Participants and caregivers provided written informed consent throughout the study at each assessment visit. Ethical approval was obtained from the University of the Witwatersrand Committee for Research on Human Subjects and the Emory University Institutional Review Board (IRB).

Results

Demographic and other background characteristics of participants are shown in **Table 1**. The samples of each gender were approximately equal in gender, with males comprising 48.92% of the 1529 total participants. The prevalence of pre-hypertension in this sample of South African young adults was 30.41% and the prevalence of hypertension was 6.87%, with an average systolic blood pressure of 113.06 mmHg. Both pre-hypertension and hypertension prevalence were higher in males than in females with 36.50% of males classified as pre-hypertensive and 8.02% classified as having hypertension, in comparison to 24.58% and 5.76% of females. Systolic blood pressure was higher in males at 117.56 mmHg than in females with a mean of 108.75, but the mean female BMI of 25.50 ± 6.18 was higher than the mean BMI of 21.61 ± 3.72 in males.

Overall rates of comorbidities were low, and did not differ significantly between genders. Males were significantly more likely than females to smoke with 61.29% of males and 27.57% of females self-identifying as smokers. The majority of participants (79.27%) reported low levels of physical activity, but females had significantly lower physical activity levels with 92.57% of females reporting the lowest level of physical activity.

Socioeconomic Factors and Determinants of Blood Pressure

Individual distributions of socioeconomic factors are shown in **Table 2**. Although there were low levels of correlation between individual measures of SES, all were considered for the construction of the SES measures.

In unadjusted bivariate analyses for potential covariates, male systolic blood pressure was significantly associated with BMI, high self-reported physical activity, and

self-reported disability of any type. In females, systolic blood pressure was significantly associated with height, BMI, parity (birth order), and self-reported disability of any type. Both males and females showed significant associations between BMI and dichotomous elevated blood pressure status, but only females showed a significant association between height and elevated blood pressure status. Results are presented in **Table 3** and **Table 4.**

Unadjusted bivariate analyses of individual socioeconomic factors are presented in **Table 5** and **Table 6**. In males, systolic blood pressure showed significant associations with only the highest grade attained by the caregiver at the time of the participant's birth and reporting of internet access, and elevated blood pressure status showed a significant association only with the highest caregiver grade attained. In the female sample, caregiver's highest grade at the time of participant's birth, wealth quintile at birth, being married or cohabitating with a romantic partner, participant completion of grade 12, ownership of MNet/DSTV/Satellite, and internet access were significantly associated with systolic blood pressure. However only wealth quintile at birth, being married or cohabitating with a partner, and internet access were significantly associated with elevated blood pressure status in females. No composite measure of SES showed a significant association with blood pressure in unadjusted analyses.

Multivariate Analysis

Height were present in all models based on prior literature, and all models were stratified by gender. Initial full models for males included the bivariate statistically significant covariates BMI ($p < 0.01$ for both outcomes), physical activity ($p = 0.05$ for both outcomes) and disability ($p = 0.02$ for SBP), and initial full models for females included BMI ($p < 0.0001$ for both outcomes), parity/birth order ($p = 0.04$ for SBP),

maternal age at birth ($p = 0.06$ for SBP), and self-reported disability of any type ($p = 0.01$ for SBP). Self-reported disability was later dropped due to potential for misclassification, and GPAQ categories were excluded due to concerns of low prevalence and sparse data. Both birth variables were dropped through backwards elimination, and final models included only height, BMI, and significant interaction variables. Consideration of excluded covariates was not found to cause significant changes in effect from the final models.

Multiple linear and logistic regression results of SES measures on SBP and presence of elevated BP are presented in **Table 7** and **Table 8**. Model 1 was used to investigate associations between separate composite measures of SES and systolic blood pressure as a continuous variable, controlling for height and BMI. Model 2 used the same measures as Model 1 with the consideration of SES-BMI interaction. Model 3 investigated associations between separate composite measures of SES and pre-hypertension / hypertension as a dichotomous variable, controlling for height and BMI. Model 3 used the same measures as Model 3 with the consideration of SES-BMI interaction. Blood pressure status was also initially investigated using categories of normal blood pressure, pre-hypertension, and hypertension. However, as only 7.9% of males and 5.7% of females were classified as hypertensive, the categories kept as a combined presence of either pre-hypertension or hypertension.

In males, no measure of SES, except for the summative household SES measure and the MCA-derived measure for individual SES after adjustment for interaction in Model 2, was significant with either outcome measure. In females, the MCA-derived measure for total SES was significantly associated with both outcome measures after adjustment for interaction, and the MCA-derived categorical measures of individual and neighborhood

SES were significantly associated with systolic blood pressure after adjustment for interaction. However no measure of SES was significant without the inclusion of SES-BMI interaction, and Model 1 showed consistent non-statistically significant negative associations for all measures of SES with systolic blood pressure.

Mediation Analysis

The results of the mediation analyses are shown in **Table 9**. A total of 18 measures were considered for potential mediation by body mass index, of which 12 showed mediation of 10% or more of the total effect of SES on SBP. For the summative household SES measure, in which both genders were found to have a significant effect of SES on SBP in multivariate adjusted regression analyses, male SBP considered exposure-mediator interaction and 89.65% of the effect of the summative household SES measure was found to be mediated by BMI. Model 2 for females did not consider exposure-mediator interaction, and 10.21% of the total effect of the summative household SES measure on SBP was mediated by obesity. Both stratum of gender were assumed to have no exposure-mediator interaction for the PCA-derived measure of total SES, and 12.25% of the effect of the primary PCA measure on SBP in males and 23.35% of the effect on SBP in females were attributable to BMI. When each PCA-derived SES category was considered individually, only 3.15% and 7.86% of the effect of individual SES on SBP in males and females, respectively, was mediated by BMI. In females, only 2.22% of the effect by SES at birth in females but 19.18% of the effect of SES at birth in males was mediated by BMI. The total effect of neighborhood SES on SBP mediated was 12.31% in males and 12.08% in females. When considering the derived measure for total SES using MCA, 27.92% of

the effect in males and 72.61% of the effect in females between SES and SBP was mediated by BMI. When considering individual categories of SES derived using MCA, 27.71% of the effect of individual SES, 36.36% of SES at birth, and 11.81% of neighborhood SES on SBP in males was found to be mediated by BMI. In females, 8.49%, 3.62%, and 78.11% of the effect of each category of SES on SBP was found to be mediated by BMI.

Discussion

Socioeconomic status and blood pressure, considered as both systolic blood pressure and as prevalence of pre-hypertension or hypertension, were not found to be associated in this population. Although the findings of this analysis do not support an association between socioeconomic status and blood pressure in this cohort of South African young adults, the results suggest that select components of SES may have independent associations with systolic blood pressure and prehypertension / hypertension status. The individual factors of highest parental grade at the time of participant's birth and internet access in males and wealth quintile at birth, being married or cohabitating with a partner in young adulthood, and internet access in females were identified as significant socioeconomic contributors to young adult systolic blood pressure, before the consideration of any covariates or interaction. Furthermore, after separating the components of SES into birth, individual/household, and neighborhood categories, the decomposed effects were found to show differing levels of significance with both outcome measures.

Mediation analyses indicated that BMI contributes to a large percentage of the effect of all statistically significant measures of SES on systolic blood pressure, with 89.65% of the effect of the summative household SES measure on systolic blood pressure mediated by BMI. None of the natural direct effects were significant, suggesting that changes in SES were not statistically significantly associated when BMI was held constant. All controlled direct effects were significant for mediation analyses that considered exposure-mediator interaction, indicating that regardless of SES, there was a significant association between BMI and SBP.

These results were supported by the change in significance for associations between SES and blood pressure following control for height and BMI, as none of the derived indices of SES were individually associated with either measure of blood pressure in bivariate analysis. Interaction between neighborhood SES factors and BMI was identified in multiple regression analyses as well, suggesting an interrelationship between neighborhood safety and weight status. However, because mediation analyses showed inconsistent statistical significance between the exposure-mediator pathway, the mediator-outcome pathway, and the total effect from the pathway between the exposure and outcome, we cannot conclude a significant mediating effect.

Birth to Twenty Context

Past investigations using Bt20 cohort data have approached the assessment of socioeconomic measures in a number of ways. While investigating residential mobility, Ginsberg et al. derived a socioeconomic index from a set of ten services and household assets (home ownership, house type, indoor water, flush toilet access, electricity, television, motor vehicle, refrigerator, washing machine, and telephone) by summing the ownership or presence of each measure and grouping the summed measure into quartiles.[93] A subsequent investigation into the effects of socioeconomic status on body composition at the age of 9 or 10 used principal component analysis to weight each of the household SES measures.[84, 89] Other approaches identified individual SES measures with unadjusted p-values for association with the outcome of less than either 0.1 or 0.5, and considered the associated measures in the final multivariate model.[94, 95] This analysis found substantial differences in effect between measures of SES indicate the need for further investigations

into the components of socioeconomic status, in order to identify specific factors that may help to develop targeted interventions in this population.

Griffiths et al. (2012) reported a systolic pre-hypertension prevalence of 11% at the age of 16 in the Bt20 cohort, and no association between SES and systolic blood pressure was found in adolescents. This investigation found a clear increase in elevated blood pressure status from adolescence to young adulthood, with 30% of participants falling under the classification of pre-hypertensive and 7% classified as hypertensive. None of the SES variables from infancy or the age of 16 years were significantly associated with systolic blood pressure in males at the age of 16, although consistent with this analysis, increased height was associated with increased systolic blood pressure. For females, the only significantly associated variables with systolic blood pressure at age 16 were obesity, post-term birth status, and being in the middle tertile of the crime prevention index in comparison to the highest tertile. Overall, SES measures in early life accounted for a small percent of variation in systolic blood pressure in South African adolescents.[94] The results of this analysis support the findings of no strong associations between SES and blood pressure into adulthood. However individual covariates that showed associations with blood pressure in adolescence, such as parity (birth order) in girls and gestational age at birth were not found to be significantly associated with systolic blood pressure in young adulthood.

Strengths and Limitations

The Birth to Twenty data was designed as a prospective birth cohort, which reduced concern of recall bias and used reliable measures of blood pressure obtained by trained research assistants rather than through participant self-report to reduce risk of information

bias. Furthermore, the longitudinal design of the study allows for the consideration of early life variables as potential covariates with young adult measures. This is particularly relevant in this population, as it allows for the comparison of SES at birth at the time of the abolishment of apartheid with current SES status over two decades later.

However a number of limitations persist, such as the lack of availability of reliable dietary and alcohol intake. Although information on patterns of alcohol intake were collected in the Young Adult Survey, the data is still being cleaned and was not available for use at the time of this analysis. Body mass index was also utilized as a proxy marker of nutritional status, but is subject to misclassification and may lack the robustness of other measures of body composition, such as fat mass. The classification of the GPAQ categories may have obscured the identification of the potentially mediating role of physical activity as well, as there was a potential sparse data issue in females. Hypertensive status (prehypertension and hypertension) was also defined using JNC 7 criteria, which considers both systolic and diastolic blood pressure. However, continuous diastolic blood pressure was not investigated, and patterns of hypertensive status using only systolic blood pressure may have shown differing patterns in systolic blood pressure after categorization.

One limitation of the use of data reduction methods in the characterization of SES is the assumed absence of measurement error. Principal component analysis and multiple correspondence analysis do not allow for the identification of individual strengths for individual assets or whether certain assets represent a significant marker of health. Variables may also be associated with multiple components, making any interpretation of results potentially ambiguous. Though asset-based measures are an established method of measuring household socioeconomic status in low- and middle-income countries, their

interpretation is limited to longer-term wealth or living standards rather than short-term reflections of socioeconomic status. Some argue that this method of calculating SES is arbitrary, as the component selection process is ill-defined. Furthermore, as LMICs continue to develop economically, the ownership of an asset may be further separated into classes, such as the ownership of a basic cell phone verses a more advanced smartphone.[60] Other studies have found that PCA based asset indexes are not reliable proxies for consumption expenditure, a standard in economics used to assess welfare and income, further limiting their interpretability.

Furthermore, SES was considered as a continuous variable without regards to participants' standing in relation to their peers, both at birth and in the Young Adult wave. However a subsample of the BT20 cohort found that SES is not static in this population, and of those in the lowest tertile of SES at birth, approximately 51% had moved into a higher tertile at the age of 9 or 10. This same subsample showed that increased lean mass at the age of 9 or 10 was associated with belonging to the highest tertile of SES at birth, while belonging to the highest SES tertile at the age of 9 or 10 was associated with increased fat mass. However no associations were found between measures of adiposity and belonging to the lowest or middle tertile of SES at any age.[84] Further sensitivity analyses are needed to examine changes in SES and potential mediator-outcome confounding as BMI, the measure of body composition used in this investigation, was shown to be a major contributor to systolic blood pressure in this cohort of South African young adults.

Chapter III: Implications

Conclusion

As population growth increases and the burden of non-communicable disease continues to rise in sub-Saharan Africa, identifying critical points of intervention are needed to address the increasing strain on already limited resources. Although this study did not find an association between SES and young adult hypertension, the differences in measurement and individually associated socioeconomic components suggest that underlying factors, as well as factors related to obesity, may play a larger role.

Public Health Implications and Future Directions

Obesity appeared to have significantly stronger associations with systolic blood pressure and prehypertension / hypertension in this cohort. However the presence of both interaction and mediation found between socioeconomic status and obesity suggest the need for further research into the pathway from SES to changes in BMI. Interaction indicates that the effect of one variable depends on the level of another, but does not assume a causal pathway. Instead, the moderator is seen as a variable that modifies the strength or direction of the relationship between an independent variable and a dependent variable, in this case, obesity modifying the strength of the relationship between SES and hypertension. Alternatively, mediating variables are assumed to lie on the pathway through which an exposure affects an outcome and the finding of significant controlled effects, representing mediation by BMI (Table 9), warrant further investigation.[96] Future research is needed to decompose how these effects interact, and how they may be targeted in future interventions and policies to reduce young adult hypertension.

Tables and Figures:

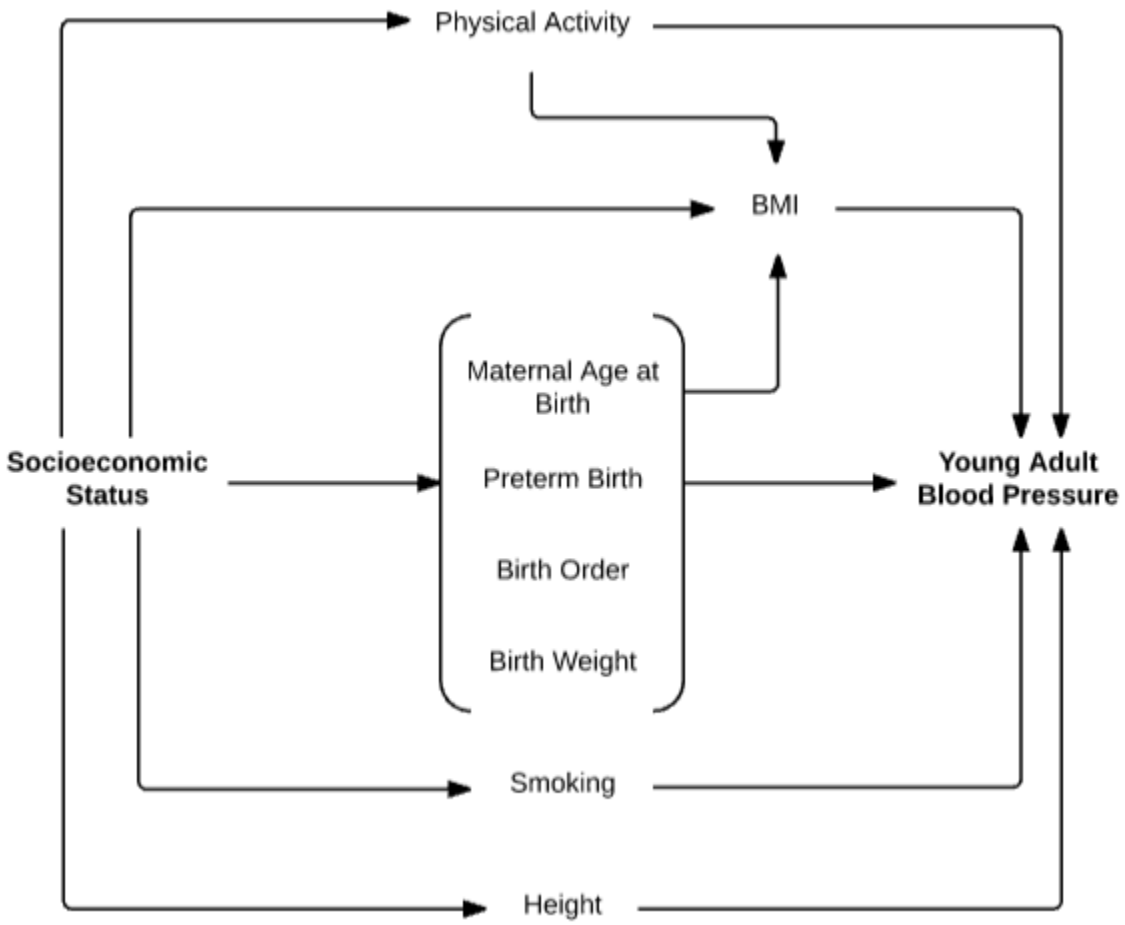

Figure 1: Directed acyclic graph (DAG) representing hypothesized causal relationships between available covariates related to socioeconomic status and blood pressure.

Table 1: Selected Demographic, Anthropometric, and Medical Characteristics of the Birth to Twenty Cohort in the Young Adult Wave (N=1550)

	Male (n = 758)	Female (n = 792)
Height (cm)	171.70 ± 6.6	159.6 ± 6.1
Weight (kg)	63.8 ± 11.7	65.2 ± 16.3
Body Mass Index (kg/m2)	21.6 ± 3.7	25.5 ± 6.2
Systolic Blood Pressure (mmHg)	117.5 ± 10.2	108.7 ± 11.7
Diastolic Blood Pressure (mmHg)	74.0 ± 10.2	74.1 ± 9.0
Blood Pressure Status, % [a]		
Normotensive	52.2	68.6
Pre-hypertensive	39.8	25.8
Hypertensive	7.9	5.7
Physical Activity, % [b]		
Low	65.6	92.7
Moderate	29.3	7.1
High	5.2	0.3
Self-reported smoking, %	61.3	27.6
Birth Characteristics		
Maternal Age at Birth [c]	25.9 ± 6.24	25.70 ± 6.2
Gestational Age, %[d]		
Normal Term	88.8	84.9
Pre-Term	11.2	15.1
Self-reported Comorbidities		
Diabetes [n (%)]	2 (0.28)	4 (0.53)	6 (0.40)
HIV [n (%)]	2 (0.28)	33 (4.35)	35 (2.36)
Malaria [n (%)]	2 (0.28)	7 (0.92)	9 (0.61)
Tuberculosis [n (%)]	12 (1.66)	14 (1.84)	26 (1.76)
Any Reported Disability [n (%)]	12 (1.69)	4 (0.55)	16 (1.11)

Data are presented as mean ± SD unless otherwise specified.

[a] Calculated using JNC 7 Guidelines: Normotensive, SBP < 120 mmHg and DBP < 80 mmHg; Pre-hypertensive, SBP between 120 and 139 mmHg OR DBP between 80 and 89 mmHg; Hypertensive, SBP ≥ 140 mmHg OR DBP ≥ 90 mmHg

[b] Defined using the WHO GPAQ Analysis Guide

[c] Refers to the participant's mother at the time of participant's birth

Table 2: Socioeconomic Characteristics of the Birth to Twenty Cohort in the Young Adult Wave (N=1550)

	Male (n = 758)	Female (n = 792)
Characteristics at Birth [a]		
Maternal Marital Status, % [b]		
Unmarried	63.1	66.2
Married	36.9	33.8
Use of Health Services, %		
No/Low Use	16.0	12.5
Intermediate Use	49.9	53.9
Highest Use	34.1	33.6
Household Flush Toilet, %	99.5	99.5
Household Water Access, %	79.8	80.1
Highest Parental Grade Attained	10.8 ± 1.6	11.3 ± 1.2
Wealth Quartiles [median (IQR)]	3 (2 - 4)	3 (2 - 4)
Neighborhood SES Characteristics[c]		
Feels Safe During Day, %	87.0	73.3
Feels Safe at Night, %	66.3	50.6
Perceived Neighborhood Safety, %		
Very Unsafe	26.5	26.6
Unsafe	27.0	29.0
Safe	37.8	36.4
Very Safe	8.7	8.0
Individual/Household SES Characteristics[c]		
Living Alone, %	8.1	5.0
Married or Cohabitating, % [d]	3.5	7.3
Completion of Grade 12, %	53.3	68.0
Home type, %		
House/Flat/Apt	89.2	88.6
Shack/Zozo/Other	10.8	11.4
Indoor Water Facilities, %	76.5	78.9
Indoor Toilet Facilities, %	65.3	69.6
Ownership of Durables, %		
Home electricity	97.8	98.1
Motor vehicle	44.6	41.9
Fridge	94.1	96.3
Microwave	83.1	84.5
Washing Machine	66.2	70.2
Landline Phone	25.3	27.4
Cell Phone	96.0	98.2
Television	96.0	97.47
Radio	90.6	89.4
Video / DVD	88.0	87.8
MNet/DSTV/Satelite	55.9	58.1
Computer/Laptop	60.7	58.2
Internet Access	53.7	63.4

Data are presented as mean ± SD or median [IQR] for continuous data and n (%) for categorical data.

[a] Self-reported by caretaker at the time of participant's birth

[b] Refers to participant's mother at the time of participant's birth

[c] Self-reported by participant in the Young Adult Survey

[d] In comparison to being single, divorced, or in a relationship but not living together

Table 3: Univariate associations of potential confounders with systolic blood pressure (as a continuous outcome) and pre-hypertension presence (as a dichotomous outcome) in males

	Systolic Blood Pressure[a]		Elevated Blood Pressure[b]	
	β (95% CI)	P-value	OR (95% CI)	P-value
Height (cm)	0.01 (-0.00, 0.03)	0.07	1.00 (1.00, 1.00)	0.06
BMI (kg/m^2)	**0.45 (0.22, 0.69)**	**<0.01**	**1.09 (1.04, 1.13)**	**<0.01**
GPAQ[c]				
Moderate	0.04 (-1.90, 1.97)	0.97	0.88 (0.64, 1.21)	0.43
High	**-4.01 (-7.99, -0.03)**	**0.05**	0.51 (0.26, 1.01)	0.05
Smoking Status	0.17 (-1.70, 2.04)	0.86	0.93 (0.69, 1.26)	0.64
Preterm Birth[d]	1.31 (-1.47, 4.10)	0.36	0.85 (0.54, 1.34)	0.47
Birth Weight (kg)	-0.32 (-2.06, 1.42)	0.72	0.96 (0.72, 1.27)	0.76
Maternal Age at Birth[e]	0.09 (-0.05, 0.23)	0.21	1.00 (0.98, 1.02)	0.96
Parity (birth order)[f]	0.55 (-0.24, 1.34)	0.18	1.00 (0.88, 1.14)	0.96
Diabetes	-3.94 (-21.0, 13.1)	0.65	<0.001 (<0.01, >999)	0.98
HIV	2.34 (-9.71, 14.39)	0.70	1.08 (0.15, 7.71)	0.94
Malaria	10.6 (-6.42, 27.59)	0.22	>999 (<0.001, >999)	0.98
Tuberculosis	-3.57 (-10.56, 3.43)	0.32	0.35 (0.10, 1.32)	0.12
Any Reported Disability	**-8.39 (-15.4, -1.39)**	**0.02**	0.54 (0.16, 1.82)	0.32

Bold = significant at $p < 0.05$

[a] Assessed using linear regression

[b] Assessed using logistic regression

[c] Reference = low

[d] Reference = normal term

[e] Refers to mother's age at the time of participant's birth

[f] Refers to number of children that participant's mother gave birth to prior at the time of participant's birth

Table 4: Univariate associations of potential confounders with systolic blood pressure (as a continuous outcome) and pre-hypertension presence (as a dichotomous outcome) in females

	Systolic Blood Pressure[a]		Elevated Blood Pressure[b]	
	β (95% CI)	P-value	OR (95% CI)	P-value
Height (cm)	**0.02 (0.00, 0.03)**	**0.02**	1.00 (1.00, 1.01)	**0.03**
BMI (kg/m^2)	**0.31 (0.18, 0.44)**	**<.0001**	1.06 (1.04, 1.09)	**<.0001**
GPAQ[c]				
Moderate	-1.00 (-4.19, 2.18)	0.54	0.95 (0.53, 1.71)	0.86
High	12.8 (-3.52, 29.02)	0.12	2.18 (0.14, 35.0)	0.58
Smoking Status	0.51 (-1.40, 2.43)	0.60	1.00 (0.93, 1.08)	0.79
Preterm Birth[d]	0.96 (-1.36, 3.28)	0.42	1.12 (0.74, 1.70)	0.60
Birth Weight (kg)	0.57 (-1.13, 2.26)	0.52	0.96 (0.72, 1.27)	0.76
Maternal Age at Birth[e]	0.13 (-0.00, 0.26)	0.06	1.02 (1.00, 1.05)	0.11
Parity (birth order)[f]	**0.80 (0.03, 1.56)**	**0.04**	1.12 (0.97, 1.29)	0.11
Diabetes	-9.67 (-21.20, 1.85)	0.10	0.74 (0.08, 7.12)	0.79
HIV	-0.85 (-4.95, 3.25)	0.68	1.12 (0.54, 2.35)	0.76
Malaria	0.10 (-8.65, 8.86)	0.98	0.88 (0.17, 4.57)	0.88
Tuberculosis	-3.26 (-9.47, 2.95)	0.30	0.60 (0.17, 2.16)	0.43
Any Reported Disability	**15.8 (4.28, 27.37)**	**<0.01**	6.83 (0.71, 66.0)	0.10
Currently Pregnant	1.99 (-2.51, 6.48)	0.39	1.12 (0.50, 2.53)	0.79
Previously Pregnant	-0.20 (-1.32, 0.92)	0.72	1.13 (0.93, 1.39)	0.23

Bold = significant at $p < 0.05$

[a] Assessed using linear regression

[b] Assessed using logistic regression

[c] Reference = low

[d] Reference = normal term

[e] Refers to mother's age at the time of participant's birth

[f] Refers to number of children that participant's mother gave birth to prior at the time of participant's birth

Table 5: Unadjusted estimates of SES components with blood pressure in males

	Systolic Blood Pressure		Elevated Blood Pressure	
	β (95% CI)	P-value	OR (95% CI)	P-value
Birth Characteristics				
Maternal Marital Status	-0.49 (-2.30, 1.32)	0.60	0.92 (0.68, 1.23)	0.57
Parental Health Service Use	0.52 (-0.87, 1.90)	0.47	1.01 (0.80, 1.28)	0.94
Toilet Access (infancy)	1.28 (-12.3, 14.83)	0.85	0.59 (0.05, 6.50)	0.66
Water Access (infancy)	-0.16 (-2.57, 2.25)	0.90	0.99 (0.66, 1.48)	0.95
Caregiver's Highest Grade	**0.75 (0..22, 1.28)**	**<0.01**	1.12 (1.02, 1.22)	**0.02**
Wealth (quintiles) at birth	0.16 (-0.58, 0.89)	0.67	1.06 (0.93, 1.19)	0.39
Neighborhood Characteristics				
Feels Safe During the Day	-0.00 (-1.16, 1.15)	1.00	1.03 (0.86, 1.25)	0.73
Feels Safe at Night	-0.59 (-1.65, 0.48)	0.28	0.94 (0.79, 1.12)	0.47
Perceived Safety	0.32 (-0.61, 1.25)	0.50	0.98 (0.84, 1.14)	0.76
Individual Characteristics				
Living Alone	-1.02 (-4.23, 2.20)	0.53	1.22 (0.72, 2.05)	0.47
Married or Cohabitating	-3.36 (-8.16, 1.44)	0.17	1.08 (0.50, 2.37)	0.84
Completion of Grade 12	0.85 (-0.90, 2.61)	0.34	1.14 (0.86, 1.52)	0.37
House Type	-0.09 (-2.93, 2.75)	0.95	0.85 (0.54, 1.35)	0.49
Water Facilities	1.33 (-0.75, 3.40)	0.21	1.22 (0.87, 1.71)	0.26
Toilet Facilities	1.05 (-0.80, 2.90)	0.27	1.24 (0.91, 1.67)	0.17
Asset Ownership				
Home electricity	-3.51 (-9.40, 2.37)	0.24	1.03 (0.39, 2.70)	0.95
Motor vehicle	-0.80 (-2.55, 0.96)	0.37	0.81 (0.61, 1.08)	0.16
Fridge	0.35 (-3.34, 4.04)	0.85	1.71 (0.92, 3.21)	0.09
Microwave	-0.04 (-2.37, 2.29)	0.97	1.20 (0.82, 1.76)	0.36
Washing Machine	-0.62 (-2.46, 1.22)	0.51	0.96 (0.71, 1.30)	0.81
Landline Phone	-1.12 (-3.12, 0.89)	0.27	0.80 (0.58, 1.12)	0.19
Cell Phone	0.53 (-3.94, 5.00)	0.82	0.91 (0.44, 1.90)	0.81
Television	3.34 (-1.13, 7.80)	0.14	1.39 (0.66, 2.93)	0.38
Radio	0.54 (-2.45, 3.54)	0.72	0.88 (0.54, 1.44)	0.61
Video / DVD	-0.06 (-2.74, 2.62)	0.96	1.13 (0.73, 1.76)	0.57
MNet/Satelite	-0.43 (-2.18, 1.33)	0.63	0.96 (0.72, 1.28)	0.14
Computer/Laptop	0.23 (-1.56, 2.01)	0.80	1.12 (0.84, 1.50)	0.54
Internet Access	**-2.11 (-3.85, -0.37)**	**0.02**	0.83 (0.63, 1.11)	
Sum of SES Assets	-0.16 (-0.50, 0.19)	0.50	0.99 (0.94, 1.04)	0.38
PCA (Full)	-0.16 (-1.20, 0.88)	0.76	0.99 (0.83, 1.18)	0.82
PCA (Individual)	-0.45 (-1.32, 0.41)	0.30	0.92 (0.80, 1.06)	0.22
PCA (Birth)	0.77 (-0.26, 1.79)	0.14	1.11 (0.93, 1.33)	0.13
PCA (Neighborhood)	-0.08 (-1.00, 0.83)	0.86	0.98 (0.84, 1.13)	0.37
MCA (Full)	-1.36 (-4.40, 1.68)	0.38	1.07 (0.66, 1.71)	0.20
MCA (Individual)	-0.85 (-2.85, 1.15)	0.40	1.00 (0.72, 1.39)	0.60
MCA (Birth)	-0.41 (-2.86, 2.05)	0.75	0.88 (0.60, 1.29)	0.72
MCA (Neighborhood)	0.41 (-0.79, 1.61)	0.50	1.05 (0.87, 1.28)	0.33

Bold = significant at $p < 0.10$

Table 6: Unadjusted estimates of SES components with blood pressure in females

	Systolic Blood Pressure		Elevated Blood Pressure	
	β (95% CI)	P-value	OR (95% CI)	P-value
Birth Characteristics				
Maternal Marital Status	1.16 (-0.577, 2.88)	0.19	1.19 (0.87, 1.63)	0.28
Parental Health Service Use	-0.02 (-1.47, 1.43)	0.98	0.91 (0.70, 1.18)	0.48
Toilet Access (infancy)	-9.73 (-22.7, 3.32)	0.14	0.84 (0.08, 9.37)	0.89
Water Access (infancy)	0.01 (-2.28, 2.30)	0.99	1.07 (0.69, 1.66)	0.75
Caregiver's Highest Grade	**-0.64 (-1.31, 0.04)**	**0.06**	0.92 (0.82, 1.04)	0.17
Wealth (quintiles) at birth	**-0.96 (-1.66, -0.26)**	**<0.01**	0.89 (0.79, 1.02)	0.09
Neighborhood Characteristics				
Feels Safe During the Day	0.46 (-0.50, 1.42)	0.35	1.04 (0.88, 1.25)	0.63
Feels Safe at Night	0.21 (-0.72, 1.13)	0.66	1.07 (0.90, 1.26)	0.46
Perceived Safety	-0.29 (-1.17, 0.58)	0.51	1.06 (0.90, 1.25)	0.47
Individual Characteristics				
Living Alone	2.31 (-1.47, 6.09)	0.23	1.23 (0.63, 2.41)	0.54
Married or Cohabitating	**-4.47 (-7.62, -1.31)**	**<0.01**	0.56 (0.29, 1.08)	0.08
Completion of Grade 12	**-1.88 (-3.64, -0.13)**	**0.04**	0.85 (0.61, 1.16)	0.30
House Type	1.19 (-1.41, 3.78)	0.37	1.05 (0.65, 1.70)	0.83
Water Facilities	0.83 (-1.19, 2.85)	0.42	1.15 (0.79, 1.67)	0.47
Toilet Facilities	-0.12 (-1.90, 1.67)	0.90	1.30 (0..93, 0.12)	0.12
Asset Ownership				
Home electricity	0.79 (-5.20, 6.79)	0.80	1.27 (0.40, 4.02)	0.69
Motor vehicle	-0.40 (-2.06, 1.26)	0.63	0.84 (0.62, 1.14)	0.25
Fridge	1.85 (-2.50, 6.20)	0.41	2.26 (0.85, 5.99)	0.10
Microwave	-0.14 (-2.40, 2.12)	0.90	1.18 (0.77, 1.81)	0.44
Washing Machine	-0.75 (-2.54, 1.03)	0.41	1.06 (0.77, 1.48)	0.71
Landline Phone	0.16 (-1.67, 2.00)	0.86	0.94 (0.67, 1.31)	0.70
Cell Phone	3.71 (-2.49, 9.91)	0.24	1.69 (0.47, 6.13)	0.42
Television	1.96 (-3.25, 7.17)	0.46	1.39 (0.50, 3.86)	0.53
Radio	0.98 (-1.67, 3.64)	0.47	0.76 (0.48, 1.22)	0.25
Video / DVD	-0.96 (-3.46, 1.53)	0.45	0.97 (0.62, 1.54)	0.91
MNet/Satelite	**-1.86 (-3.51, -0.21)**	**0.03**	0.79 (0.59, 1.08)	0.14
Computer/Laptop	-0.57 (-2.24, 1.11)	0.60	0.91 (0.67, 1.23)	0.54
Internet Access	**-3.06 (-4.74, -1.38)**	**<0.01**	**0.68 (0.50, 0.92)**	**0.01**
Sum of SES Assets	-0.23 (-0.57, 0.11)	0.14	0.98 (0.92, 1.03)	0.38
PCA (Full)	-0.85 (-1.94, 0.24)	0.13	1.03 (0.83, 1.27)	0.82
PCA (Individual)	-0.55 (-1.40, 0.29)	0.20	0.91 (0.78, 1.06)	0.22
PCA (Birth)	**-0.97 (-2.04, 0.10)**	**0.08**	0.86 (0.70, 1.05)	0.13
PCA (Neighborhood)	0.14 (-0.67, 0.96)	0.73	1.07 (0.92, 1.25)	0.37
MCA (Full)	-1.01 (-3.93, 1.91)	0.50	0.70 (0.40, 1.20)	0.20
MCA (Individual)	-1.16 (-2.88, 0.56)	0.19	0.92 (0.67, 1.26)	0.60
MCA (Birth)	1.26 (-0.92, 3.45)	0.26	1.07 (0.73, 1.59)	0.72
MCA (Neighborhood)	-0.62 (-1.78, 0.53)	0.29	0.90 (0.73, 1.11)	0.33

Bold = significant at $p < 0.10$

Table 7: Multivariate regression coefficients, odds ratios, and 95% confidence intervals comparing adjusted associations between socioeconomic status and blood pressure in males

	Systolic Blood Pressure				Elevated Blood Pressure			
	Model 1		Model 2		Model 3		Model 4	
	[β (95% CI)]	P	[β (95% CI)]	P	[OR (95% CI)]	P	[OR (95% CI)]	P
Summative Household SES measure								
Asset Index[a]	-0.25 (-0.57, -0.07)	0.13	**2.96 (0.97, 4.96)**	**	0.97 (0.92, 1.02)	0.22	1.42 (0.99, 2.03)	0.06
Height	**0.02 (0.00, 0.03)**	**0.03**	**0.02 (0.00, 0.03)**	**0.02**	1.00 (1.00, 1.01)	0.05	**1.00 (1.00, 1.01)**	**0.04**
BMI	**0.50 (0.26, 0.73)**	***	**2.27 (1.15, 3.38)**	***	**1.09 (1.05, 1.14)**	***	**1.35 (1.10, 0.66)**	**
Interaction[b]			**-0.15 (-0.24, -0.06)**	**			**0.98 (0.9, 1.00)**	**0.03**
Total SES: PCA Measure								
1° Component[c]	-0.20 (-1.24, 0.84)	0.70	1.15 (-6.0, 8.30)	0.75	0.98 (0.82, 1.17)	0.81	0.65 (0.18, 2.32)	0.48
Height	0.02 (-0.00, 0.03)	0.08	0.02 (-0.00, 0.03)	0.08	1.00 (1.00, 1.00)	0.76	1.00 (1.00, 1.00)	0.79
BMI	0.27 (-0.01, 0.54)	0.06	0.28 (-0.00, 0.56)	0.05	1.05 (1.00, 1.10)	0.05	1.05 (1.00, 1.10)	0.07
Interaction[b]			-0.06 (-0.3, 0.26)	0.71			1.02 (0.96, 1.08)	0.53
SES categories: PCA Measures[d]								
Individual	-0.58 (-1.70, 0.53)	0.30	-0.58 (-1.68, 0.53)	0.31	0.87 (0.71, 1.05)	0.15	0.87 (0.71, 1.06)	0.16
Birth	0.72 (-0.37, 1.80)	0.20	0.64 (-0.45, 1.73)	0.25	1.12 (0.93, 1.36)	0.24	1.11 (0.91, 1.34)	0.31
Neighborhood	-0.13 (-1.23, 0.98)	0.82	6.14 (-0.22, 12.50)	0.06	1.00 (0.83, 1.22)	0.98	**3.54 (1.08, 11.6)**	**0.04**
Height	0.01 (-0.00, 0.03)	0.09	0.01 (-0.00, 0.03)	0.10	1.00 (1.00, 1.00)	0.74	1.00 (1.00, 1.00)	0.80
BMI	0.24 (-0.04, 0.52)	0.10	**0.35 (0.05, 0.65)**	**0.02**	1.05 (0.99, 1.10)	0.08	**1.07 (1.01, 1.13)**	**0.02**
Individual int.[b]			NS				NS	
Birth int.[b]			NS				NS	
Neighborhood int.[b]			**-0.29 (-0.58, -0.00)**	**0.05**			**0.94 (0.89, 1.00)**	**0.03**
Total SES: MCA Measure								
Dimension 1[e]	-2.18 (-5.18, 0.82)	0.16	-2.74 (-6.41, 0.93)	0.14	0.94 (0.58, 1.53)	0.79	0.05 (0.00, 2.09)	0.12
Height	**0.02 (0.01, 0.04)**	0.01	**0.03 (0.01, 0.06)**	**0.02**	**1.00 (1.00, 1.01)**	**0.01**	**1.00 (1.00, 1.01)**	**0.01**
BMI	**0.72 (0.34, 1.10)**	***	**0.51 (0.06, 0.96)**	**0.03**	**1.12 (1.05, 1.19)**	***	**1.12 (1.05, 1.19)**	**
Interaction[b]			-0.03 (-0.09, 0.04)	0.41			1.14 (0.97, 1.35)	0.12
SES categories: MCA Measures[f]								

Individual	-1.22 (-3.75, 1.31)	0.35	**-20.5 (-39.4, -1.51)**	**0.03**	0.96 (0.64, 1.45)	0.85
Birth	-0.32 (-2.74, 2.11)	0.80	-0.34 (-2.76, 2.07)	0.78	0.88 (0.60, 1.31)	0.53
Neighborhood	1.08 (-0.54, 2..70)	0.19	1.03 (-0.58, 2.65)	0.21	1.23 (0.95, 1.61)	0.12
Height	**0.02 (0.00, 0.04)**	**0.03**	**0.02 (0.00, 0.04)**	**0.03**	**1.00 (1.00, 1.01)**	**0.02**
BMI	**0.54 (0.18, 0.90)**	******	**0.58 (0.22, 0.94)**	******	**1.10 (1.03, 1.17)**	******
Individual int.[b]			**0.91 (0.02, 1.80)**	**0.04**		
Birth int.[b]			NS			
Neighborhood int.[b]			NS			

Bold indicates significance at p<0.05. ** indicates a p-value of <0.01. *** indicates a p-value of <0.0001.
Model 1 controlled for height and BMI using the continuous outcome of systolic blood pressure.
Model 2 controlled for Model 1 + potential interaction using the continuous outcome of systolic blood pressure.
Model 3 controlled for height and BMI using the binary outcome of elevated blood pressure (either hypertension or pre-hypertension).
Model 4 controlled for Model 3 + potential interaction using the binary outcome of elevated blood pressure (either hypertension or pre-hypertension).
[a] Summative household asset index
[b] Continuous by continuous interaction term between SES and BMI
[c] Represents the primary component derived using principal component analysis
[d] Includes measures categorized as individual (incl. household), birth, and neighborhood SES, derived using principal component analysis
[c] Represents the primary dimension derived using multiple correspondence analysis
[d] Includes measures categorized as individual (incl. household), birth, and neighborhood SES, derived using multiple correspondence analysis

Table 8: Multivariate regression coefficients, odds ratios, and 95% confidence intervals comparing adjusted associations between socioeconomic status and blood pressure in females

	Systolic Blood Pressure				Elevated Blood Pressure			
	Model 1		Model 2		Model 3		Model 4	
	[β (95% CI)]	P	[β (95% CI)]	P	[OR (95% CI)]	P	[OR (95% CI)]	P
Summative Household SES measure								
Asset Index[a]	-0.25 (-0.55, 0.06)	0.11	-1.01 (-2.31, 0.29)	0.13	0.97 (0.92, 1.03)	0.37	0.88 (0.69, 1.13)	0.32
Height	**0.02 (0.00, 0.03)**	**	**0.02 (0.01, 0.03)**	**	**1.00 (1.00, 1.01)**	**0.02**	**1.00 (1.00, 1.01)**	**0.02**
BMI	**0.33 (0.19, 0.46)**	***	-0.01 (-0.59, 0.56)	0.96	**1.07 (1.04, 1.10)**	***	1.02 (0.92, 1.14)	0.67
Interaction[b]			0.03 (-0.02, 0.08)	0.23			1.00 (1.00, 1.01)	0.42
Total SES: PCA Measure								
1° Component[c]	-1.01 (-2.10, 0.08)	0.07	3.02 (-3.19, 9.22)	0.34	0.01 (-0.20, 0.24)	0.96	1.31 (0.37, 4.58)	0.68
Height	**0.02 (0.00, 0.04)**	**0.02**	**0.02 (0.00, 0.04)**	**0.02**	**0.00 (0.00, 0.01)**	**0.04**	**1.00 (1.00, 1.01)**	**0.04**
BMI	**0.28 (0.10, 0.46)**	**	**0.31 (0.13, 0.49)**	**	**0.05 (0.02, 0.08)**	**	**1.06 (1.02, 1.09)**	**
Interaction[b]			-0.18 (-0.44, 0.09)	0.20			0.99 (0.94, 1.04)	0.68
SES categories: PCA Measures[d]								
Individual	-0.77 (-1.86, 0.32)	0.16			-0.12 (-0.33, 0.10)	0.28		
Birth	-0.88 (-1.99, 0.23)	0.12			-0.15 (-0.37, 0.06)	0.16		
Neighborhood	-0.27 (-1.33, 0.78)	0.61			-0.01 (-0.22, 0.19)	0.91		
Height	**0.02 (0.00, 0.04)**	**0.02**			**0.00 (0.00, 0.01)**	**0.04**		
BMI	**0.26 (0.08, 0.44)**	**			**0.05 (0.02, 0.08)**	**		
Individual int.[b]								
Birth int.[b]								
Neighborhood int.[b]								
Total SES: MCA Measure								
Dimension 1[e]	-0.72 (-3.65, 2.22)	0.63	**-16.1 (-30.4, -1.69)**	**0.02**	-0.32 (-0.88, 0.25)	0.27	**0.05 (0.00, 0.86)**	**0.04**
Height	**0.02 (0.01, 0.04)**	**0.01**	**0.02 (0.00, 0.04)**	**0.01**	0.00 (-0.00, 0.01)	0.14	1.00 (1.00, 1.01)	0.16
BMI	**0.34 (0.18, 0.52)**	**	**0.38 (0.20, 0.56)**	***	**0.06 (0.03, 0.09)**	**	**1.07 (1.03, 1.11)**	***
Interaction[b]			**0.62 (0.05, 1.19)**	**0.03**			1.11 (1.00, 1.25)	0.06
SES categories: MCA Measures[f]								

Individual	-1.97 (-4.07, 0.12)	0.07	**-2.14 (-4.23, -0.04)**	**0.05**	0.96 (0.65, 1.42)	0.82
Birth	1.11 (-1.06, 3.28)	0.32	1.27 (-0.90, 3.43)	0.25	1.12 (0.75, 1.68)	0.59
Neighborhood	-0.64 (-2.16, 0.87)	0.41	**-7.85 (-14.7, -1.04)**	**0.02**	0.94 (0.70, 1.24)	0.65
Height	**0.03 (0.01, 0.04)**	**	**0.03 (0.01, 0.04)**	**	1.00 (1.00, 1.01)	0.11
BMI	**0.35 (0.18, 0.52)**	***	**0.36 (0.19, 0.53)**	***	**1.07 (1.03, 1.10)**	**
Individual int.[b]			NS			
Birth int.[b]			NS			
Neighborhood int.[b]			**11.5 (10.8, 12.2)**	**0.03**		

Bold indicates significance at p<0.05. ** indicates a p-value of <0.01. *** indicates a p-value of <0.0001.
Model 1 controlled for height and BMI using the continuous outcome of systolic blood pressure.
Model 2 controlled for Model 1 + potential interaction using the continuous outcome of systolic blood pressure.
Model 3 controlled for height and BMI using the binary outcome of elevated blood pressure (either hypertension or pre-hypertension).
Model 4 controlled for Model 3 + potential interaction using the binary outcome of elevated blood pressure (either hypertension or pre-hypertension).
[a] Summative household asset index
[b] Continuous by continuous interaction term between SES and BMI
[c] Represents the primary component derived using principal component analysis
[d] Includes measures categorized as individual (incl. household), birth, and neighborhood SES, derived using principal component analysis
[c] Represents the primary dimension derived using multiple correspondence analysis
[d] Includes measures categorized as individual (incl. household), birth, and neighborhood SES, derived using multiple correspondence analysis

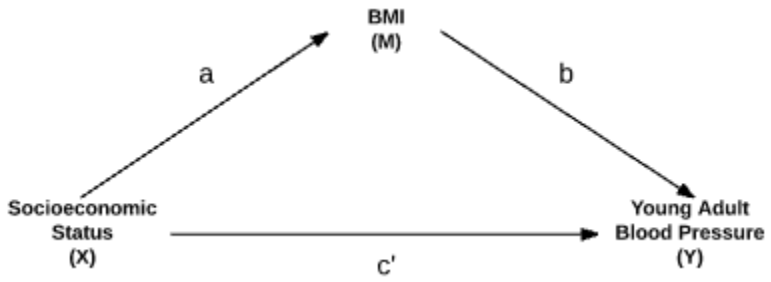

Figure 2: Exposure-mediator interaction between

The direct effect (a) represents the effect of the exposure (SES) on the outcome (SBP) at a fixed counterfactual level of the mediator (BMI). In models with no interaction between SES and BMI, the controlled direct effect is equal to the natural direct effect. In models with exposure-mediator interaction between SES and BMI, the controlled direct effect represented changes in the outcome with a constant level of the mediator (BMI), but a contrast between the exposure (SES) levels from low to high. The natural direct effect measured changes in the outcome by levels of exposure (SES), keeping the mediator (BMI) at the same level it would have been if SES was set as moderate. The indirect effect (b) represents the extent to which the effect of the exposure on the outcome changes throughout levels of the mediator, and as a result, was used to calculate the percentage of the total effect that was mediated by BMI. Finally, the total effect (c') represents the sum of the natural direct effect and the natural indirect effect.[91]

Table 9: Direct and indirect effects of body mass index as a mediator of the effect of SES on continuous systolic blood pressure (assuming exposure–mediator interaction between SES and BMI when included in the final model)

	Males		Females	
	β (SE)	P-value	β (SE)	P-value
Summative Household SES measure				
Natural direct effect	0.05 (0.21)	0.82	-0.25 (0.16)	0.11
Natural indirect effect	0.40 (0.14)	0.01	0.02 (0.03)	0.40
Controlled direct effect				
Mediator = Low	3.04 (1.05)	0.00		
Mediator = High	2.89 (1.00)	0.00		
Total effect (TE)	0.44 (0.31)	0.15	-0.22 (0.16)	0.16
% Total Effect Mediated	**89.65%**		**10.21%**	
Primary PCA Measure for Total SES only (No Interaction)				
Natural direct effect	-0.20 (0.53)	0.84	-1.01 (0.56)	0.07
Natural indirect effect	0.02 (0.05)	0.65	0.19 (0.10)	0.06
Total effect (TE)	-0.18 (0.53)	0.73	-0.82 (0.56)	0.14
% Total Effect Mediated	**12.25%**		**23.35%**	
Theory-driven PCA by SES type (household/individual, at birth, neighborhood)				
Individual Factors				
Natural direct effect	-0.58 (0.57)	0.31	-0.77 (0.56)	0.17
Natural indirect effect	-0.02 (0.05)	0.68	-0.07 (0.08)	0.41
Total effect (TE)	-0.60 (0.57)	0.29	-0.84 (0.56)	0.14
% Total Effect Mediated	**3.15%**		**7.86%**	
Birth Factors				
Natural direct effect	0.72 (0.56)	0.20	-0.88 (0.57)	0.12
Natural indirect effect	0.17 (0.11)	0.13	0.02 (0.08)	0.81
Total effect (TE)	0.89 (0.55)	0.11	-0.86 (0.58)	0.13
% Total Effect Mediated	**19.18%**		**2.22%**	
Neighborhood Factors				
Natural direct effect	-0.17 (0.57)	0.77	-0.27 (0.54)	0.61
Natural indirect effect	0.02 (0.06)	0.74	0.03 (0.07)	0.69
Controlled direct effect				
Mediator = Low	6.29 (3.34)	0.06		
Mediator = High	6.14 (3.27)	0.06		
Total effect (TE)	-0.15 (0.57)	0.79	-0.24 (0.55)	0.66
% Total Effect Mediated	**12.31%**		**12.08%**	
Primary MCA Measure for Total SES				
Natural direct effect	-2.18 (1.54)	0.16	-0.38 (1.52)	0.80
Natural indirect effect	0.47 (0.30)	0.11	-1.00 (0.85)	0.24
Controlled direct effect				
Mediator = Low			-16.4 (7.51)	0.03
Mediator = High			-15.7 (7.23)	0.03
Total effect (TE)	-1.70 (1.56)	0.27	-1.38 (1.71)	0.42
% Total Effect Mediated	**27.92%**		**72.61%**	
Theory-driven MCA by SES type (household/individual, at birth, neighborhood)				
Individual Factors				
Natural direct effect	-0.94 (1.31)	0.47	0.15 (0.20)	0.44
Natural indirect effect	-0.36 (0.51)	0.48	-1.82 (1.09)	0.10
Controlled direct effect				

Mediator = Low	-20.9 (9.97)	0.04		
Mediator = High	-20.0 (9.51)	0.04		
Total effect (TE)	-1.31 (1.39)	0.35	-1.97 (1.08)	0.07
% Total Effect Mediated	**27.71%**		**8.49%**	
Birth Factors				
Natural direct effect	-0.12 (1.24)	0.80	1.11 (1.11)	0.32
Natural indirect effect	-0.16 (0.18)	0.32	-0.04 (0.20)	0.85
Total effect (TE)	-0.28 (1.25)	0.69	1.07 (1.13)	0.35
% Total Effect Mediated	**36.36%**		**3.62%**	
Neighborhood Factors				
Natural direct effect	1.08 (0.83)	0.19	-0.68 (0.78)	0.39
Natural indirect effect	0.14 (0.12)	0.24	0.30 (0.27)	0.27
Controlled direct effect				
Mediator = Low			-7.99 (3.56)	0.03
Mediator = High			-7.71 (3.43)	0.02
Total effect (TE)	1.22 (0.84)	0.14	-0.38 (0.82)	0.64
% Total Effect Mediated	**11.81%**		**78.11%**	

The percentage of the total effect from socioeconomic status on systolic blood pressure that was mediated by body mass index was determined by dividing the natural indirect effect by the marginal total effect.

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