2021

The Predictive Relationship of Allostatic Load in Asthma

Mohamed Mustafa Hassan
Walden University

Walden University

College of Health Professions

This is to certify that the doctoral dissertation by

Mohamed. M. Hassan

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. Peter Anderson, Committee Chairperson, Public Health Faculty
Dr. Montrece Ransom, Committee Member, Public Health Faculty
Dr. Zin Htway, University Reviewer, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
2021

Abstract

The Predictive Relationship of Allostatic Load in Asthma

by

Mohamed. M. Hassan

M.Sc., University of Nottingham, 1999

BS, University of Portsmouth, 1998

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

August 2021

Abstract

Research on populations emphasizes the influence of allostatic overload, a marker of biophysical and biochemical stress, in driving adverse health outcomes. Unknown is the impact of allostatic load and its cardiovascular, metabolic, and inflammatory components as they pertain to asthma prevalence in U.S. populations. Specifically, there is a need to understand the nature of the relationship between allostatic load and asthma in light of confounders such as socioeconomic status, race, education, and gender. Using Bronfenbrenner's bioecological model as a theoretical underpinning and binary logistic regression as a statistical modality, the predictive relationship between allostatic load and asthma was examined in a representative U.S. population. Using binary logistic regression, contemporary data from the National Health and Nutrition Examination Study covering the most recent available data (2017-2018) were analyzed for predictive association with results reported for effect size, significance, and confidence intervals. Study results highlighted the statistically significant predictive nature of allostatic load in asthma and the outsized role of inflammation in driving the relationship. Having high allostatic load predicted 28% higher odds for reporting asthma ($p = .021$) whereas inflammatory allostatic load predicted asthma with 36% higher odds, ($p < .01$). Insights from the current research study contribute a scientific basis to support the development of a validated allostatic load index for asthma where none currently exists. Additionally, clinical translation of results can inform the development of future prognostic tools for asthma that account for allostatic load and possibly reduce the associated health disparity and inequity leading to improved lives for individuals, families, and communities.

The Predictive Relationship of Allostatic Load in Asthma

by

Mohamed M. Hassan

M.Sc., University of Nottingham, 1999

BS, University of Portsmouth, 1998

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

August 2021

Dedication

I dedicate this dissertation to my family, whose support has enabled me to pursue my passion. To my wife Kelly, you are my rock. I love you. Thank you for constantly picking up where I have slacked, being my sounding board and voice for reason. Throughout this ordeal you are the glue that kept our family thriving. To my son Oliver, thank you for being patient with dad when he couldn't always play or had to work. You are so kind and generous, even to your parents. To my mother and late father, thank you for your unwavering encouragement and support, irrespective of circumstance. Your faith in me made believe this journey was possible. To my siblings, Dahlia and Hassan, thank you for leading the way with compassion and humbleness. Your counsel has allowed me to see the path forward and envisage what is truly possible. I love you all.

Acknowledgments

I wish to acknowledge my committee chair, Professor Peter B. Anderson. From the first instance I connected with Professor Anderson, he has been an engaged and collaborative guide on this journey. Every interaction I have had with Professor Anderson was one made with thoughtful reflection and compassionate delivery to progress further in the dissertation journey. Thank you. My committee member, Professor Montrece Ransom, thank you for your enthusiastic counsel on translation and application of my research. I would also like to acknowledge Dr. Zin Hitway for his valuable statistical insight. The three of you have made the journey very rewarding, thank you.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Introduction

Allostasis describes how social environments impact an individual's physical and mental health, characterizing the capacity to adapt to stressful environments in order to support homeostasis (Carlson & Chamberlain, 2005). Sterling and Eyer (1988) first introduced allostasis as a way to explain how adaptive variability complements homeostasis in an effort to keep the organism healthy. While allostasis allows the body to respond to a changing environment, sustained allostasis leads to disease (McEwen, 2016). This led to the coining of the term *allostatic load* to refer to the cumulative "wear and tear" that results from sustained allostasis (McEwen, 2016). In addition to adverse health outcomes, excess allostatic load has been implicated in health disparity and inequity (Beydoun et al., 2016).

The means by which allostatic load exerts its harmful effects are complex, spanning the psychosocial and biophysical realms. Under normal conditions, allostasis is achieved by an interplay between the hypothalamus, pituitary, and adrenal glands termed the HPA axis (McEwen, 2015). In response to a stressful event, the hypothalamus releases corticotropin-releasing factor (CRF) that stimulates the subsequent release of adrenocorticotropic hormone (ACTH) from the pituitary gland (Picard et al., 2017). ACTH travels via the systemic circulation to the adrenal gland, where it, in turn, stimulates the release of cortisol. Cortisol subsequently initiates physiological events such as heightened anxiety, increased blood pressure, and blood glucose elevations (Picard et al., 2017). The HPA axis returns to balance as high levels of systemic cortisol

act on the hypothalamus and pituitary gland through a negative feedback loop to shut down production of CRF and ACTH.

Chronic activation of the HPA axis results in a dysregulation of stress hormones that lead to clinical disease. As allostatic load increases, a state of exhaustion sets in at the HPA axis (Bahreinian et al., 2013). At this juncture, the negative feedback loop system that controls the HPA axis becomes dysregulated, causing changes in metabolic and cardiovascular systems. Such changes include increased glucose, elevated blood pressure, and reduced lipid metabolism as a means to compensate for the dysregulated hormonal systems (Picard et al., 2017). The final stage of allostatic load progression is allostatic overload, whereby the culmination of physiological and subclinical dysregulations transforms into chronic disease (Fava et al., 2019).

Asthma represents an ongoing health issue with a pressing need for added research that guides practice to lower adverse health outcomes. In the United States, medical, absenteeism, and mortality costs associated with asthma exceed $89.1 billion, with a higher burden evidenced across racial and socioeconomic lines (Nurmagambetov et al., 2018). Indeed, asthma's disparity among race and ethnic lines translates into twice the prevalence in African American children as compared to their Caucasian counterparts. Asthma exacerbation in this population manifests as more hospital visits, higher steroid use, and reduced exercise capacity (Federico et al., 2020).

Socioeconomic status functions as an important nexus point between allostatic load and asthma. Data tying socioeconomic status to adverse asthma outcomes are prolific in the academic literature with ties to reduced stress coping capacity and higher

disparity (Beck et al., 2016). Central to socioeconomic status's ill effects is a direct link to distinct biological inflammatory pathways that predispose individuals to chronic respiratory disease (E. Chen et al., 2016, 2017, 2019; Kwong & Bacharier, 2019; Lee et al., 2017). Moreover, there is a strong link between allostatic load and asthma, with similar biological dysregulation that leaves the individual more prone to disease (Johnson et al., 2017). Indeed, the linkages to allostatic load are so strong that it has led several authors to hypothesize that socioeconomic status might be primarily responsible for embedding allostatic load (Gagné & Ghenadenik, 2018; Graves & Nowakowski, 2017; McCrory et al., 2019).

Research that quantifies the associations between allostatic load and asthma imparts positive social change as it can inform future interventions that aim to reduce disparities. As such, I examined and reported on the association between allostatic load and asthma, quantifying the influence of key confounders such as socioeconomic status, gender, race, and education.

The current paper is composed of five chapters that aim to provide a detailed overview of the topic of allostatic load, socioeconomic status, and asthma; an introduction, literature review, research method, results, and finally, a chapter covering discussions and conclusions. In the following sections of this first chapter, I provide a brief background and problem statement before framing the purpose of the study. Subsequent sections of this chapter detail the research questions of interest, including the theoretical framework and the quantitative nature of the study. The chapter ends with

reference to definitions, assumptions, delimitations, limitations, significance, and a general summary.

Background

Allostatic overload reflects a breakdown between psychosocial and biophysical stress mitigation systems and is associated with health disparity and inequity (Delpierre et al., 2016). Correspondingly, the study of the relationship between allostatic load, socioeconomic status, and asthma is influenced by several variables that transect multiple disciplines and include the differential impact on populations, allostatic calculation, markers of disease, and public health.

Tomfohr et al. (2016) examined whether allostatic load independent of traditional sociobehavioral risk factors is associated with mortality disparities between Caucasian and African American subjects and found higher associations between allostatic load and mortality for African American men and women as opposed to their Caucasian counterparts. This finding represents how race is a key differentiation in allostatic load and part of a large body of evidence to the fact (Allen et al., 2019; Beydoun et al., 2016; Delpierre et al., 2016; Suvarna et al., 2020). Equally as significant, socioeconomic status has been demonstrated as a key influencer of adverse health outcomes with connections to both asthma and allostatic load. Christensen et al. (2018b) assessed the mechanisms underlying the association between parental socioeconomic conditions with later life allostatic load. Here, parental socioeconomic condition was inversely associated with allostatic load in midlife. Current literature supports the need to examine the influence of

socioeconomic status in any study that considers allostatic load and asthma (E. Chen et al., 2016; Gagné & Ghenadenik, 2018; Johnson et al., 2017; McCrory et al., 2019).

Within the allostatic load schema, there is strong evidence that social and environmental stress-related factors can result in impaired biological pathways, leading to subclinical and eventual chronic disease (McEwen, 2016). Indeed, several factors have been found to be associated with an increased allostatic load, including older age, female gender, and low educational attainment (Ding et al., 2019; Doamekpor & Dinwiddie, 2015; Howard & Sparks, 2015; Juster et al., 2019; Juster et al., 2016; Piazza et al., 2019). Additionally, family functioning also plays a role in increasing the allostatic load. Ehrlich et al. (2015) examined the prospective connections among familial dysfunction and eosinophilic activity in children with asthma over 1 year, showing a direct biological link between stressors and increased adverse asthma outcomes.

Of interest, allostatic load calculation varies within the academic literature with no singular biomarker "mix" adopted as the standard upon which to measure allostatic load (Duong et al., 2017; Wiley et al., 2016). Howard and Sparks (2016) highlighted the utility of using summary measures of allostatic load, the outsized importance of metabolic markers, and the inherent variation present as a function of race, gender, and education in allostatic load calculations, and the need for a standard index. McEwen (2015) detailed the successful validation of diagnostic clinimetric tools to assess allostatic load using a combined approach that includes allostatic load biomarkers and clinimetric criteria. Taken in aggregate, the outlined literature points to how allostatic load features in the complex interplay between the biophysical and psychosocial domains that result in

adverse outcomes in asthma. Confounders complicate this relationship and must be accounted for. Additionally, a weighted and standardized calculation of the allostatic load index is necessary to align with seminal research on the topic.

Problem Statement

Allostatic load overburden refers to how stress-based events in childhood leave lifelong psychosocial and biochemical imprints that manifest as inflammatory disease in midlife (Jackson et al., 2010). Several scholars have reported adverse health outcomes and health disparity associated with AL, including ties to cardiovascular, cognitive, and respiratory disorders (Bahreinian et al., 2013; Goldstein, 2012; Steptoe et al., 2014). Central to this association between ill-health and allostatic load is the breakdown of internal mechanisms that regulate psychosocial stress, resulting in an uninhibited inflammatory cytokine response that subsequently manifests as a chronic inflammatory disease (Jackson et al., 2010).

Asthma, in particular, remains a disease state with profound unmet need, illustrated by higher prevalence in communities associated with lower socioeconomic status and racial disparity (Gordon et al., 2016; Lee et al., 2017). The Centers for Disease Control and Prevention (CDC, 2018) estimated that more than 6.1 million children under 18 have asthma, representing 8% of the population. Although literature separately links socioeconomic status and allostatic load to inflammatory disorders, a gap exists as to their mutual role in asthma (E. Chen et al., 2017; Graves & Nowakowski, 2017; Logan & Barksdale, 2008; Oren et al., 2017). Notably, socioeconomic status is a known modulator of stress and thereby allostatic load (E. Chen et al., 2016). As such, insights gleaned from

this research delineating the combined effect of socioeconomic status and allostatic load in asthma can inform health promotion campaigns that attempt to mitigate adverse outcomes in adolescents and bolster resiliency against asthma.

Purpose

In the current study, I used a quantitative cross-sectional approach to ascertain the relationship between allostatic load and asthma, taking into account the influence of confounders in the relationship. Specifically, I statistically analyzed secondary data from the National Health and Nutrition Examination Survey (NHANES) was for variable association using binary logistic regression. Here, total allostatic load index was expressed as a composite of metabolic, cardiovascular, and inflammatory biomarkers, including systolic blood pressure (SBP), diastolic blood pressure (DBP), high density lipoprotein cholesterol (HDL), total cholesterol (TC), pulse, albumin, estimated glomerular filtration rate (eGFR), and C-reactive protein. The analysis was also thought to determine how categorical components of allostatic load impact the relationship. Here cardiovascular components include SBP, DBP, HDL, TC, and pulse. Metabolic components include albumin and eGFR. Lastly, the inflammatory component of allostatic load is composed of CRP.

Confounding variables of interest included socioeconomic status expressed as poverty to income ratio, educational attainment stratified by years of schooling, gender, and ethnicity. Educational attainment was also examined for moderation effects. As for the dependent variable in the study, I utilized the presence of asthma as outlined in the medical questionnaire to analyze the occurrence in the dataset.

Research Questions

RQ1: Is there a relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education?

$H_0$1: There is no relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

$H_1$1: There is a relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

RQ2: Is there a relationship between cardiovascular, metabolic, and inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education?

$H_0$2: There is no relationship between cardiovascular, metabolic, and inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

$H_1$2: There is a relationship between cardiovascular, metabolic, and inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

RQ3: Does educational attainment moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and gender?

$H_0$3: Educational attainment does not moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and gender.

$H_1$3: Educational attainment moderates moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and gender.

RQ4: Does educational attainment moderate the relationship between cardiovascular, metabolic, and inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and gender?

$H_0$4: Educational attainment does not moderate the relationship between cardiovascular, metabolic, and inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and gender.

$H_1$4: Educational attainment moderates moderate the relationship between cardiovascular, metabolic, and inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and gender.

Theoretical Framework

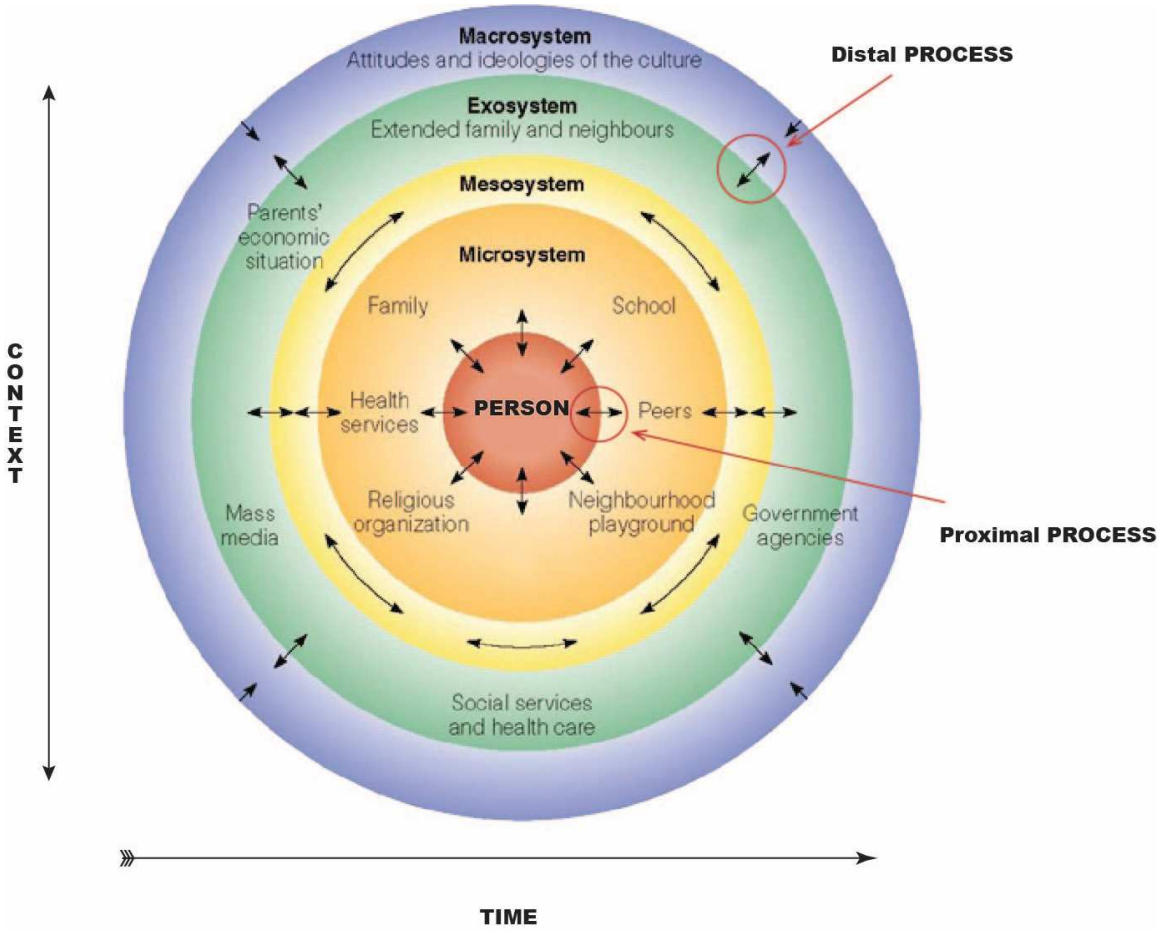
Theories provide researchers with a systemic way of explaining or predicting events by illustrating the relationships between variables (Glanz et al., 2015). Of significance to this study, Bronfenbrenner's ecological system's theory (EST) and its subsequent iteration, the bioecological model, delineating the role of ongoing interactions as the key influencers of development, serve as suitable frameworks for studying allostatic load (Bronfenbrenner, 1974, 1977). EST divides an individual's environment into five interrelated spheres of influence: the microsystem, the mesosystem, the exosystem, the macrosystem, and the chronosystem (Bronfenbrenner, 1977). The microsystem is the inner-most sphere of influence and describes factors that have a direct

exchange with the developing child. Next comes the mesosystem, which frames interactions between the developing child's different microsystems. The exosystem is the third level of influence and describes social structures that influence microsystems. External to the exosystem is the macrosystem, which describes the influence of cultural elements and their effect on development. The outermost sphere of influence is the chronosystem, which describes life transitions over time. Further refinements of the EST by Bronfenbrenner expanded on the original EST by defining four domains: process, person, context, and time. In this new bioecological model, the microsystem, mesosystem, exosystem, and macrosystem spheres of influence are nested under context.

Bronfenbrenner's bioecological model helps frame the current research by identifying and mapping key variables of interest, delineating intervariable relationships, and ascertaining variable impact on the individual. Key variables of interest in allostatic load research such as socioeconomic status, ethnicity, gender, and education are framed within the model to accurately describe their context and to determine their relationship to the individual to quantify their direct impact on health outcomes.

Figure 1

Bronfenbrenner's Bioecological Model



Note. Bronfenbrenner's bioecological model showing the relationship between person, process, context, and time. Person characteristics sit at the center of the model and determine how the individual is impacted by proximal processes. Distal processes, while less influential, also shape experiences through their action on successive contexts that eventually reach the individual as a proximal process. Adapted from Ferguson, K. T., & Evans, G. W. (2019). Social ecological theory: Family systems and family psychology in bioecological and bioecocultural perspective. In B. H. Fiese, M. Celano, K. Deater-Deckard, E. N. Jouriles, & M. A. Whisman (Eds.), APA handbook of contemporary family psychology: Foundations, methods, and contemporary issues across the lifespan., Vol. 1. (2018-59956-009; pp. 143–161). American Psychological Association; APA PsycInfo. https://doi.org/10.1037/0000099-009

Nature of the Study

Using a cross-sectional research design, the current study assessed whether a relationship between allostatic load and asthma exists, including which categorical components of allostatic load (cardiovascular, metabolic, inflammatory) might have led to the associations to asthma. To that pursuit, I statistically examined contemporary NHANES data that included variables of interest using the statistical package SPSS version 25. A weighted allostatic load index and its categorical components served as the independent variables of interest in the analysis, whereas asthma was the dependent variable or outcome. Using binary logistic model analysis, I quantified and reported on the influence of confounding variables in the study including socioeconomic status, gender, education, and race. For the study results, I calculated odds ratios for associations to provide a measure of effect size. Additionally, I also reported confidence intervals (CI) and *p*-values to test whether any observed effects where statistically significant (Mann, 2003; Ressing et al., 2010).

Definitions

Allostatic load: A state of biological exhaustion where long-term stress exposure results in dysregulation of biological coping systems leading to subclinical and inflammatory disease (Edes & Crews, 2017)

Asthma: A medical condition in which a person's airways become inflamed, narrow, and swell, making it difficult to breathe (Mims, 2015).

Educational attainment: Highest grade or level of school completed based on descriptive criteria in the NHANES survey instrument (CDC, 2020). Five categories

compose the variable: less than 9th grade, 9th-11th grade, less than high school, some college, college graduate, or above.

Ethnicity: Race of participant classed as Mexican American, non-Hispanic Black, non-Hispanic White, or Other, based on the NHANES (CDC, 2020).

Gender: Binary, biological sex of individual categorized as male or female mirroring the NHANES instrument (CDC, 2020).

Socioeconomic status: A measure of social and economic status that aligns with health (Baker, 2014). In the current study, I selected poverty to income ratio as a descriptor with categories representing below five or five and above (CDC, 2020).

Assumptions

Assumptions pertaining to accurate reporting and allostatic load calculation methodology should be noted for the current study. Firstly, I assumed accurate respondent self-reporting for both presences of asthma and confounders within the study. Although NHANES conducts robust validation of its survey instrument, the presence of self-reporting bias cannot be ruled out (Pfeiffer et al., 2017). The assumption is worth noting considering current research that points to a difference between self-reported and data-driven asthma in NHANES (Amaral et al., 2019). Secondly, and to the issue of allostatic load calculation, no standardized measurement exists, although there are calls to create such a standard (Gallo et al., 2014). The need for a standardized allostatic load calculation is illustrated by the myriad calculations present for allostatic load within NHANES (Duong et al., 2017). Indeed, scholars have openly questioned whether allostatic calculation matters if a sufficient number of key metabolic, cardiovascular, and

inflammatory markers are used in a base calculation (Howard & Sparks, 2016). That being said, for the current study, I chose a calculation method described by Doamekpor and Dinwiddie (2015) that has gained wide acceptance in the published literature (Duong et al., 2017; Howard & Sparks, 2016; Wiley et al., 2016).

Scope and Delimitations

In this study I aimed to determine the presence and magnitude of associations between allostatic load, confounders, and asthma in a representative U.S. population. I assessed allostatic load as a composite marker of cardiovascular, metabolic, and inflammatory biomarkers using a calculation posited by Doamekpor and Dinwiddie et (2006). Contemporary NHANES data covering the most recent iterations of the survey (2017-2018) was analyzed for potential associations in the dataset. To that end, I employed a quantitative, cross-sectional research design that used binary logistic regression to create models that quantify possible associations and moderating effects by confounders. Effect size was reported as odds ratios and included corresponding significance measures such as probability values and CIs.

As for delimitations, this study was limited to a U.S. population from the NHANES database. There exists a significant research body that details allostatic load and its adverse effects from non-U.S. populations (Dich et al., 2015; Matzer et al., 2018; Tampubolon & Maharani, 2018; van Deurzen & Vanhoutte, 2019; Viljoen & Claassen, 2017). A decision to limit sources to U.S. populations was based on how stress-based events differ by geographic region (Robertson & Watts, 2016). Moreover, an examination of the literature on the topic of allostatic load highlighted the need for analysis from

representative U.S. data upon which to draw conclusions. Accordingly, while the analysis contained herein is generalizable to a large swathe of the U.S. population, it should be stressed that such generalizability cannot be extrapolated to populations outside the United States.

Limitations

Limitations of the current study stem from its cross-sectional design. The cross-sectional design affords researchers the ability to identify patterns and prevalence of an outcome within a population at a given time (Creswell & Creswell, 2018). This utility of cross-sectional research makes it a good choice for consideration when resources are limited or when working from secondary datasets. Additionally, the ability to consider multiple variables in a single study makes it an attractive option for research (Salkind, 2010). Conversely, cross-sectional studies offer no input on causality, giving no explanation of the sequence of events between cause and outcome (Creswell & Creswell, 2018). Moreover, nonresponse bias and small sample size can detrimentally impact results from such a research design. Having a large sample size and predetermining inclusion and exclusion criteria can go a long way in ensuring that results from such an analysis remain relevant (Salkind, 2010).

Significance

By conducting this study, I aimed to answer an identified gap in the published academic research. A large body of research has detailed the adverse impact of excess allostatic load in health, with linkages to health disparity and inequity in cardiovascular, metabolic, and psychological disease (Beydoun et al., 2016; Mocayar Marón et al., 2019;

Nobel et al., 2017; Vaccarino et al., 2018). Unfortunately, the research for allostatic load and asthma outcomes is far less robust, with an observed gap as it pertains to representative U.S. populations. Indeed, asthma as a disease area remains one with a continuing unmet need where in spite of recent advances, disparities persist (Martinez, 2019). Accordingly, by conducting this research I aimed to inform future research on allostatic load and provide a possible evidence base to support the formulation of new health treatment modalities based on observed associations. Such an approach might support the use of allostatic load component pathways as prognostic tools in asthma treatment and may contribute to the reduction of disparity and health inequity therein.

Summary

In this chapter, I outlined and introduced the topic of allostatic load and its adverse effects on asthma outcomes, providing a synopsis and background that described current gaps in the knowledge base. This was followed by stating the research problem, study purpose, distilled research questions, and their placement within Bronfenbrenner's bioecological model. The chapter ended with a description of definitions, assumptions, delimitations, limitations, and significance. What follows in Chapter 2 is a deeper synthesis of contemporary research on the topic of allostatic load and associated variables of interest, focusing on their place in theory and relative association to the individual.

Chapter 2: Literature Review

Introduction

Allostatic overload describes how chronic stress exposure affecting neural and systemic physiological response exceeds coping resources and results in adverse outcomes for the individual (Fava et al., 2019). The impact of allostatic load on the population's health is demonstrated by its linkages to multiple adverse outcomes and health disparity (Beydoun et al., 2016; Delpierre et al., 2016; Rodriquez et al., 2019). Associations between allostatic overload and ill-health have been noted for metabolic, cardiovascular, respiratory, and mental health domains (Barry et al., 2020; Berger et al., 2015; Bey et al., 2018; Wiley et al., 2016).

Asthma, in particular, is an area where the implications of allostatic load and its associated social and individual elements detrimentally impact health (Barry et al., 2020). As a disease state, asthma afflicts upwards of 8% of the U.S. population, with children, adolescents, and the elderly representing vulnerable groups (Martinez, 2019). Social factors such as low socioeconomic status and African American ethnicity exacerbate asthma morbidity, manifesting as increased disease severity and more acute clinical outcomes (Ehrlich et al., 2015; Goodman et al., 2017; Lam et al., 2018; Lee et al., 2017; Rastogi & Holguin, 2017).

While literature exists that describes the linkages between allostatic load and asthma and socioeconomic status and asthma, a gap exists into how socioeconomic status and allostatic load combined impact asthma incidence (E. Chen et al., 2017; Graves & Nowakowski, 2017; Oren et al., 2017). As such, I aimed to determine the relationship

between allostatic load and asthma prevalence in a representative U.S. sample, reporting on the impact of ethnicity, gender, education, and socioeconomic status. I aimed to report the magnitude of effect between total and component-based allostatic load and asthma while controlling for socioeconomic status, gender, and race. Additionally, I aimed to determine the existence and magnitude of any moderation effects from education, while controlling for socioeconomic status, gender, and race. In the analysis, logistic regression provided an estimate of any observed effect size between the independent and dependent variables, any confounding from covariates, and moderation effects from education. In the following sections, I provide information relating to literature search strategy, theoretical foundation, as well as a synopsis of recent literature covering topics and variables of interest.

Literature Search Strategy

For the current manuscript, I conducted a systematic review of the literature covering the past 5 years to determine current knowledge gaps and answer the outlined research questions. I reviewed and synthesized contemporary research relating to allostatic load, personal characteristics, social factors, and asthma to ascertain key variables and concepts of interest using a combined CINAHL & MEDLINE search. Peer-reviewed articles, case studies, systemic reviews, books, and evidence-based reports were screened for key search terms such as *allostatic load, allostasis, allostatic overload socioeconomic status, race, ethnicity, gender,* and combinations thereof. Results were limited to human data from the United States covering the year 2015 onwards and thematically coded into clinical, individual factors, and social factors. I included seminal

research extending beyond the 5-year range when current sources were unavailable, too few to engender consensus, or when historical perspective was needed. This was indeed the case for literature covering allostatic load and asthma, allostatic load and ecological theory, and ecological theory genesis, including the bioecological model.

Theoretical Foundation

As a theoretical underpinning, Bronfenbrenner's EST and associated bioecological model served as ideal accompaniments for the current doctoral study. The development of Bronfenbrenner's EST rose from the realization that life aspects and their interaction with the child are influential in development (Bronfenbrenner, 1974). Such influencing factors and their context were termed "ecology," giving rise to ecological systems theory that takes into account dynamic interactions and environments as developmentally impactful. In EST, Bronfenbrenner argued that five spheres of influence exist when studying development: microsystem, mesosystem, exosystem, macrosystem, and chronosystem (Bronfenbrenner, 1977). Further refinement of the EST by Bronfenbrenner resulted in the emergence of the bioecological model that espoused four domains related to development: process, person, context, and time (Bronfenbrenner & Evans, 2000; Rosa & Tudge, 2013). In this newly created bioecological model, (Figure 1), the spheres of influence, microsystem, mesosystem, exosystem, and macrosystem, are nested under the context domain. (Ferguson & Evans, 2019).

Proximal Processes and Allostatic Load

Proximal processes lie at the heart of the bioecological model and describe the sustained exchange between the developing person, people, objects, and symbols within

their environment (Bronfenbrenner & Evans, 2000). Bronfenbrenner termed these exchanges as critical drivers of development and noted that factors that interfere with these processes have an outsized impact on the individual (Bronfenbrenner & Evans, 2000). In the allostatic load model, proximal processes are analogous to stress-based events that "wear and tear" at compensatory mechanisms (Edes & Crews, 2017). These repetitive stress-based events act as psychosocial trauma and lead to an overload of stress-based mitigation capacity (McEwen, 2016). As a result of this breakdown, powerful biochemical modulators of acute response are left unregulated, powering a harmful biochemical cascade that ends in inflammatory disease (Fava et al., 2019).

Person Characteristics and Allostatic Load

The person domain describes how personality traits, behavioral dispositions, resources, and demand characteristics shape the impact of proximal processes (Rosa & Tudge, 2013). Allostatic load researchers have illustrated how factors such as coping capacity, education, and behavioral disposition that are associated with the person domain moderate allostatic load and as such are responsible for reduced mortality and morbidity (Ding et al., 2019; Levy et al., 2016; Suvarna et al., 2020).

The Context Domain in Allostatic Load

The third domain of Bronfenbrenner's theory is context, and it is described as the impact of physical and psychosocial environments on development, stratified as the microsystem, mesosystem, exosystem, and macrosystems (Ferguson & Evans, 2019).

Allostatic Load in the Microsystem

Microsystems are described as environments experienced directly by the person such as family, peers, and neighbors and are the only level in which proximal processes occur (Rosa & Tudge, 2013). Evidence connecting allostatic load to interactions at the microsystem is seen in studies of toddler anxiety and adolescents victimization, where the higher allostatic load was predictive of increased internalized problems across childhood and into adulthood (Barr, 2017; Buss et al., 2011; Zimmer□Gembeck, 2016).

Allostatic Load in the Mesosystem

Mesosystems are described as the interrelationships between individual microsystems (Ferguson & Evans, 2019). Individuals are influenced by the interactions between the microsystems they live in, such as the home, school, or work (Rosa & Tudge, 2013). As such, what happens in one microsystem impacts other microsystems, which might directly impact the individual. In allostatic load, this mirrors how impoverished neighborhoods that could not support sustained parental income negatively impacted child development (Robinette et al., 2016).

Allostatic Load in the Exosystem

The exosystem is used to describe the impact of environments of which the individual is not a member, yet still influence proximal processes (Rosa & Tudge, 2013). Although the individual is not part of the exosystem per se, the influence on microsystems, proximal processes, and the individual is profound (Lehman et al., 2017). Here, the connection to allostatic load is evidenced through parental socioeconomic

status, where reduced financial well-being adversely impacts child health (Christensen et al., 2018a).

Allostatic Load in the Macrosystem

In the bioecological model, macrosystems are used to describe the intersections between microsystems, mesosystems, and exosystem as they relate to a specific culture or subculture (Rosa & Tudge, 2013). Factors such as ethnicity, socioeconomic status, geographic location, and culture dominate this sphere (Ferguson & Evans, 2019). Cultural influence shapes the structure and function of microsystems that subsequently impact the proximal process and the individual. The connection of this domain to allostatic load is quite strong, with a large literature body describing such linkages and adverse health outcomes in cardiovascular, metabolic, and mental health domains (Borrell et al., 2020; Christensen et al., 2018a; Graves & Nowakowski, 2017; Johnson et al., 2017; Juster et al., 2016; Lunyera et al., 2020).

The Time Domain in Allostatic Load

The final component domain of Bronfenbrenner's model is time (chronosystem), which describes life transitions over time and their impact on the individual (Ferguson & Evans, 2019). Within this domain lie factors that impact allostatic load such as adverse childhood experiences, traumatic familial dynamics such as divorce, and parental death. Collectively, these time-based events impact the individual through the person domain and contribute to increased allostatic load through proximal processes (Christensen et al., 2018a; Delpierre et al., 2016; Schulz et al., 2012).

Literature Review of Key Variables

Allostatic Load and Clinical Outcomes

Adverse clinical outcomes resultant from allostatic overload have been linked to dysfunctionality at the hypothalamic-adrenal-pituitary axis (Edes & Crews, 2017). Here, in response to repeated acute stressors and the "wear and tear" of regulatory mechanisms, unabated hormonal release ensues and results in excess cytokine production leading to high inflammatory states and endothelial dysfunction (Picard et al., 2017; Wiley et al., 2016). The terminal result of this dysfunctionality is a biological system that is less capable of coping with acute stressors and more prone to inflammatory mediated disease states such as cardiovascular disease and asthma (Edes & Crews, 2017).

Allostatic Load and Asthma

Although allostatic load driven asthma development mirrors the molecular mechanisms seen in allostatic load driven cardiovascular disease, the literature is not as prevalent on the topic (Hill et al., 2018). Barry et al. (2020) aimed to parse the relationship between allostatic load, asthma, and corticosteroid use and detailed how subjects with an allostatic load index equivalent to mild controlled asthma presented similarly to more aged patients without asthma; the differential being eight years. In their study, higher allostatic load indices of non-asthmatic patients made them clinically present as older patients. This 'early weathering' is a key feature of allostatic load and places individuals at greater risk. The authors noted that therapeutic approaches that reduce stress and increase coping capacity might show benefits in terms of improved morbidity and mortality rates. The study did not report on which components of allostatic

load drove the observed associations. Similarly, Bahreinian et al. (2013) reported on the relationship that exists between higher allostatic load biomarker indices for 10-year-olds and subsequent higher asthma incidence by age 12. The relationship was quantified as a 60% increased likelihood of prevalent asthma for each additional unit of allostatic load (Bahreinian S et al., 2013). Notably, the authors stated that observed atopic and non-atopic asthma phenotypes in boys and girls were driven by increases in different biomarkers (Bahreinian S et al., 2013). Here, elevated cortisol in boys and insulin levels in girls increased the likelihood of non-atopic asthma. Chen et al. (2019) detailed the association between stress and asthma as it relates to Black and Latino adolescent youth compared to their Caucasian peers. Examining how the response to stress-based school events influences mental health and asthma outcomes, the authors noted an observable difference in immunological and clinical outcomes. In their analysis, Black and Latino youth with asthma who experienced high levels of school stress and had self-control experienced better mental health but worse clinical and immunologically assessed asthma. Of note, the study did not report on the impact of individual components of allostatic load.

Collectively, the literature supports that allostatic load events are linked to worsening asthma outcomes and that this association is present for children, adolescents, and adults alike (Bahreinian et al., 2013; Barry et al., 2020; E. Chen, Hayen, et al., 2019). Moreover, there is an observable asthma disparity in outcomes, one that is based on race (Beydoun et al., 2016). A critical assessment of the data also reveals that the majority of available data suffers from either small sample sizes, lack of representative populations,

or having been conducted outside of the United States (Beydoun et al., 2016; Fernandez, 2015; Tomfohr et al., 2016). There is also a distinct difference in how allostatic load was calculated with differences in chosen biomarkers and associated weighting (Duong et al., 2017; Gallo et al., 2014; Geronimus et al., 2006; Howard & Sparks, 2016; Wiley et al., 2016). Additionally, few studies reported on which components of allostatic load drove the associations (Howard & Sparks, 2016). What remains to be seen is if the trends and disparity observed for asthma and allostatic load are present in a representative US population using a verified measure for allostatic load. Additionally, what specific components of allostatic load drive this association. Answering these questions is the main focus of the current study.

Allostatic Load and Individual Characteristics

Ethnicity

Several studies point to the role of allostatic load in racial mortality disparity and adverse outcomes. Beydoun et al. (2016) reported on all-cause and cause-specific mortality disparities by race/ethnicity from a representative US adult population after adjusting for confounding factors. The analysis utilized data from the Third National Health and Nutrition Examination Survey (NHANES III) and included over 16,000 individuals and 4000 deaths with a median follow-up time of 170 months. The allostatic load was indicated as a mediator of all-cause mortality for Non-Hispanic Blacks (NHBs). Additionally, NHBs experienced higher cause-specific cardiovascular and cancer mortality compared to their respective Mexican American and Non-Hispanic White cohorts. The study illustrated how allostatic load mediates differences in racial mortality,

with evidence of its effect mediated by different categorical components of allostatic load. Borrell et al. (2020) reconfirmed these results using NHANES III and Linked Mortality data. Similar to earlier findings, the higher allostatic load was associated with increased all-cause and cardiovascular (CVD) specific mortality. Of interest, all-cause mortality rates for each racial/ethnic group differed with age and education, whereas for CVD-specific mortality rates, this difference was observed for gender (Borrell et al., 2020). Analogous to this data, Shalowitz et al. (2019) looked at Allostatic load in terms of cardiometabolic risk following delivery and as a function of race, poverty status, and pregnancy risk factors. In a population that included 2,448 predominantly low-income African American, Latina, and White women immediately after delivery, African American women fared worse than their Latina and White counterparts. The data corresponded with a higher allostatic load for African American women.

Researchers also pointed to the role of negative affect and allostatic load showing distinct racial associations. Tomfohr et al. (2016) examined how differential exposure to discrimination, negative affect, and health practices mediated allostatic load in a group of healthy, middle-aged African American and White American participants. Using parallel and serial mediation, the authors noted that allostatic load in the African American group persisted even when controlling for age, gender, and socioeconomic status. The authors surmised that discrimination was not a direct mediator of the relationship between allostatic load and race but was part of a chain of negative-effect variables that, in turn, were influenced by allostatic load. Notably, no discussion of what categorical component of allostatic load drove the observed associations.

From the reviewed sources, it is clear that racial disparity represented a key influencer of allostatic load, with associations to all-cause mortality and cardiovascular-specific mortality (Delpierre et al., 2016; Doamekpor & Dinwiddie, 2015). Moreover, confounding this association are significant interactions for age, gender, socioeconomic status, and education with allostatic load (Beckles et al., 2019; Beydoun et al., 2016; E. Chen et al., 2016; Ding et al., 2019). The data also makes it clear that discrimination was not the main mediator for this association but that it played a role in a chain of negative influences that subsequently affected allostatic load (Allen et al., 2019).

Although the derived associations stem from large representative US databases, the data itself is not current, with a majority being derived from NHANES III that covered the years 1988-1994. Time and changing societal norms might render the described associations as non-representative of current perspectives. Similarly, as is the case for other studies that have researched variables associated with allostatic load, the reviewed sources cite a myriad of different allostatic calculation methodologies (Duong et al., 2017; Howard & Sparks, 2016). The outstanding question that remains is 'does contemporary US representative data mirror the differences seen in allostatic load by race, and to what extent do individual components drive that difference.' I aim to answer this question in the current study.

Gender

The data for allostatic load and gender can be described as lacking consensus with a need for contemporary US population data. It is important to understand that in addition to binary sex determinations, gender refers to a spectrum of socially constructed roles,

identities, and expressions (Kerr et al., 2020). Here, we report on US data for sex-based differences and gender-based differences.

U.S.-based studies that map sex to allostatic load can be broadly classified into those that report no sex-based differences and those that show women with a lower allostatic load burden than men. Brody et al. (2013) reported on sex-based differences in African American adolescent youth residing in the "Black Belt" states that include South Carolina, Georgia, Alabama, Mississippi, and Louisiana. The authors noted that men, as opposed to women, experienced higher externalizing behavior, although depressive symptoms were higher in the female group. That being said, the authors commented that no apparent sex differences were found in the dataset. Chen et al. (2014) drew similar conclusions by examining NHANES 2005-2008 data for allostatic load and sleep. Results from their statistical analysis showed that although African American women experienced higher allostatic load compared to their Mexican American and Caucasian counterparts, no sex-based differences were noticed in the study.

As for studies that show lower allostatic load burden in women, Hawkley et al. (2011) reported such an association when examining allostatic load differences in a racially stratified Illinois population from the Chicago Health, Aging, and Social Relations Study (CHASRS). Fernandez et al. (2015) presented similar results when examining sex-based differences in coping style and their impact on allostatic load in a sample population from the Jackson Heart Study. The Jackson Heart Study authors noticed that while there was no difference in allostatic load between men and women, higher disengagement coping styles were seen in women. The notion of female advantage

was furthered by the work of Tampubolon and Maharani (2018) that not only showed a distinct female advantage but hypothesized that it might account for the increased longevity seen in women when compared to men.

While it is unclear from the data whether women show no difference or have a lower allostatic load than men, it is clear is that no studies to date show women with a higher allostatic load compared to men. However, there is an emerging consensus that approaches to measure allostatic load in men and women must be different (Juster et al., 2016). At issue is the cutoff biomarker values that dictate high allostatic load in statistical analysis, biomarkers that show differential baselines by sex and as such should be appropriately weighted in any cutoff calculation.

As for gender-based differences, the academic literature is less robust and points to a need for more research on the topic (Kerr et al., 2020). Nonetheless, a small number of researchers have taken on the challenge of deciphering allostatic load differences in this important population. Juster et al. (2016), when examining allostatic load and depressive symptoms amongst a gender diverse population, reported that increased masculine gender roles relative to feminine gender roles were associated with high allostatic load for both sexes. Moreover, the authors reported that gay/bisexual men had a lower allostatic load than heterosexual men, whereas lesbian/bisexual women had a higher allostatic load than heterosexual women. More recently, Juster et al. (2019) showed that masculinity and age predicted high allostatic load levels, while sex did not. Here, masculinity and being female predicted increased physical complaints that corresponded to high allostatic load. The research points to the fact that higher

masculinity irrespective of sexual orientation results in increased physiological dysregulation and suggests an overall increased vulnerability to hyper-arousal pathologies such as cardiovascular disease among masculine-typed individuals. Taken in aggregate, the outlined studies point to the fact that when it comes to allostatic load, sex, gender roles, and sexual orientation reveal associations that are impossible to discern by assessing sex solely as a binary classification.

As outlined in the review, there remains a lack of consensus regarding how sex and gender-based differences pertain to allostatic load. Whether this lack of association is an actual signal from the data, or a product of inappropriate allostatic load calculation remains to be seen. There is, however, emerging evidence that might indicate that the male sex or masculine gender might predispose the individual to a higher allostatic load (Juster et al., 2019).

As with other studies in allostatic load, allostatic load calculations differed from study to study, highlighting the need for standardization of allostatic load score (Duong et al., 2017). Additionally, gender-based studies rarely point to differences in allostatic load components as they pertain to outcomes (Fernandez, 2015; Juster et al., 2019; Tampubolon & Maharani, 2018). Similarly, sex and gender-based studies determining associations to allostatic load lacked current representative US data, which is especially the case for gender-based studies (Juster et al. , 2019; Juster et al., 2016; van Deurzen & Vanhoutte, 2019). As such, through results from this study, I aim to report on sex-based differences from a current representative US sample using appropriately sex-weighted allostatic load indices and chronicle the findings as they pertain to asthma as an outcome.

Education

An assessment of current literature regarding allostatic load and educational attainment highlights complex associations influenced by race and discrimination that are difficult to ascertain as causal in nature.

Howard and Sparks (2015) reported on the importance of educational attainment in allostatic load from four recent waves of NHANES, stating that education is an important predictor of allostatic load, but cautioning that the association is only significant when comparing college-educated to less than high school diploma educated participants. Moreover, the degree of benefit was predicated by racial/ethnic and socioeconomic background, with individuals with less than high school attainment exhibiting similar allostatic load irrespective of race/ethnicity. That being said, racial differences in allostatic load began to diverge with increasing education, culminating in large variance for college-educated individuals.

The observed racial/ethnic differences in allostatic load profiles seen across educational attainment raised the question of whether distinct biological pathways existed for allostatic load. Howard and Sparks (2016) examined biomarkers from NHANES data to determine if, indeed, distinct biological pathways were responsible for the observed variance. Results showed that Non-Hispanic Blacks specifically exhibit inflammatory pathways as opposed to metabolic pathways in non-Hispanic Whites. Additionally, results showed that low educational attainment displayed both inflammatory and metabolic allostatic pathways, whereas higher education individuals exhibited predominantly metabolic pathways.

Allen et al. (2019) sought to determine the association between racial discrimination and allostatic load in African American women and the influence of education. Biomarker data from the African American Women's Heart & Health Study were analyzed to reveal inherent associations. Study results showed that participants with higher education who have experienced low or very high levels of racial discrimination had lower allostatic load than those with lower educational attainment. Of note, results also showed that cardiometabolic biomarkers drove high allostatic load.

Doamekpor and Dinwiddie (2015) used pooled data from the 2001-2010 NHANES to examine the association between education and allostatic load among foreign- and US-born Blacks. In their analysis, the authors noted that education did not impart a moderating benefit upon recent immigrants. Hormenu et al. (2020) reconfirmed the lack of benefit, adding that neither education, income, health insurance, or marital status affected a high allostatic load score in immigrant cohorts. Collectively the data adds credence to the *acculturation* hypothesis that states that an allostatic load protective ability wears down after a ten-year stay in the US as unhealthy behaviors and diet become the norm (Doamekpor & Dinwiddie, 2015; Hormenu et al., 2020)

Seeking to establish whether a distinct biological causal relationship existed between allostatic load and educational level, Hamdi et al. (2016) utilized biomarker data and a co-twin control design to infer causality. Twins from the Midlife Development in the United States (MIDUS) study who had participated in the biomarker study were used for analysis. Individual regression results pointed to a significantly negative relationship between allostatic load and education, inferring that education imparts better health.

Controversially, the Co-Twin Control (CTC) analysis explained all of the significance seen from the individual regression as being due to familial influences between the shared twins. As such, the current study concludes that no causal relationship between allostatic load and education exists.

Ding et al. (2019) thought to determine if causality does indeed exist between educational attainment and allostatic load by using a Mendelian Randomization design and data from the Health and Retirement Study. The authors hypothesized that using Mendelian Randomization is more suitable in inferring causality from observational studies. Intervening variable analysis that employed a polygenic score of educational attainment showed a significant, negative relationship between education and allostatic load. Moreover, the authors reported that years of education were significantly associated with reduced risk for BMI and Hba1c, which are indicators for metabolic dysregulation.

Synthesizing the outlined research, it is apparent that education is an important moderator of allostatic load when comparing college-educated to less than high school educated individuals and that the relationship is influenced by race (Ding et al., 2019; Dinwiddie et al., 2015; Howard & Sparks, 2016). Moreover, distinct biological pathways exist by race, and African Americans exhibit inflammatory pathways for allostatic load (Howard & Sparks, 2015). However, tying causality to the significant association between allostatic load and education remains an ongoing topic of discourse. Also, of note, the benefit imparted by education does not translate to recent immigrants, reinforcing the acculturation hypothesis and highlighting nativity as a confounder for the education variable (Hamdi et al., 2016).

As for the strengths and weaknesses of reviewed sources, it can be seen that while the data does indeed reflect a diverse and representative U.S. population with adequate sample size, there is a need to quantify how education moderates allostatic load in asthma outcomes. Correspondingly, the current study aims to fill this research gap and report any confounding by nativity therein.

Socioeconomic Status

Low socioeconomic status in childhood has often been linked to disease in adulthood. Chen et al. (2016) discussed the differential impact of socioeconomic status using resource and prestige groupings on asthma development in 150 adolescents noting distinct biological pathways. Their research notes that prestige was associated with asthma management behaviors related to environmental control, whereas resources were consistently associated with profiles of cytokine production. Chen et al. (2017) further examined the links of socioeconomic status to asthma outcomes in the same population, focusing on parental socioeconomic status. Results from their research point to significant differences in children's asthma control by parents' childhood socioeconomic status. Parents who experienced low socioeconomic status as children had children with worse asthma control than parents with higher socioeconomic childhoods and exhibit higher inflammatory cytokine production.

Graves and Nowakowski (2017) added to the research body by examining the association inherent between low socioeconomic status in childhood and stress in later adulthood using a longitudinal approach that relies on allostatic load scores. Using successive data from the National Social Life, Health, and Aging Project (NSHAP), the

authors measured allostatic load longitudinally over a 5-year period. The authors noted that low childhood socioeconomic status is significantly associated with increased allostatic load in late adulthood and that this relationship persists even after controlling for education and wealth. That being said, the authors note that the data does support a moderating effect by college-level education on the relationship.

Beckles et al. (2019) investigated whether allostatic load explained the association between life-course socioeconomic status and type II diabetes in an African American population, noting whether the relationship was modified by gender. Using records from the Jackson Heart Study, the authors note that life-course socioeconomic status influences type II diabetes in women and not men and that allostatic load did not explain the observed result. Conversely, Lunyera et al. (2020) confirmed the relationship between life-course socioeconomic status and allostatic load when examining kidney health in an African American population. The authors note that low lifetime socioeconomic status was associated with 8% higher odds of CKD incidence and modestly faster eGFR decline via its association with higher allostatic load at baseline.

Taking a different approach to classifying socioeconomic status, Rodriguez et al. (2019) argued that using a social stratification approach, where socioeconomic and demographic characteristics jointly conform to actual social structures, better explains health outcomes attributable to allostatic load. Analyzing longitudinal data from the National Survey of Midlife Development in the United States (MIDUS), the authors revealed that allostatic load was associated with socioeconomic gradients that impact health and that low gradients were observed more often in the African American cohorts,

especially women and the elderly compared to their non-African American counterparts. More importantly, the data point to the importance of differential exposure to ecological, political, social, economic, and historical contexts that dictate social stratification.

A review of the recent literature shows that socioeconomic status is independently linked to asthma with distinct inflammatory profiles associated with resource availability and parental socioeconomic status (E. Chen et al., 2016; Gagné & Ghenadenik, 2018; McCrory et al., 2019). As for the allostatic load, longitudinal data links low socioeconomic status in childhood to higher allostatic load in adulthood (Rodriguez et al., 2019). While no current literature describes associations between socioeconomic status, allostatic load, and asthma outcomes, there is research that describes how allostatic load and socioeconomic status contribute to adverse type II diabetes and chronic kidney disease (Lunyera et al., 2020). The remaining unanswered question in the research is whether socioeconomic status impacts allostatic load and results in adverse asthma outcomes, a question I aim to answer in the current research study.

Summary and Conclusion

Major themes apparent from the literature review point to the outstanding research gaps, some of which align with the current study's research questions. From an outcome's perspective, although allostatic load has secured a position as a mediator of all-cause mortality, that linkage is strongest for cardiovascular-specific mortality. This association is influenced particularly by race, education, gender, and socioeconomic status. For asthma, research points to different allostatic load biomarkers concurrent with different phenotypes, however, the evidence base is not as robust, and there remains a

need to understand asthma-based mortality from a representative US population. Moreover, there is a need to understand which specific components of allostatic load (cardiovascular, metabolic, inflammatory) power the possible association between allostatic load and asthma.

Differences in allostatic load burden by race are by far the most prominent in research, with several key factors in this association mapped at the biological and social levels. African Americans suffer from the highest allostatic load burden compared to Mexican Americans and Caucasians. There is also a distinct difference in metabolic and inflammatory allostatic profile by race, with African Americans having a higher inflammatory burden as opposed to a metabolic burden in their Caucasian counterparts.

Education has emerged as an important area of research focus, with a propensity of research mapping low educational attainment to an increase in both metabolic and inflammatory profiles. College-level education has been demonstrated as a moderator for this relationship through a decrease in metabolic pathways. That being said, it is important to note that this moderation only holds true for US-born African Americans. This highlights the importance of nativity as an important differentiating factor, with time in the US and 'acculturation' having adverse impacts on allostatic load that is not moderated by education. What is missing from the research is what role education plays when it comes to allostatic load and asthma in a representative US population.

As for sex and gender-based differences in allostatic load, it is fair to say that observed differences remain unresolved, with proponents and opponents reporting differences in mortality and causality. As is the case for other key factors, there remains a

research gap as to how sex in particular moderates or mediates allostatic load in asthma-based outcomes. This need also extends to socioeconomic status, where in spite of a large body of research tying parental socioeconomic position, resources, and prestige to asthma, linkages that pertain to allostatic load, socioeconomic status, and asthma have not been recently defined for a representative US population. As such, our current research attempts to answer the noted questions from a representative US sample as a way to further the body of research and provide positive social change.

Chapter 3: Research Method

Introduction

The current study used a quantitative cross-sectional approach to determine the relationship between total allostatic load, its categorical components, and asthma including the influence of confounders in the relationship. To that end, I statistically analyzed contemporary secondary data from the NHANES dataset using binary logistic regression and noting the presence, if any, of confounding by socioeconomic status, educational attainment, gender, and ethnicity.

In this analysis, total allostatic load index was expressed as a composite of metabolic, cardiovascular, and inflammatory biomarkers and included SBP, DBP, HDL, TC, pulse pressure, albumin, eGFR, and C-reactive protein. Here, cardiovascular components included SBP, DBP, HDL, TC, and pulse pressure whereas metabolic components include albumin and eGFR. As for the inflammatory component, it was comprised of a singular measure, CRP. These categorical classifications of allostatic load were analyzed for associations as well.

In the following sections of this chapter, I outline the research design and rationale, methodology, identify threats to validity, and end with a brief summary highlighting the major takeaways from the chapter. Included in the summary is a preview of the major section of Chapter 4.

Research Design and Rationale

The independent variables in this study were total allostatic load index, cardiovascular allostatic load, metabolic allostatic load, and inflammatory allostatic load. Each measure of allostatic load comprised a corresponding set of biomarkers identified from laboratory and physical examination components of the NHANES survey. For total allostatic load index, biomarkers included SBP, DBP, HDL, TC, pulse, albumin, eGFR, and C-reactive protein. As for cardiovascular allostatic load, the category included SBP, DBP, HDL, TC, and pulse pressure. Metabolic allostatic load comprised eGFR and albumin biomarkers whereas inflammatory allostatic load was denoted through CRP measurement.

The dependent variable for this study was asthma as noted on the NHANES medical conditions questionnaire. A study participant is classed as having asthma if they answer in the affirmative to whether a health professional has ever stated to the respondent that they have asthma.

As for covariates in the study, they included socioeconomic status, educational attainment, gender, and ethnicity. Socioeconomic status was assessed through family income to poverty ratio (INDFMPIR) as stated in the NHANES demographic survey instrument (CDC, 2020). Here the ratio was a binary value of less than five and more than five.

Educational attainment was assessed using the NHANES adult educational attainment instrument (DMDEDUC2), which asks adults over the age of 20 what their highest level of education is. Answers are grouped into five separate groups representing

less than 9th grade, 9th-11th grade, high school, some college, or college graduate (CDC, 2020). Education also served as a moderating variable in the logistic regression analysis.

Race in the study was assessed using the NHANES descriptor RIDRETH3, which classifies respondents into six categories representing Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian and Other/Mixed Race. As for gender, it was assessed as a binary male or female categorization.

In the current study I used a cross-sectional design to determine the existence, if any, of any associations between allostatic load, its constituent components and asthma. Using a cross-sectional research design is useful in identifying patterns and prevalence of an outcome within a population at a given time point (Allen, 2017). By applying such a research design to the study of allostatic load, I aimed to discern the presence, if any, of associations between the independent, confounding, mediating, and dependent variables. Also of benefit, cross-sectional studies are relatively easy to conduct, with no lag in data collection resulting in brevity and cost-effectiveness for the researcher (Mertens & McLaughlin, 2004). Moreover, the research design choice was consistent with other research on the topic of allostatic load (Doamekpor & Dinwiddie, 2015; Duong et al., 2017; Howard & Sparks, 2016; Tomfohr et al., 2016).That being said, it is important to note that cross-sectional studies do not provide the sequence of events resulting in an outcome and as such are not able to confer causality (Allen, 2017).

Methodology

Population

The population of interest in this study were noninstitutionalized civilian residents of the United States residing in the 50 states and the District of Columbia. Every year, NHANES selects approximately 5,000 individuals of all ages and interviews them in their homes, with corresponding health and laboratory examinations in a mobile examination center (MEC). Sample sizes are fixed in any year due to operational constraints, with public use data presented in 2-year cycles annually (CDC, 2020).

It is estimated that the prevalence of asthma in the United States is approximately 8% (Nurmagambetov et al., 2018). With that in mind, it is reasonable to estimate that each 2-year iteration of NHANES includes approximately 800 individuals with asthma.

Sampling and Sampling Procedures

Detailed sampling design and estimation for NHANES are described in analytic publications by the National Center for Health Statistics (T. C. Chen et al., 2020). NHANES uses a multistage, probability sampling design to select participants representative of the civilian, noninstitutionalized U.S. population. The sampling procedure consists of four stages: (a) primary sampling units (PSUs; counties or combinations of adjacent counties), (b) segments within PSUs (census blocks or combinations of blocks), (c) dwelling units (households) within segments, and (d) individuals within households (T. C. Chen et al., 2020). PSUs are sampled from all U.S. counties with screening conducted at the dwelling unit level to identify sampled persons, based on oversampling criteria (CDC, 2020).

Oversampling is a key benefit and feature of NHANES that aids reliability and precision of estimates concerning the health status of specific populations (CDC, 2020). Oversampled populations include Hispanics, non-Hispanic Blacks, non-Hispanic Asians, older adults, and low-income populations (CDC, 2020). Here, low income populations are considered persons at or below 185% of the Department of Health and Human Services poverty guidelines, whereas older adults are classed as persons aged 80 years and older (T. C. Chen et al., 2020).

Power Analysis

Power analyses are useful in helping determine the required sample size to detect a significant association with small effect size in data (Creswell & Creswell, 2018). The U.S. asthma prevalence rate is approximately 8%, which would translate to about 800 cases in every 2-year cycle. However, such a general estimate does not take into account oversampling in NHANES, which might lead to higher asthma instances as oversampled populations carry a higher burden of asthma (Amaral et al., 2019). Moreover, an examination of the 2017-2018 NHANES Codebook for the variable MCQ010 (asthma) revealed that 1,325 records exist (CDC, 2020).

Using G*Power 3.1, I was able to estimate the needed sample size to detect a small effect size in the proposed dataset (see Erdfelder et al., 1996). A small effect size (Cohen's $d = 0.2$) was assumed as no data delineating allostatic load effect size and asthma currently exists (Bahreinian et al., 2013). Accordingly, I chose an odds ratio of 1.68, equivalent to a Cohen's d equal to 0.2, for the sample size calculation (see H. Chen et al., 2010). Selecting for a priori logistic regression testing with an estimated odds ratio

of 1.68, statistical significance level at an α of 0.05, power (1-β err prob) set at 80% and a 95% CI, G*Power calculated the needed sample size to be 1,070. As such, it was possible to utilize the most current available NHANES cycle (2017-2018) for the analysis.

Recruitment, Participation and Data Collection

On average, 15 PSUs are selected each cycle, with scheduling considerations based on geographic location, transit, and weather (T. C. Chen et al., 2020). Prior to arrival, county officials including public health directors, executives, and mayors are notified of NHANES arrival and asked to notify the community as well as provide endorsements for NHANES. Press kits are also distributed to local media with a goal to publish articles about NHANES in the local press and drive awareness.

Recruitment

Approximately 12,000 individuals per 2-year cycle are asked to participate in NHANES (Zipf et al., 2013). These individuals are located in 30 counties across the United States representing the four regions of the United States. Of these 12,000, about 10,500 agree to participate and accordingly complete home interviews and participate in data collection activities at MECs.

Participation

For NHANES 2017-2018, the screener response rate was 90.9% (CDC, 2020). In total, 16,211 participants were screened, representing a weighted population equal to 320,842,721 individuals, which approximates the totality of the US population. 8,233 of the screened 16,211 were male with 7,978 females. Of the 16,211 screened, 9,254

completed the interview, and 8,704 were examined. Survey participation in NHANES is bolstered by the use of remuneration as a way to boost participation (Zipf et al., 2013).

Data Collection

To aid in the reliability and security of generated data, NHANES developed the Integrated Survey Information System (ISIS), a system-wide architecture that relies on automated data collection and storage (Zipf et al., 2013). Tablet computers are used by field staff to capture interview data which are subsequently encrypted and sent to ISIS central servers. Similarly, automated data captured from biomedical and health examinations at the MEC are encrypted and transmitted securely to ISIS central servers. At the conclusion of operations for an NHANES 2-year cycle, data are edited for consistency, deidentified, and reviewed by a disclosure review board before being made available to the public (Zipf et al., 2013).

National Health and Nutrition Examination Study Data Access

At the conclusion of the disclosure review board editing process, all data are released in a SAS-readable file format using standardized variable naming (CDC, 2020). Codebooks, associated documentation, field operations, and analytic guides are provided for each component in the survey and are available at the NHANES website. Simplified search tools allow researchers to quickly locate data on topics of interest.

Instrumentation

As a continuous, annual survey, NHANES is uniquely situated to provide prevalence data, monitor disease trends, and explore emerging public health needs of the US population (Zipf et al., 2013). Central to this capacity is the survey's structure that

combines a personal interview with standardized physical examinations and laboratory tests.

Personal interviews are conducted at the respondent's home or in rare instances at a MEC (Zipf et al., 2013). The interview consists of four main sections: a screener questionnaire, relationship questionnaire, sample participant questionnaire, and a family questionnaire. Trained staff administer the interview and record answers on a computer tablet. Interpreters are utilized for non-English or non-Spanish participants.

Physical examinations and laboratory tests are conducted exclusively at the MEC, where standardized processes ensure valid, accurate, and high-quality data (Zipf et al., 2013). Here, detailed physical examinations on a range of topics are conducted in a manner identical to each survey location. Once complete, respondents travel to the biospecimen collection area of the MEC for laboratory analysis.

Variables in the Study

The current study includes both total and categorical allostatic load as independent variables, with asthma as a dependent variable. Gender, ethnicity, education, and socioeconomic status serve as covariates. Additionally, education serves as a moderating variable in the study. Components and operational definitions for each variable are as follows.

Total and Categorical Allostatic Load

For total and categorical allostatic load, I determined a high threshold for each biomarker on the basis of increased risk and in line with previously published studies (Doamekpor & Dinwiddie, 2015; Duong et al., 2017). Specifically, 75th percentiles for

specific variables were used to categorize respondents at greater risk of developing disease relative to the rest of the sample. The 75th percentile threshold were used for all biomarkers with the exception of high-density lipoprotein, which utilized the 25th percentile.

Table 1

Biomarkers for Total and Categorical Allostatic Load Calculation.

Component	Definition	Category	NHANES variable
SBP	Systolic blood pressure, 2nd reading mm/Hg	Cardiovascular	BPXSY2
DBP	Diastolic blood pressure, 2nd reading mm/Hg	Cardiovascular	BPXBI2
PP	60 second pulse pressure	Cardiovascular	BPXPLS
TC	Total Cholesterol mg/ml	Cardiovascular	LBXTC
HDL	Direct HDL level mg/ml	Cardiovascular	LBDHDD
eGFR	Urine creatinine clearance mg/ml	Metabolic	URXUCR
Albumin	Urine albumin mg/ml	Metabolic	URXUMS
CRP	High sensitivity C-reactive protein mg/ml	Inflammatory	LBXHSCRP

Asthma

The occurrence of asthma in the NHANES dataset is determined by respondent's answers to whether a doctor or other health professional has ever informed them that they asthma. Responses are tabulated and categorized according to Table 2.

Table 2

Self-Reported Asthma Categories

Code	Description
1	Yes
2	No
7	Refused
9	Don't know
.	Missing

Gender, Race, Education and Socioeconomic Status

For the covariates of race, gender, education, and socioeconomic status, the selected NHANES variables include RIDRETH3, RIAGENDR, DMDEDUC2, and INDFMPIR, respectively. Data categorizations for these variables are outlined in Table 3, Table 4, Table 5, and Table 6.

Table 3

Self-Reported Gender Categories

Code	Description
1	Male
2	Female
.	Missing

Table 4

Self-Reported Race Categories.

Code	Description
1	Mexican American
2	Other Hispanic
3	Non-Hispanic White
4	Non-Hispanic Black
6	Non-Hispanic Asian
7	Other race-multiracial
.	Missing

Table 5

Self-Reported Educational Categories.

Code	Description
1	Less than 9th grade
2	9th-11th grade
3	High school graduate
4	Some college
5	College graduate
7	Refused
9	Don't know
.	Missing

Table 6

Socioeconomic Status as PIR Categories.

Code	Description
0 to 4.98	Range of values
5	Value greater than or equal to 5

Data Analysis Plan

To analyze the data for this study, I used SPSS version 25 (IBM Corporation, 2018). Publicly available deidentified NHANES data covering the most recent release (2017-2018) was being used to answer the stated research questions:

RQ1: Is there a relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education?

$H_0$1: There is no relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

$H_1$1: There is a relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

RQ2: Is there a relationship between cardiovascular, metabolic, and inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education?

$H_0$2: There is no relationship between cardiovascular, metabolic, and inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

$H_1$2: There is a relationship between cardiovascular, metabolic, and inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

RQ3: Does educational attainment moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and gender?

$H_0$3: Educational attainment does not moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and gender.

$H_1$3: Educational attainment moderates moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and gender.

RQ4: Does educational attainment moderate the relationship between cardiovascular, metabolic, and inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and gender?

$H_0$4: Educational attainment does not moderate the relationship between cardiovascular, metabolic, and inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and gender.

$H_1$4: Educational attainment moderates moderate the relationship between cardiovascular, metabolic, and inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and gender.

Statistical Analysis

I carried out descriptive statistics to determine frequencies, means and standard deviations within the 2017-2018 NHANES dataset. Additionally, I also analyzed the data through inferential statistics to answer the stated research questions. Here, binary logistic regression was employed to report on effect size, probability measures and associated CIs.

The use of binary logistic regression is well suited when determining associations between multiple independent variables and a binary dependent variable such as asthma (Frankfort-Nachmias & Leon-Guerrero, 2018). Effect sizes for logistic regression produce odds ratios which represent the change in odds for every 1.0 increase in the

independent variable (Osborne, 2015). As for the moderation analysis, I used the method outlined by Dawson et al. (2014) to determine if any significant interactions exist in the data. The Dawson approach is deemed necessary as moderation through logistic regression results in logit transformation of the moderation effects, thereby skewing results (Hess et al., 2014). To counter such an effect, the Dawson approach probes for significant interactions and then interprets findings by generating non-linear slopes upon which calculations of effect size and power are generated (Dawson, 2014).

Threats to Validity

Threats to validity raise concerns as to whether researcher-reported observations are due to manipulated variables of interest or some other factor (Creswell & Creswell, 2018). These threats are classified as either internal threats to validity or external threats to validity.

Internal Validity

Internal validity determines the degree to which the observed effect is related to the perceived cause and where the absence of a relationship implies an absence of a link between the cause and observed effect (Burkholder et al., 2016). Threats to internal validity include history, maturation, testing, instrumentation, regression, selection, experimental mortality, and interaction of threats (Flannelly et al., 2018). Of importance to the current study, rigorous protocols and standardized procedures minimize threats to internal validity in the NHANES design, although threats from experimental mortality persist (CDC, 2020).

Missing Data

Experimental mortality is the term used to describe study participants that have been enrolled in the study but not included in the final analysis due to ineligibility, nonadherence, missing data, or competing effects (Slack & Draugalis, 2001). Notably, NHANES includes missing data from both participant and component non-response (CDC, 2020). To address participant non-response, NHANES adjusts sample weights in the survey. Additionally, NHANES performs and publishes a detailed non-response bias analysis for each cycle (CDC, 2020). As for component non-response, NHANES advises researchers that it is acceptable to continue analysis if a specific component missing values are less than 10% for the outcome variable of interest (CDC, 2020). For our dependent variable of asthma, an examination of frequencies in the examination codebook shows no missing values above the threshold of 10%.

External Validity

External validity, on the other hand, refers to the prospect that extraneous factors obscured the treatment's outcome, with the impact from such factors wholly dependent upon research design (Slack & Draugalis, 2001). Threats to external validity include interactions of observed causal relationship, treatment variations, outcome measures used, treatment delivery setting and context dependent mediation (Burkholder et al., 2016). Of significance to this study, its cross-sectional design restricts the conferring of causality outside the studied parameters (Creswell & Creswell, 2018). Accordingly, it is important to take note of all threats to validity in the current study.

Ethical Considerations

Ethical considerations in social research pertain to the ultimate goal of doing no harm. In this regard privacy concerns, informed consent and a thorough understanding of the study goals and treatment considerations are essential (Babbie, 2017).

For NHANES, ethical considerations are addressed through healthcare laws, ethical review boards (ERBs) and informed consent (Zipf et al., 2013). Specifically, the NHANES protocol is reviewed to be in compliance with the Policy for Protection of Human Research Subjects which is part of Code of the Federal Regulations. The NHANES protocol is also approved by the National Center for Health Statistics (NCHS) through an ERB on an annual basis. Additionally, all staff are required to sign non-disclosure agreements that prevent disclosure to unauthorized persons and adhere to NCHS confidentiality practices. This process ensures ethical treatment of participants including children, the elderly and vulnerable populations.

NHANES also includes the use of informed consent forms to help participants understand their rights in participating in the survey (Zipf et al., 2013). Documented signed consent forms are required from all participants aged 18 year or older, with parental or guardian consent for participants aged 7 years to 17 years. Taken in aggregate, the laws, ERBs and consent forms help protect participant's rights and privacy in the survey.

Summary

The current research study utilized a cross-sectional design to examines the association between allostatic load, its categorical components, and asthma, taking into

account confounding by gender, race, education, and socioeconomic status. Data covering the most recent release of NHANES (2017-2018) was analyzed using logistic regression through SPSS version 25. Associations and interaction effects were reported as odds ratios with their corresponding significance and CI values. Here, I have determined significance as an alpha of 5% with a CI at 95%. A priori power analysis determined that 1188 responses for the dependent variable would suffice to significantly detect an effect size of 0.15.

In Chapter 4, I provide details on data collection, give detailed results of the descriptive and inferential analysis as well as provide a brief summary highlighting answers to the stated research questions.

Chapter 4: Results

Introduction

In the current study I sought to delineate the association between allostatic load, its categorical constituents, and asthma, taking the influence of gender, ethnicity, education, and socioeconomic status into consideration. I analyzed total and categorical allostatic load comprising biomarkers relating to cardiovascular, metabolic, and inflammatory subsets through binary logistic regression and analysis of variance to quantify associations and moderation effects by education. Data from the NHANES 2017-2018 cycle served as the source data for the analysis. What follows in this chapter is a review of the research questions, data collection and organization methodology, and results from the inferential analysis of the research questions. The chapter ends with a brief summary of the findings.

Research Questions and Hypotheses

The stated research questions are displayed below. To account for the impact of the specific categorical components on allostatic load stated in RQ2, the research question was parsed and labelled as follows: RQ2a, RQ2b, RQ2c. The same notation was used when accounting for specific categorical components on RQ4, specifically RQ4a, RQ4b, and RQ4c respectively.

RQ1: Is there a relationship between total allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$1: There is no relationship between total allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$1: There is a relationship between total allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

RQ2a: Is there a relationship between the cardiovascular components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$2a: There is no relationship between the cardiovascular components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$2a: There is a relationship between the cardiovascular components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

RQ2b: Is there a relationship between the metabolic components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$2b: There is no relationship between the metabolic components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$2b: There is a relationship between the metabolic components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

RQ2c: Is there a relationship between the inflammatory component of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$2c: There is no relationship between the inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$2c: There is a relationship between the inflammatory component of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

RQ3: Does educational attainment moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and sex?

$H_0$3: Educational attainment does not moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and sex.

$H_1$3: Educational attainment moderates the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and sex.

RQ4a: Does educational attainment moderate the relationship between cardiovascular components of allostatic load and asthma when controlling for socioeconomic status, race, and sex?

$H_0$4a: Educational attainment does not moderate the relationship between cardiovascular components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

$H_1$4a: Educational attainment moderates the relationship between cardiovascular components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

RQ4b: Does educational attainment moderate the relationship between metabolic components of allostatic load and asthma when controlling for socioeconomic status, race, and sex?

$H_0$4b Educational attainment does not moderate the relationship between metabolic components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

$H_1$4b Educational attainment moderates the relationship between metabolic components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

RQ4c: Does educational attainment moderate the relationship between inflammatory component of allostatic load and asthma when controlling for socioeconomic status, race, and sex?

$H_0$4c: Educational attainment does not moderate the relationship between inflammatory component of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

$H_1$4c: Educational attainment moderates the relationship between inflammatory component of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

Data Collection

For the current study, I obtained data from the 2017-2018 NHANES release cycle. Every year, approximately 5,000 individuals are interviewed and complete a health examination component of the NHANES survey. The health examination portion of the survey is conducted in an MEC to ensure that the data are of high-quality and collected in a standardized environment (CDC, 2020). For the 2017-2018, release, 16,211 persons were selected for NHANES from 30 different survey locations. Of those selected, 9,254 completed the interview and 8,704 were examined. The oversampled subgroups in the 2017-2018 survey cycle included Hispanic persons, non-Hispanic Blacks, non-Hispanic Asians, and non-Hispanic Whites.

Before data was downloaded and loaded into SPSS, I obtained Institutional Review Board (IRB) approval from Walden University (approval number 03-05-21-0970939). Downloaded questionnaire data included datasets relating to demographic data (DEMO_J.XPT), medical condition data (MCQ_J.XPT), and laboratory data (ALB_CR_J.XPT, BPQ_J.XPT, BPX_J.XPT, HDL_J.XPT, HSCRP_J.XPT, TCHOL_J.XPT). The selected files contained all variables of interest including the dependent variable of asthma, constituents of the independent variable of allostatic load, and covariates gender, ethnicity, educational attainment, and socioeconomic status. Files

were merged into a single dataset by SPSS using sequence number as the key identifier variable.

Results

Descriptive Statistics

Of the 9,254 interviewed participants, 1,325 said they had asthma whereas 7,563 respondents answered that they did not (Table 7). Additionally, there were 357 missing values and nine cases where the respondents were unsure as to whether they have asthma. The missing and unsure cases totaling 366 cases and equivalent to 4.0% of total population were removed from all subsequent analysis, leaving a total of 8,888 cases to draw inferences from. Also removed were 2 Refused and 11 Don't Know cases from the education category, leaving a total of 8,875 cases to draw inferences from. These 8,875 cases served as the study population.

Table 7

Descriptive Statistics for Asthma

Covariate	Frequency	%
Asthma		
Present	1325	14.3
Not present	7563	81.7
Don't know	9	0.1
Missing	357	3.9

Table 8 highlights descriptive statistics for the covariates gender, ethnicity, educational attainment, and socioeconomic status.

Table 8

Descriptive Statistics for Gender, Ethnicity, Education, and Poverty Income Ratio

Covariate	Frequency	%
Gender		
Male	2700	30.4
Female	2864	32.2
Missing	3324	37.4
Ethnicity		
Mexican American	735	8.3
Other Hispanic	517	5.8
Non-Hispanic White	1933	21.7
Non-Hispanic Black	1296	14.6
Non-Hispanic Asian	810	9.1
Multiracial/Other	273	3.1
Missing	3324	37.4
Education		
Less than 9th Grade	476	5.4
9th-11th Grade	638	7.2
High school/GED	1323	14.9
Some college/AA	1778	20
College grad or above	1336	15
Refused	2	0
Don't know	11	0.1
Missing	3324	37.4
Poverty to income ratio		
0 - 4.98	3938	44.3
5+	838	9.4
Missing	4112	46.3

Allostatic Load Index Calculation

Allostatic load calculation mirrored the process described by Doamekpor and Dinwiddie (2015). Specifically, values from all eight constituent biomarkers (SBP, DBP, PP, TC, HDL, eGFR, Albumin, CRP) were quantized and ranked into quartiles. For all

observations, with the exception of HDL, values equal to or in excess of the 75% quartile were assigned a point to signify a high disease state. For HDL, values equal to or below the 25% quartile were assigned a point to signify disease. Table 9 displays quartiles produced from this iteration.

Accordingly, an allostatic load index was calculated by summation of all the points from the individual markers ranging from zero to eight. In keeping with previous research, an allostatic load equal to or above 4 from the index was chosen as signifying high allostatic load burden to be utilized in the analysis (Doamekpor & Dinwiddie, 2015; Duong et al., 2017; Howard & Sparks, 2016).

Table 9

Descriptive Statistics and Associated Quartiles for Allostatic Load Index

		Albumin	eGFR	PP	SBP	DBP	CRP	TC	HDL
N	Valid	5122	5122	5013	4882	4882	4905	4933	4933
	Missing	3766	3766	3875	4006	4006	3983	3955	3955
Mean		53.2825	128.2241	71.68	127.00	72.53	4.2051	188.09	53.26
Median		9.2000	113.0000	70.00	124.00	72.00	1.9900	185.00	51.00
Percentiles	25	4.6000	64.0000	64.00	112.00	64.00	.9100	160.00	42.00
	50	9.2000	113.0000	70.00	124.00	72.00	1.9900	185.00	51.00
	75	19.1250	172.0000	78.00	138.00	80.00	4.5350	213.00	61.00

Statistical Assumptions

To confer validity and appropriateness of results from statistical analyses, it is imperative to not violate associated assumptions (Millsap & Maydeu-Olivares, 2009). For binary logistic regression these assumptions include a dichotomous dependent variable, one or more independent variables, independence of observations, mutually exclusive and

exhaustive categories for the dependent and independent variables, and a minimum of 15 cases per independent variable (Warner, 2013). As for moderation, the Dawson approach to moderation in logistic regression was utilized to determine moderation effects by education on the relationship between allostatic load and asthma (Dawson, 2014). Here, a two-step approach that first determines if moderation is present is followed by slope analysis (Dawson, 2014).

Logistic Regression

Binary logistic regression was employed to answer the first and second research questions. Total allostatic load, coded as a point value more than four of the allostatic load index, was selected as the independent variables while asthma was selected as the dependent variable. Also coded in the model were the categorical components of allostatic load. Here, cardiovascular allostatic load was represented as three or more points in the allostatic load index, metabolic was two and inflammatory allostatic load as a single component measure of inflammation. Covariates in the model included gender, ethnicity, educational attainment, and poverty to income ratio. Statistical significance was set at 5% and CIs were reported at 95%.

Total Allostatic Load and Asthma

RQ1: Is there a relationship between total allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$1: There is no relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

$H_1$1: There is a relationship between total allostatic load index and asthma when controlling for socioeconomic status, gender, race, and education.

A binary logistic regression was performed to determine the relationship between allostatic load and asthma, controlling for gender, ethnicity, education, and socioeconomic status. The logistic regression model was statistically significant, $\chi^2(12) = 73.01$, $p < .001$. The model explained 2.6% (Nagelkerke R^2) of the variance in asthma and correctly classified 84.6% of cases. As shown in Table 10, high allostatic load (AL > 4), was a statistically significant predictor of the dependent variable asthma. Using low allostatic load as the reference standard (AL < 4), the unstandardized Beta weight for the predictor variable total allostatic load (AL > 4) was B = .249, S.E. = .108, Wald = 5.352, $p = .021$. The estimated unadjusted odds ratio indicates statistically significant higher odds of 28% [Exp (B) = 1.283, 95% CI (1.039, 1.584)] for reporting asthma.

When taking the covariates into consideration in the model, gender, ethnicity, and education were found to be statistically significant predictors (Table 11). Female gender compared to male gender was a statistically significant predictor with the unstandardized B = .327, S.E. = .082, Wald = 15.840, $p < .001$. The estimated unadjusted odds ratio indicates significantly higher odds of 39% [Exp (B) = 1.387, 95% CI (1.181, 1.629)] for reporting asthma when taking ethnicity, allostatic load, education, and socioeconomic status into consideration.

Ethnicity was also a significant predictor of resilience against allostatic load in the model. Data for Mexican Americans, Non-Hispanic Whites and Non-Hispanic Asians all showed positive protective effect from asthma when compared to the reference multi-

Racial population. Here, for Mexican Americans, Non-Hispanic Whites and Non-Hispanic Asians, unstandardized B= -.695, S.E. = .208, Wald = 11.152, p =.001, B = -.372, S.E. = .172, Wald = 4.683, *p* =.030 and B = - .748, S.E. = .207, Wald = 13.100, *p* <.001 respectively. Corresponding unadjusted odds ratio indicates statistically significant lower odds of 50% [Exp (B) = .499, 95% CI (.332, .750)], 31% [Exp (B) = .690, 95% CI (.493, .966)] and 53% [Exp (B) = .473, 95% CI (.315, .710)] respectively.

As for education, when taking less than 9th grade education as a reference standard, high school graduates and those with some college or an associate degree showed significant associations with high allostatic load in the model with unstandardized B = .395, S.E. = .195, Wald = 4.095, *p* =.043 and B = .408, S.E. = .192, Wald = 4.516, *p* =.034 respectively. The estimated unadjusted odds ratio indicates significantly higher odds of 48% [Exp (B) = 1.484, 95% CI (1.012, 2.167)] for high school graduates and 50% [Exp (B) = 1.503, 95% CI (1.032, 2.189)] for those with some college when reporting asthma and taking allostatic load, ethnicity, gender, and socioeconomic status into account.

The statistically significant associations observed between total allostatic load and asthma in the presence of covariates provide support to reject the null hypothesis of no association in favor of the alternate hypothesis.

Table 10

Logistic Regression of Allostatic Load without Covariates

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Allostatic load > 4(1)	.289	.106	7.468	1	.006	1.336
	Constant	-1.750	.044	1570.523	1	.000	.174

a. Variable(s) entered on step 1: Allostatic Load >4.

Table 11

Logistic Regression of Total Allostatic Load with Covariates

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Allostatic load > 4(1)	.249	.108	5.352	1	.021	1.283	1.039	1.584
	Female gender	.327	.082	15.840	1	.000	1.387	1.181	1.629
	Ethnicity			29.103	5	.000			
	Mexican American	-.695	.208	11.152	1	.001	.499	.332	.750
	Other Hispanic	-.149	.206	.523	1	.470	.861	.575	1.291
	Non-Hispanic White	-.372	.172	4.683	1	.030	.690	.493	.966
	Non-Hispanic Black	-.159	.177	.814	1	.367	.853	.603	1.205
	Non-Hispanic Asian	-.748	.207	13.100	1	.000	.473	.315	.710
	Education level			7.062	4	.133			
	9th-11th Grade	.386	.212	3.327	1	.068	1.471	.972	2.228
	High School Graduate/GED	.395	.195	4.095	1	.043	1.484	1.012	2.176
	Some College/AA	.408	.192	4.516	1	.034	1.503	1.032	2.189
	College and above	.211	.206	1.053	1	.305	1.235	.825	1.848
	Family PIR <4.98	.167	.122	1.885	1	.170	1.182	.931	1.502
	Constant	-2.034	.271	56.473	1	.000	.131		

a. Variable(s) entered on step 1: Allostatic Load >4, Gender, Race/Hispanic origin w/ NH Asian, Education level - Adults 20+, Ratio of family income to poverty.

Cardiovascular Allostatic Load and Asthma

RQ2a: Is there a relationship between cardiovascular components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$2a: There is no relationship between the cardiovascular components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$2a: There is a relationship between the cardiovascular components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

For the cardiovascular component of allostatic load, the binary logistic regression model was statistically significant, $\chi^2(12) = 67.86$, $p < .001$. The model explained 2.4% (Nagelkerke R^2) of the variance in asthma and correctly classified 84.6% of cases. As shown in Table 11, the cardiovascular component of allostatic load was not statistically significant with unstandardized B = -.022, S.E. = .122, Wald = .032, $p = .858$. As such, the data does not support rejection of the null hypothesis of no association between cardiovascular allostatic load and asthma.

Table 12

Logistic Regression of Cardiovascular Allostatic Load

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Cardio>3(1)	-.022	.122	.032	1	.858	.978	.770	1.243
	Female gender	.311	.082	14.358	1	.000	1.365	1.162	1.603
	Ethnicity			30.766	5	.000			
	Mexican American	-.704	.208	11.445	1	.001	.495	.329	.744
	Other Hispanic	-.153	.206	.552	1	.458	.858	.573	1.285
	Non-Hispanic White	-.379	.172	4.866	1	.027	.685	.489	.959
	Non-Hispanic Black	-.152	.176	.740	1	.390	.859	.608	1.214
	Non-Hispanic Asian	-.763	.207	13.641	1	.000	.466	.311	.699
	Education level			7.505	4	.111			
	9th-11th grade	.391	.212	3.410	1	.065	1.478	.976	2.238
	High school graduate/GED	.400	.195	4.200	1	.040	1.491	1.018	2.185
	Some college/AA	.413	.192	4.639	1	.031	1.511	1.038	2.199
	College and above	.205	.206	.995	1	.319	1.228	.820	1.837
	Family PIR <4.98	.177	.122	2.106	1	.147	1.193	.940	1.515
	Constant	-1.988	.271	54.018	1	.000	.137		

Note. a. Variable(s) entered on step 1: Cardio>3, Gender, Race/Hispanic origin w/ NH Asian, Education level - Adults 20+, Ratio of family income to poverty.

Metabolic Allostatic Load and Asthma

RQ2b: Is there a relationship between the metabolic components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$2b: There is no relationship between the metabolic components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$2b: There is a relationship between the metabolic components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

To answer if metabolic allostatic load was the predictor in the relationship with asthma, the binary logistic model was setup with the high metabolic allostatic load index components for albumin and creatinine serving as the independent variable. The logistic regression model was statistically significant, $\chi^2(12) = 69.22$, $p < .001$ and explained 2.5% (Nagelkerke R^2) of the variance in asthma, correctly classifying 84.6% of cases. As shown in Table 12, Metabolic allostatic load was a non-significant predictor of the relationship between asthma, unstandardized B = .161, S.E. = .134, Wald = 1.434, p = .231. Accordingly, the data does not support the rejection of the null hypothesis for the research question.

Table 13

Logistic Regression of Metabolic Allostatic Load

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Metabolic>2	.161	.134	1.434	1	.231	1.174	.903	1.528
	Female gender	.316	.082	14.880	1	.000	1.372	1.168	1.611
	Ethnicity			29.391	5	.000			
	Mexican American	-.699	.208	11.275	1	.001	.497	.331	.748
	Other Hispanic	-.147	.206	.509	1	.475	.863	.576	1.293
	Non-Hispanic White	-.374	.172	4.733	1	.030	.688	.492	.964
	Non-Hispanic Black	-.161	.177	.833	1	.361	.851	.602	1.203
	Non-Hispanic Asian	-.754	.207	13.298	1	.000	.470	.314	.706
	Education level			7.444	4	.114			
	9th-11th grade	.389	.212	3.371	1	.066	1.475	.974	2.233
	High school graduate/GED	.398	.195	4.175	1	.041	1.490	1.016	2.183
	Some college/AA	.413	.192	4.654	1	.031	1.512	1.039	2.201
	College and above	.207	.206	1.012	1	.314	1.230	.822	1.840
	Family PIR < 4.98	.171	.122	1.963	1	.161	1.186	.934	1.507
	Constant	-2.006	.270	55.147	1	.000	.135		

Note. a. Variable(s) entered on step 1: Metabolic>2, Gender, Race/Hispanic origin w/ NH Asian, Education level - Adults 20+, Ratio of family income to poverty.

Inflammatory Allostatic Load and Asthma

RQ2c: Is there a relationship between the inflammatory component of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education?

$H_0$2c: There is no relationship between the inflammatory components of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

$H_1$2c: There is a relationship between the inflammatory component of the allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

Binary logistic regression was performed to determine the relationship between inflammatory allostatic load and asthma. The logistic regression model was statistically significant, $\chi^2(12) = 78.82$, $p < .001$. The model explained 2.8% (Nagelkerke R^2) of the variance in asthma and correctly classified 84.6% of cases. Using low allostatic load as the reference standard, the unstandardized Beta weight for inflammatory allostatic load was B = .308, S.E. = .092, Wald = 11.301, $p < .001$ (Table 14). The estimated unadjusted odds ratio indicates significantly higher odds of 36% [Exp (B) = 1.361, 95% CI (1.137, 1.630)] for reporting asthma.

As was the case for total allostatic load, ethnicity, gender, and education were all significant predictors in the model (Table 15). Here, female gender was a statistically significant predictor with the unstandardized B = .285, S.E. = .082, Wald = 12.005, p < .001. The estimated unadjusted odds ratio indicates significantly higher odds of 33%

[Exp (B) = 1.330, 95% CI (1.132, 1.563)] for female respondents reporting asthma when taking ethnicity, allostatic load, education, and socioeconomic status into consideration in the model.

Additionally, education was also a significant predictor in the model for inflammatory allostatic load. High school graduates and those with some college or an associate degree showed statistically significant association to allostatic load in the model with unstandardized B = .387, S.E. = .195, Wald = 3.929, p =.047 and B = -.403, S.E. = .192, Wald = 4.411, p =.036 respectively. The estimated unadjusted odds ratio indicates higher susceptibility odds of 47.3% [Exp (B) = 1.473, 95% CI (1.004, 2.159)] and 49.6% [Exp (B) = 1.496, 95% CI (1.027, 2.179)] for high school graduates and those with some college reporting asthma compared to those with a less than 9th grade education when taking inflammatory allostatic load, ethnicity, gender, and socioeconomic status into account.

As for ethnicity, Mexican Americans, Non-Hispanic Whites and Non-Hispanic Asians showed protective effect against allostatic load in the model with unstandardized B= -.694, S.E. = .208, Wald = 11.090, p =.001, B = -.360, S.E. = .172, Wald = 4.383, p =.036 and B = -.710, S.E. = .208, Wald = 11.712, p =.001 respectively. Estimated unadjusted odds ratio reveals significantly lower odds of 50% [Exp (B) = .500, 95% CI (.332, .752)], 30.2% [Exp (B) = .698, 95% CI (.498, .977)] and 50.9% [Exp (B) = .491, 95% CI (.327, .738)] for Mexican Americans, Non-Hispanic Whites and Non-Hispanic Asians respectively.

Accordingly, the data does indeed support rejection of the null hypothesis in favor of the alternate for inflammatory allostatic load.

Table 14

Logistic Regression of Inflammatory Allostatic Load without Covariates

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Inflammatory allostatic load	.412	.090	20.970	1	.000	1.510
	Constant	-1.806	.047	1462.923	1	.000	.164

Note. a. Variable(s) entered on step 1: Inflammatory Allostatic Load.

Table 15

Logistic Regression of Inflammatory Allostatic Load with Covariates

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Inflammatory allostatic load	.308	.092	11.301	1	.001	1.361	1.137	1.630
	Female gender	.285	.082	12.005	1	.001	1.330	1.132	1.563
	Ethnicity			27.872	5	.000			
	Mexican American	-.694	.208	11.090	1	.001	.500	.332	.752
	Other Hispanic	-.145	.206	.496	1	.481	.865	.577	1.296
	Non-Hispanic White	-.360	.172	4.383	1	.036	.698	.498	.977
	Non-Hispanic Black	-.145	.177	.675	1	.411	.865	.612	1.223
	Non-Hispanic Asian	-.710	.208	11.712	1	.001	.491	.327	.738
	Education level			6.742	4	.150			
	9th-11th grade	.376	.212	3.146	1	.076	1.456	.961	2.207
	High school graduate/GED	.387	.195	3.929	1	.047	1.473	1.004	2.159
	Some college/AA	.403	.192	4.411	1	.036	1.496	1.027	2.179
	College and above	.211	.206	1.050	1	.306	1.235	.825	1.848
	Family PIR <4.98	.168	.122	1.887	1	.170	1.182	.931	1.502
	Constant	-2.056	.271	57.616	1	.000	.128		

Note. a. Variable(s) entered on step 1: Inflammatory Allostatic Load, Gender, Race/Hispanic origin w/ NH Asian, Education level - Adults 20+, Ratio of family income to poverty.

Moderation Analysis

The Dawson approach for moderation in binary logistic regression was employed to answer the third and fourth research questions to delineate whether educational attainment moderated the relationship between total and categorical components of allostatic load when controlling for gender, ethnicity, and socioeconomic status. In the model, asthma served as the dependent variable, educational attainment as the moderator and gender, ethnicity, and socioeconomic status as covariates.

Total Allostatic Load and Asthma

RQ3: Does educational attainment moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and sex?

$H_0$3: Educational attainment does not moderate the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and sex.

$H_1$3: Educational attainment moderates the relationship between total allostatic load index and asthma when controlling for socioeconomic status, race, and sex.

To determine whether education moderated the relationship between total allostatic load and asthma, a logistic regression for the interaction between education and total allostatic load was carried out. As shown in Table 16, there was a non-statistically significant interaction between education and total allostatic load on the presence of asthma, for all levels of education. This result indicates that educational attainment does

not moderate the relationship between total allostatic load and asthma, rendering the null hypothesis valid.

Table 16

Moderation Effects between Total Allostatic Load and Education

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Total allostatic load	.664	.622	1.139	1	.286	1.942
	Education			8.017	4	.091	
	9th-11th grade	1.163	.657	3.136	1	.077	3.200
	High school graduate/GED	1.172	.626	3.509	1	.061	3.228
	Some college/AA	1.514	.614	6.077	1	.014	4.545
	College and above	1.129	.645	3.065	1	.080	3.093
	Education * Total allostatic load			4.816	4	.307	
	Allostatic load * 9th-11th Grade	-.787	.693	1.290	1	.256	.455
	Allostatic load * High school graduate/GED	-.748	.656	1.302	1	.254	.473
	Allostatic load * Some college/AA	-1.124	.644	3.051	1	.081	.325
	Allostatic load * College and above	-1.055	.675	2.441	1	.118	.348
	Constant	-2.708	.596	20.626	1	.000	.067

Note. a. Variable(s) entered on step 1: Allostatic Load >4, Education level - Adults 20+, Education level - Adults 20+ * Allostatic Load >4.

Cardiovascular Allostatic Load and Asthma

RQ4a: Does educational attainment moderate the relationship between cardiovascular components of allostatic load and asthma when controlling for socioeconomic status, race, and sex?

$H_0$4a: Educational attainment does not moderate the relationship between cardiovascular components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

$H_1$4a: Educational attainment moderates the relationship between cardiovascular components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

Binary logistic interaction analysis was also carried out to answer whether education moderated the relationship between cardiovascular allostatic load and asthma. As shown in Table 17, there was a non-statistically significant interaction between cardiovascular allostatic load and all levels of education on the presence of asthma. This indicates that educational attainment does not moderate the relationship between cardiovascular allostatic load and asthma. As such, the data does not support rejection of the null hypothesis stating no moderation by education.

Table 17

Moderation Effects Between Cardiovascular Allostatic Load and Education

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Cardiovascular allostatic load	.147	.504	.085	1	.771	1.158
	Education			5.143	4	.273	
	9th-11th grade	.101	.601	.028	1	.867	1.106
	High school graduate/GED	.456	.522	.765	1	.382	1.578
	Some college/AA	.792	.503	2.482	1	.115	2.208
	College and above	.392	.538	.530	1	.466	1.480
	Education * Cardiovascular allostatic load			3.345	4	.502	
	Allostatic load * 9th-11th grade	.415	.640	.421	1	.516	1.515
	Allostatic load * High school graduate/GED	.058	.559	.011	1	.917	1.060
	Allostatic load * Some college/AA	-.286	.540	.280	1	.597	.751
	Allostatic load * College and above	-.233	.575	.164	1	.686	.792
	Constant	-2.241	.470	22.690	1	.000	.106

Note. a. Variable(s) entered on step 1: Cardio > 3, Education level - Adults 20+, Cardio > 3 * Education level - Adults 20+.

Metabolic Allostatic Load and Asthma

RQ4b: Does educational attainment moderate the relationship between metabolic components of allostatic load and asthma when controlling for socioeconomic status, race, and sex?

$H_0$4b Educational attainment does not moderate the relationship between metabolic components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

$H_1$4b Educational attainment moderates the relationship between metabolic components of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

Table 18 shows the results of the binary logistic regression interaction analysis for education on the relationship between metabolic allostatic load and asthma. There was a non-statistically significant interaction between education at all levels and metabolic allostatic load on the presence of asthma. This indicates that educational attainment does not moderate the relationship between metabolic allostatic load and asthma. Accordingly, the data does not support rejection of the null hypothesis.

Table 18

Moderation Effects between Metabolic Allostatic Load and Education

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Metabolic allostatic load	1.243	1.033	1.449	1	.229	3.466
	Education level - Adults 20+			3.736	4	.443	
	9th-11th Grade	1.707	1.076	2.516	1	.113	5.510
	High school graduate/GED	1.961	1.043	3.535	1	.060	7.105
	Some college/AA	1.874	1.040	3.249	1	.071	6.517
	College and above	1.877	1.058	3.145	1	.076	6.532
	Education * Metabolic allostatic load			3.538	4	.472	
	Allostatic load * 9th-11th grade	-1.307	1.097	1.420	1	.233	.271
	Allostatic load * High school graduate/GED	-1.549	1.060	2.134	1	.144	.212
	Allostatic load * Some college/AA	-1.406	1.056	1.771	1	.183	.245
	Allostatic load * College and above	-1.793	1.076	2.777	1	.096	.166
	Constant	-3.296	1.018	10.475	1	.001	.037

Note. a. Variable(s) entered on step 1: Metabolic > 2, Education level - Adults 20+, Education level - Adults 20+ * Metabolic > 2.

Inflammatory Allostatic Load and Asthma

RQ4c: Does educational attainment moderate the relationship between inflammatory components of allostatic load and asthma when controlling for socioeconomic status, race, and sex?

$H_0$4c: Educational attainment does not moderate the relationship between inflammatory component of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

$H_1$4c: Educational attainment moderates the relationship between inflammatory component of allostatic load and asthma when controlling for socioeconomic status, race, and sex.

To delineate whether education moderated the relationship between inflammatory allostatic load and asthma, a logistic regression interaction effects analysis was carried out. As shown in Table 19, there was a non-statistically significant interaction between inflammatory allostatic load and all education levels on the presence of asthma. As such, we fail to reject the null hypothesis that states education does not moderate the relationship between inflammatory allostatic load and asthma.

Table 19

Moderation Effects between Inflammatory Allostatic Load and Education

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Inflammatory allostatic load	-.043	.420	.011	1	.918	.958
	Education level - Adults 20+			10.346	4	.035	
	9th-11th grade	.981	.424	5.349	1	.021	2.667
	High school graduate/GED	.482	.406	1.409	1	.235	1.620
	Some college/AA	.878	.394	4.963	1	.026	2.405
	College and above	.533	.421	1.599	1	.206	1.703
	Education * Inflammatory allostatic load			8.415	4	.077	
	Allostatic load * 9th-11th grade	-.747	.488	2.346	1	.126	.474
	Allostatic load * High school graduate/GED	.031	.458	.005	1	.946	1.032
	Allostatic load * Some college/AA	-.465	.445	1.091	1	.296	.628
	Allostatic load * College and above	-.422	.473	.796	1	.372	.656
	Constant	-2.079	.375	30.749	1	.000	.125

Note. a. Variable(s) entered on step 1: Inflammatory allostatic load, Education level - Adults 20+, Education level - Adults 20+ * Inflammatory allostatic load.

Summary

The current study assessed whether allostatic load and its categorical components predicted the presence of asthma in a representative population when controlling for gender, ethnicity, educational attainment, and socioeconomic status. The study also examined whether educational attainment moderated this association for both total allostatic load and its categorical components.

Total Allostatic Load and Asthma

For total allostatic load, results indicated that allostatic load was a statistically significant predictor for the dependent variable asthma with an odds ratio of 1.283, equivalent to an increase of 28% in probability. Also significant in the total allostatic load model were predictive associations from gender, ethnicity, and educational attainment.

Female gender when compared to male gender was a statistically significantly predictor for the association between total allostatic load and asthma, responsible for an increase of 39% in the model. For ethnicity, Non-Hispanic Whites and Non-Hispanic Asians showed statistically significant reductions in the prediction of asthma, indicating a protective effect of 31% and 53% respectively compared to multi-Racial populations.

Educational attainment also showed predictive associations in the study, albeit only statistically significant for those educated to the level of high school graduate and some college or associate degree. Odds ratios predicted an increase in asthma of approximately 32% when compared to those with a less than 9^{th} grade education.

Assessing the null hypothesis stated in the first research question in light of the observed results, the data supports rejection of the null hypothesis in favor of the

alternate hypothesis, stating that there is a relationship between total allostatic load index and asthma when controlling for socioeconomic status, sex, race, and education.

Categorical Allostatic Load and Asthma

Analysis of the categorical components of allostatic load did not show statistical significance in the binary logistic model for cardiovascular or metabolic allostatic load. However, inflammatory allostatic load did show a statistically significant predictive association with asthma, one that corresponds to an odds ratio of approximately 36% in reporting asthma when taking ethnicity, gender, education, and socioeconomic status into consideration.

As was the case for the total allostatic model, significant associations were also present for gender, educational attainment, and ethnicity in the inflammatory allostatic load component model. Female gender predicted higher odds for asthma equivalent to 39% when compared to male gender. Also significant were the negative predictive associations for Non-Hispanic Whites and Non-Hispanic Asians which showed a protective effect equivalent to 30% and 50% respectively when compared to multi-Racial populations.

Educational attainment also was a statistically significant predictor in the inflammatory allostatic load model. Here, as was the case for total allostatic load, those with a high school education or those with some college showed a statistically significant increase in the predictive association for asthma, equating to an odds ratio of 47% and 50% respectively.

Considering the non-significant associations observed for cardiovascular and metabolic allostatic load and the significant association for inflammatory allostatic load, the data advocates accepting the null hypothesis of no relation for cardiovascular and metabolic allostatic load while rejecting the null hypothesis and accepting the alternate hypothesis for inflammatory allostatic load.

Moderation by Education in Allostatic Load

Regarding the moderation of allostatic load by education, interaction effects analysis revealed that education did not moderate total allostatic load, cardiovascular allostatic load, metabolic allostatic load, or inflammatory allostatic load in a statistically significant manner. For this reason, we accept the null hypothesis of no effect for total, cardiovascular, metabolic, and inflammatory components of allostatic load.

In Chapter 5, I interpret the current findings and evaluate the implications for social change including review of conclusions from this project, and recommendations for future research.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The current study was undertaken to examine the predictive relationship between allostatic load and asthma when accounting for known covariates of interest. Using a quantitative cross-sectional approach, I assessed secondary data from NHANES 2017-2018 coding for biomarkers of total and categorical allostatic load for association to the dependent variable asthma. Biomarkers included SBP, DBP, HDL, TC, pulse, albumin, eGFR, and C-reactive protein. Covariates of interest in the study included gender, ethnicity, educational attainment, and socioeconomic status. To determine inherent associations in the data, I ran a series of statistical analyses that included binary logistic regression to quantify associations and interaction effects analysis to determine if education moderated the relationship between allostatic load and asthma.

Total allostatic load was a statistically significant predictor of asthma, irrespective of whether covariates were included in the model. Covariates that were significant in the full model included gender, ethnicity, and education, albeit for specific categories. As for categorical allostatic load, cardiovascular and metabolic components were nonsignificant predictors of asthma in the regression analysis. Inflammatory allostatic load was found to be a significant predictor of asthma with and without covariates. Similar to the total allostatic load model, gender, ethnicity and education were all significant in the full covariate model.

For the moderation analysis, results revealed education was not a statistically significant moderator for the relationship between allostatic load and asthma be it for total or categorical components of allostatic load.

Interpretation of Findings

Allostatic Load and Asthma

The finding that total allostatic load is a statistically significant predictor of asthma is in line with previous research outlining the adverse impact of allostatic load on health (Delpierre et al., 2016; Edes & Crews, 2017; Gillespie et al., 2019; Shalowitz et al., 2019). The current study adds asthma to the disease states upon which allostatic load exerts its harmful actions (Berger et al., 2015; Guidi et al., 2021; Shalowitz et al., 2019; Viljoen & Claassen, 2017). Additionally, the finding that inflammatory components of allostatic load were found to be significant predictors of asthma in the study lends credence to the inflammation hypothesis for allostatic load injury (Hill et al., 2018; Picard et al., 2017; Rastogi & Holguin, 2017).

Of note, the study did not find cardiovascular and metabolic components of allostatic load to be significant predictors of asthma. Two possible explanations for the lack of an observed relationship include medication use and differential activation pathways for allostatic load in asthma. Medication use may artificially mask higher levels for cardiovascular and metabolic biomarkers such as blood pressure and cholesterol raising the possibility of a type II error (see Doamekpor & Dinwiddie, 2015). Conversely, it could be that inflammatory processes are the predominant drivers in allostatic load driven asthma, outsizing any effect from cardiovascular or metabolic components. There

is evidence in the academic literature that supports this latter hypothesis, suggesting activation of different biomarkers in allostatic load for different disease states (Edes & Crews, 2017). Whether medication use, differential pathways, or a combination of both were responsible for the observations seen was not revealed by the current study.

The Differential Impact of Covariates in Significant Models

When covariates were added to total allostatic load and inflammatory allostatic load in the regression analysis, a distinct pattern emerged. Specifically, being of female gender, possessing a high school/GED or some college/AA degree conferred a statistically significant increase in the prediction of asthma. The current finding of a statistically significant prediction in allostatic load based on gender is in line with previous research on the topic (Beckie et al., 2016; Christensen et al., 2018a). However, the case for educational attainment is not as clear. To date, there remains much discourse on the subject of education in allostatic load (Assari et al., 2019; Dinwiddie et al., 2015; Hamdi et al., 2016; Howard & Sparks, 2015).

Also seen in the data was a protective-resilience effect from allostatic load for Mexican Americans, non-Hispanic Whites and non-Hispanic Asians as compared to multiracial populations. Of note is the lack of protective resiliency seen for non-Hispanic Blacks and other Hispanics, suggesting that these populations are at higher risk for developing allostatic load driven asthma. Indeed, a significant body of evidence ties higher allostatic load indices to non-Hispanic Blacks and Hispanics of non-Mexican ethnicity (Beydoun et al., 2016; Borrell et al., 2010; Duru et al., 2012; Tomfohr et al.,

2016). Collectively, these findings suggest differential susceptibility for allostatic load driven asthma in these populations.

Not seen in the data was a significant predictive association between socioeconomic status, depicted as a poverty-to-income ratio less than 4.98, and asthma. This finding differs significantly from a large body of evidence that suggests that challenged socioeconomic status contributes to higher allostatic load (Beckles et al., 2019; E. Chen et al., 2016; Johnson et al., 2017; Lunyera et al., 2020; McCrory et al., 2019; Rodriguez et al., 2019).

The Role of Education in Allostatic Load

Of particular interest in the current study is the lack of significance seen at higher educational attainment level in the regression analysis that indicates a nonlinear relationship between increasing education and allostatic load. This finding possibly is indicative of moderation at higher levels of education, a theory put forward by many scholars (Ding et al., 2019; Hamdi et al., 2016; Howard & Sparks, 2015). This moderating effect was not borne out by the data in the current study, as none of the models examined showed a statistically significant moderation effect by education.

Limitations of the Study

A number of limitations exist for the current study inherent to research design and indicators of interest. From a research design perspective, the cross-sectional, observational and secondary nature of the study predicates a lack of causation in any found associations rendering them only predictive in application (Mann, 2003; Millsap & Maydeu-Olivares, 2009). In addition, the categorical cardiovascular and metabolic

components for allostatic load might have been subject to type II errors. This error was possibly due to masking from medication use, providing artificially low levels that might have underreported significant associations from cardiovascular and metabolic allostatic load.

Recommendations

A number of recommendations are warranted based on the results observed in the current study. Firstly, there is a need to document and validate an allostatic load index for asthma, one that relies on a validated set of readily available biomarkers and takes into consideration possible masking by medication use. Such a scale could inherently strengthen the meaningfulness of any stated results and resolve a key area of discourse regarding what constitutes an allostatic load biomarker for asthma (Duong et al., 2017; Howard & Sparks, 2016). Moreover, I recommend that subscales should be established for varying disease etiologies, as current evidence suggest that the progression of allostatic load can differ by disease state (Picard et al., 2017). For example, a different set of biomarkers might drive the relationship in cardiovascular disease more than respiratory disease, and the use of cardiovascular allostatic load subscale might provide more insights into the inherent associations. Indeed, findings from the current study reaffirm the importance of inflammation in allostatic load-driven asthma and serve as evidence to include inflammatory components in future models.

Secondly, further research is needed in allostatic load translational medicine as an approach to integrate evidence-based current allostatic load research into effective clinimetric tools that improve patient outcomes. Such research holds great promise,

paving the way for allostatic load burden screening during routine blood work. Accordingly, identified at-risk individuals can receive individualized care plans in an attempt to reduce the health inequity seen from allostatic load (E. Chen, Shalowitz, et al., 2019; Fava et al., 2019; Martinez, 2019).

Implications

Results from the current study offer a number of key drivers for positive social change. The current study adds asthma to the list of disease states upon which allostatic load contributes to disease progression and adversity with evidence presented highlighting the vulnerability of minority populations to the associated adversity. Also of import to social change is the development of an allostatic load index for asthma, one that uses readily available biomarker data to determine whether an individual is at elevated risk for adverse asthma outcomes related to allostatic load overburden. Such information could be useful to health practitioners who can now use biomarker data to adequately screen for high allostatic load and intervene as necessary, lowering health inequity and improving asthma outcomes.

Conclusion

The current study offers an evidence-based approach to the predictive nature of allostatic load in asthma, one that utilizes a contemporary representative sample and takes covariates of interest into account. Using secondary biomarker data from the 2017-2018 release cycle of NHANES, I analyzed the predictive nature of allostatic load in asthma, highlighting the role of inflammatory components in the association. To my knowledge no such analysis for asthma using NHANES currently exists (Duong et al., 2017).

In addition to the evidenced statistically significant prediction of asthma outcomes from high allostatic load indices, study results also showed the lack of protection and resiliency to high allostatic load for non-Hispanic Blacks and other Hispanics. Education did not moderate the relationship between allostatic load and asthma even though higher allostatic load was observed in the data for respondents with less than a college degree.

Although the current study answered the stated research questions, further research is needed on the topic of allostatic load. Specifically, there is a need to define and validate a biomarker scale for allostatic load, ideally with subset scales for varying disease etiologies (Duong et al., 2017; Gallo et al., 2014; Geronimus et al., 2006; Howard & Sparks, 2016). Secondly there remains an unmet need as it pertains to translational research for allostatic load, with a lack of actual clinimetric tools to apply much of the current knowledge regarding allostatic load and underlying disease (Fava et al., 2019). It is hoped that the current research will further aid in the development of such tools to reduce adversity and health inequity from allostatic load driven disease.

References

Allen, A. M., Thomas, M. D., Michaels, E. K., Reeves, A. N., Okoye, U., Price, M. M., Hasson, R. E., Syme, S. L., & Chae, D. H. (2019). Racial discrimination, educational attainment, and biological dysregulation among midlife African American women. *Psychoneuroendocrinology*, *99*, 225–235. https://doi.org/10.1016/j.psyneuen.2018.09.001

Allen, M. (Ed.). (2017). *The SAGE encyclopedia of communication research methods*. SAGE.

Amaral, R., Pereira, A. M., Jacinto, T., Malinovschi, A., Janson, C., Alving, K., & Fonseca, J. A. (2019). Comparison of hypothesis and data-driven asthma phenotypes in NHANES 2007–2012: The importance of comprehensive data availability. *Clinical and Translational Allergy*, *9*. https://doi.org/10.1186/s13601-019-0258-7

Assari, S., Chalian, H., & Bazargan, M. (2019). High education level protects European Americans but not African Americans against chronic obstructive pulmonary disease: National Health Interview Survey. *International Journal of Biomedical Engineering and Clinical Science*, *5*(2), 16–23. https://doi.org/10.11648/j.ijbecs.20190502.12

Babbie, E. R. (2017). *The basics of social research* (7th ed.). Cengage Learning.

Bahreinian, S., Ball, G. D. C., Vander Leek, T. K., Colman, I., McNeil, B. J., Becker, A. B., & Kozyrskyj, A. L. (2013). Allostatic load biomarkers and asthma in

adolescents. *American Journal of Respiratory and Critical Care Medicine*, *187*(2), 144–152. https://doi.org/10.1164/rccm.201201-0025OC

Baker, E. H. (2014). Socioeconomic status, definition. In W. C. Cocerkam, R. Dingwall, & S. R. Quah (Eds.), *The Wiley Blackwell Encyclopedia of Health, Illness, Behavior, and Society* (pp. 2210–2214). Wiley Blackwell. https://doi.org/10.1002/9781118410868.wbehibs395

Barr, D. A. (2017). The childhood roots of cardiovascular disease disparities. *Mayo Clinic Proceedings*, *92*(9), 1415–1421. https://doi.org/10.1016/j.mayocp.2017.06.013

Barry, L. E., O'Neill, C., & Heaney, L. G. (2020). Association between asthma, corticosteroids and allostatic load biomarkers: A cross-sectional study. *Thorax*, *75*(10), 835–841. https://doi.org/10.1136/thoraxjnl-2019-214139

Beck, A. F., Huang, B., Auger, K. A., Ryan, P. H., Chen, C., & Kahn, R. S. (2016). Explaining racial disparities in child asthma readmission using a causal inference approach. *JAMA Pediatrics*, *170*(7), 695–703. https://doi.org/10.1001/jamapediatrics.2016.0269

Beckie, T. M., Duffy, A., & Groer, M. W. (2016). The relationship between allostatic load and psychosocial characteristics among women veterans. *Women's Health Issues*, *26*(5), 555–563. https://doi.org/10.1016/j.whi.2016.05.008

Beckles, G. L., McKeever Bullard, K., Saydah, S., Imperatore, G., Loustalot, F., & Correa, A. (2019). Life course socioeconomic position, allostatic load, and incidence of type 2 diabetes among African American adults: The Jackson Heart

Study, 2000-04 to 2012. *Ethnicity & Disease*, *29*(1), 39–46. https://doi.org/10.18865/ed.29.1.39

Berger, M., Juster, R.-P., & Sarnyai, Z. (2015). Mental health consequences of stress and trauma: Allostatic load markers for practice and policy with a focus on Indigenous health. *Australasian Psychiatry*, *23*(6), 644–649. https://doi.org/10.1177/1039856215608281

Bey, G. S., Jesdale, B. M., Ulbricht, C. M., Mick, E. O., & Person, S. D. (2018). Allostatic load biomarker associations with depressive symptoms vary among us Black and White women and men. *Healthcare*, *6*(3). https://doi.org/10.3390/healthcare6030105

Beydoun, M. A., Beydoun, H. A., Mode, N., Dore, G. A., Canas, J. A., Eid, S. M., & Zonderman, A. B. (2016). Racial disparities in adult all-cause and cause-specific mortality among us adults: Mediating and moderating factors. *BMC Public Health*, *16*(1), 1113. https://doi.org/10.1186/s12889-016-3744-z

Borrell, L. N., Dallo, F. J., & Nguyen, N. (2010). Racial/ethnic disparities in all-cause mortality in U.S. adults: The effect of allostatic load. *Public Health Reports*, *125*(6), 810–816. https://doi.org/10.1177/003335491012500608

Borrell, L. N., Rodríguez-Álvarez, E., & Dallo, F. J. (2020). Racial/ethnic inequities in the associations of allostatic load with all-cause and cardiovascular-specific mortality risk in U.S. adults. *PLOS ONE*, *15*(2), e0228336. https://doi.org/10.1371/journal.pone.0228336

Brody, G. H., Yu, T., Chen, E., Miller, G. E., Kogan, S. M., & Beach, S. R. H. (2013). Is resilience only skin deep?: Rural African Americans' socioeconomic status–related risk and competence in preadolescence and psychological adjustment and allostatic load at age 19. *Psychological Science*. https://doi.org/10.1177/0956797612471954

Bronfenbrenner, U. (1974). Developmental research, public policy, and the ecology of childhood. *Child Development*, *45*(1), 1–5. https://doi.org/10.2307/1127743

Bronfenbrenner, U. (1977). Toward an experimental ecology of human development. *American Psychologist*, *32*(7), 513–531. https://doi.org/10.1037/0003-066X.32.7.513

Bronfenbrenner, U., & Evans, G. W. (2000). Developmental science in the 21st century: Emerging questions, theoretical models, research designs and empirical findings. *Social Development*, *9*(1), 115–125. https://doi.org/10.1111/1467-9507.00114

Burkholder, G., Cox, K., & Crawford, L. (Eds.). (2016). *The scholar-practitioner's guide to research design* (1st ed.). Laureate Publishing.

Buss, K. A., Davis, E. L., & Kiel, E. J. (2011). Allostatic and environmental load in toddlers predicts anxiety in preschool and kindergarten. *Development and Psychopathology*, *23*(4), 1069–1087. https://doi.org/10.1017/S0954579411000502

Carlson, E. D., & Chamberlain, R. M. (2005). Allostatic load and health disparities: A theoretical orientation. *Research in Nursing & Health*, *28*(4), 306–315. https://doi.org/10.1002/nur.20084

Centers for Disease Control and Prevention. (2018). *Asthma's impact on the nation*. https://www.cdc.gov/asthma/impacts_nation/default.htm

Centers for Disease Control and Prevention. (2020). *NHANES Questionnaires, Datasets, and Related Documentation*. https://wwwn.cdc.gov/nchs/nhanes/default.aspx

Chen, E., Hayen, R., Le, V., Austin, M. K., Shalowitz, M. U., Story, R. E., & Miller, G. E. (2019). Neighborhood social conditions, family relationships, and childhood asthma. *Pediatrics*, *144*(2), e20183300. https://doi.org/10.1542/peds.2018-3300

Chen, E., Shalowitz, M. U., Story, R. E., Ehrlich, K. B., Levine, C. S., Hayen, R., Leigh, A. K. K., & Miller, G. E. (2016). Dimensions of socioeconomic status and childhood asthma outcomes: Evidence for distinct behavioral and biological associations. *Psychosomatic Medicine*, *78*(9), 1043–1052. https://doi.org/10.1097/PSY.0000000000000392

Chen, E., Shalowitz, M. U., Story, R. E., Ehrlich, K. B., Manczak, E. M., Ham, P. J., Le, V., & Miller, G. E. (2017). Parents' childhood socioeconomic circumstances are associated with their children's asthma outcomes. *The Journal of Allergy and Clinical Immunology*, *140*(3), 828-835.e2. https://doi.org/10.1016/j.jaci.2016.11.040

Chen, E., Shalowitz, M. U., Story, R. E., Hayen, R., Leigh, A. K. K., Hoffer, L. C., Austin, M. K., Lam, P. H., Brody, G. H., & Miller, G. E. (2019). The costs of high self-control in Black and Latino youth with asthma: Divergence of mental health and inflammatory profiles. *Brain, Behavior, and Immunity*, *80*, 120–128. https://doi.org/10.1016/j.bbi.2019.02.031

Chen, H., Cohen, P., & Chen, S. (2010). How big is a big odds ratio? Interpreting the magnitudes of odds ratios in epidemiological studies. *Communications in Statistics - Simulation and Computation*, *39*(4), 860–864. https://doi.org/10.1080/03610911003650383

Chen, T. C., Clark, J., Riddles, M. K., Mohadjer L. K., & Fakhouri, T. H. I.. (2020). National Health and Nutrition Examination Survey, 2015−2018: Sample design and estimation procedures. *National Center for Health Statistics Vital Health Statistics*, *2*(184). https://www.cdc.gov/nchs/data/series/sr_02/sr02-184-508.pdf

Chen, X., Redline, S., Shields, A. E., Williams, D. R., & Williams, M. A. (2014). Associations of allostatic load with sleep apnea, insomnia, short sleep duration, and other sleep disturbances: Findings from the National Health and Nutrition Examination Survey 2005 to 2008. *Annals of Epidemiology*, *24*(8), 612–619. https://doi.org/10.1016/j.annepidem.2014.05.014

Christensen, D. S., Flensborg-Madsen, T., Garde, E., Hansen, Å. M., Masters Pedersen, J., & Mortensen, E. L. (2018a). Early life predictors of midlife allostatic load: A prospective cohort study. *PloS One*, *13*(8), e0202395. https://doi.org/10.1371/journal.pone.0202395

Christensen, D. S., Flensborg-Madsen, T., Garde, E., Hansen, Å. M., Masters Pedersen, J., & Mortensen, E. L. (2018b). Parental socioeconomic position and midlife allostatic load: A study of potential mediators. *BMC Public Health*, *18*. https://doi.org/10.1186/s12889-018-5956-x

Creswell, J. W., & Creswell, J. D. (2018). *Research design: Qualitative, quantitative, and mixed methods approaches* (5th ed.). SAGE.

Dawson, J. F. (2014). Moderation in management research: What, why, when, and how. *Journal of Business and Psychology*, *29*(1), 1–19. https://doi.org/10.1007/s10869-013-9308-7

Delpierre, C., Barboza-Solis, C., Torrisani, J., Darnaudery, M., Bartley, M., Blane, D., Kelly-Irving, M., Getz, L., Tomasdottir, M. O., Robertson, T., & Gustafsson, P. E. (2016). Origins of health inequalities: The case for allostatic load. *Longitudinal and Life Course Studies*, *7*(1), 79–103. https://doi.org/10.14301/llcs.v7i1.325

Dich, N., Hansen, Å. M., Avlund, K., Lund, R., Mortensen, E. L., Bruunsgaard, H., & Rod, N. H. (2015). Early life adversity potentiates the effects of later life stress on cumulative physiological dysregulation. *Anxiety, Stress, & Coping*, *28*(4), 372–390. https://doi.org/10.1080/10615806.2014.969720

Ding, X., Barban, N., & Mills, M. C. (2019). Educational attainment and allostatic load in later life: Evidence using genetic markers. *Preventive Medicine*, *129*, 105866. https://doi.org/10.1016/j.ypmed.2019.105866

Dinwiddie, G. Y., Zambrana, R. E., Doamekpor, L. A., & Lopez, L. (2015). The impact of educational attainment on observed race/ethnic disparities in inflammatory risk in the 2001-2008 national health and nutrition examination survey. *International Journal of Environmental Research and Public Health*, *13*(1). https://doi.org/10.3390/ijerph13010042

Doamekpor, L. A., & Dinwiddie, G. Y. (2015). Allostatic load in foreign-born and US-born Blacks: Evidence from the 2001–2010 national health and nutrition examination survey. *American Journal of Public Health*, *105*(3), 591–597. https://doi.org/10.2105/AJPH.2014.302285

Duong, M. T., Bingham, B. A., Aldana, P. C., Chung, S. T., & Sumner, A. E. (2017). Variation in the calculation of allostatic load score: 21 Examples from NHANES. *Journal of Racial and Ethnic Health Disparities*, *4*(3), 455–461. https://doi.org/10.1007/s40615-016-0246-8

Duru, O. K., Harawa, N. T., Kermah, D., & Norris, K. C. (2012). Allostatic load burden and racial disparities in mortality. *Journal of the National Medical Association*, *104*(1–2), 89–95. https://doi.org/10.1016/s0027-9684(15)30120-6

Edes, A. N., & Crews, D. E. (2017). Allostatic load and biological anthropology. *American Journal of Physical Anthropology*, *162*(S63), e23146. https://doi.org/10.1002/ajpa.23146

Ehrlich, K. B., Miller, G. E., & Chen, E. (2015). Family functioning, eosinophil activity, and symptoms in children with asthma. *Journal of Pediatric Psychology*, *40*(8), 781–789. https://doi.org/10.1093/jpepsy/jsv045

Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power analysis program. *Behavior Research Methods, Instruments & Computers*, *28*(1), 1–11. https://doi.org/10.3758/BF03203630

Fava, G. A., McEwen, B. S., Guidi, J., Gostoli, S., Offidani, E., & Sonino, N. (2019). Clinical characterization of allostatic overload. *Psychoneuroendocrinology*, *108*, 94–101. https://doi.org/10.1016/j.psyneuen.2019.05.028

Federico, M. J., McFarlane, A. E., Szefler, S. J., & Abrams, E. M. (2020). The impact of social determinants of health on children with asthma. *Journal of Allergy and Clinical Immunology. In Practice; Amsterdam*, *8*(6), 1808–1814. https://doi.org/10.1016/j.jaip.2020.03.028

Ferguson, K. T., & Evans, G. W. (2019). Social ecological theory: Family systems and family psychology in bioecological and bioecocultural perspective. In B. H. Fiese, M. Celano, K. Deater-Deckard, E. N. Jouriles, & M. A. Whisman (Eds.), *APA handbook of contemporary family psychology: Foundations, methods, and contemporary issues across the lifespan* (Vol. 1, pp. 143–161). American Psychological Association. https://doi.org/10.1037/0000099-009

Fernandez, C. A. (2015). Evaluating the effects of coping style on allostatic load, by sex: The Jackson Heart Study, 2000–2004. *Preventing Chronic Disease*, *12*. https://doi.org/10.5888/pcd12.150166

Flannelly, K. J., Flannelly, L. T., & Jankowski, K. R. B. (2018). Threats to the internal validity of experimental and quasi-experimental research in healthcare. *Journal of Health Care Chaplaincy*, *24*(3), 107–130. https://doi.org/10.1080/08854726.2017.1421019

Frankfort-Nachmias, C., & Leon-Guerrero, A. (2018). *Social statistics for a diverse society* (8th ed.). SAGE.

Gagné, T., & Ghenadenik, A. E. (2018). Rethinking the relationship between socioeconomic status and health: Challenging how socioeconomic status is currently used in health inequality research. *Scandinavian Journal of Public Health*, *46*(1), 53–56. https://doi.org/10.1177/1403494817744987

Gallo, L. C., Fortmann, A. L., & Mattei, J. (2014). Allostatic load and the assessment of cumulative biological risk in biobehavioral medicine: Challenges and opportunities. *Psychosomatic Medicine*, *76*(7), 478–480. https://doi.org/10.1097/PSY.0000000000000095

Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among Blacks and Whites in the United States. *American Journal of Public Health*, *96*(5), 826–833. https://doi.org/10.2105/AJPH.2004.060749

Gillespie, S. L., Anderson, C. M., Zhao, S., Tan, Y., Kline, D., Brock, G., Odei, J., O'Brien, E., Sims, M., Lazarus, S. A., Hood, D. B., Williams, K. P., & Joseph, J. J. (2019). Allostatic load in the association of depressive symptoms with incident coronary heart disease: The Jackson Heart Study. *Psychoneuroendocrinology*, *109*, 104369. https://doi.org/10.1016/j.psyneuen.2019.06.020

Glanz, K., Rimer, B. K., & Viswanath, K. (Eds.). (2015). *Health behavior: Theory, research, and practice* (5th ed). Jossey-Bass.

Goldstein, D. S. (2012). Stress, allostatic load, catecholamines, and other neurotransmitters in neurodegenerative diseases. *Cellular and Molecular Neurobiology*, *32*(5), 661–666. https://doi.org/10.1007/s10571-011-9780-4

Goodman, J. E., Loftus, C. T., Liu, X., & Zu, K. (2017). Impact of respiratory infections, outdoor pollen, and socioeconomic status on associations between air pollutants and pediatric asthma hospital admissions. *PLOS ONE*, *12*(7), e0180522. https://doi.org/10.1371/journal.pone.0180522

Gordon, B., Hassid, A., Bar-Shai, A., Derazne, E., Tzur, D., Hershkovich, O., & Afek, A. (2016). Association between asthma and body mass index and socioeconomic status: A cross-sectional study on 849,659 adolescents. *Respirology*, *21*(1), 95–101. https://doi.org/10.1111/resp.12645

Graves, K. Y., & Nowakowski, A. C. H. (2017). Childhood socioeconomic status and stress in late adulthood: A longitudinal approach to measuring allostatic load. *Global Pediatric Health*, *4*. https://doi.org/10.1177/2333794X17744950

Guidi, J., Lucente, M., Sonino, N., & Fava, G. A. (2021). Allostatic load and its impact on health: A systematic review. *Psychotherapy and Psychosomatics*, *90*(1), 11–27. https://doi.org/10.1159/000510696

Hamdi, N. R., South, S. C., & Krueger, R. F. (2016). Does education lower allostatic load? A co-twin control study. *Brain, Behavior, and Immunity*, *56*, 221–229. https://doi.org/10.1016/j.bbi.2016.01.014

Hawkley, L. C., Lavelle, L. A., Berntson, G. G., & Cacioppo, J. T. (2011). Mediators of the relationship between socioeconomic status and allostatic load in the Chicago Health, Aging, and Social Relations Study (CHASRS). *Psychophysiology*, *48*(8), 1134. https://doi.org/10.1111/j.1469-8986.2011.01185.x

Hess, J. D., Hu, Y., & Blair, E. (2014). *On testing moderation effects in experiments using logistic regression* (SSRN Scholarly Paper ID 2393725). Social Science Research Network. https://doi.org/10.2139/ssrn.2393725

Hill, M. R., Philp, C. J., Billington, C. K., Tatler, A. L., Johnson, S. R., O'Dea, R. D., & Brook, B. S. (2018). A theoretical model of inflammation- and mechanotransduction-driven asthmatic airway remodelling. *Biomechanics and Modeling in Mechanobiology*, *17*(5), 1451–1470. https://doi.org/10.1007/s10237-018-1037-4

Hormenu, T., Shoup, E. M., Osei-Tutu, N. H., Hobabagabo, A. F., DuBose, C. W., Mabundo, L. S., Chung, S. T., Horlyck-Romanovsky, M. F., & Sumner, A. E. (2020). Stress measured by allostatic load varies by reason for immigration, age at immigration, and number of children: The Africans in America study. *International Journal of Environmental Research and Public Health*, *17*(12). https://doi.org/10.3390/ijerph17124533

Howard, J. T., & Sparks, P. J. (2015). The role of education in explaining racial/ethnic allostatic load differentials in the United States. *Biodemography and Social Biology*, *61*(1), 18–39. https://doi.org/10.1080/19485565.2014.937000

Howard, J. T., & Sparks, P. J. (2016). Does allostatic load calculation method matter? Evaluation of different methods and individual biomarkers functioning by race/ethnicity and educational level. *American Journal of Human Biology: The Official Journal of the Human Biology Council*, *28*(5), 627–635. https://doi.org/10.1002/ajhb.22843

Jackson, Knight, & Rafferty. (2010). Race and unhealthy behaviors: Chronic stress, the HPA axis, and physical and mental health disparities over the life course. *American Journal of Public Health*, *100*(5), 933–939. https://doi.org/10.2105/AJPH.2008.143446

Johnson, S. C., Cavallaro, F. L., & Leon, D. A. (2017). A systematic review of allostatic load in relation to socioeconomic position: Poor fidelity and major inconsistencies in biomarkers employed. *Social Science & Medicine*, *192*, 66–73. https://doi.org/10.1016/j.socscimed.2017.09.025

Juster, R.-P., de Torre, M. B., Kerr, P., Kheloui, S., Rossi, M., & Bourdon, O. (2019). Sex differences and gender diversity in stress responses and allostatic load among workers and LGBT people. *Current Psychiatry Reports*, *21*(11), 110. https://doi.org/10.1007/s11920-019-1104-2

Juster, R.-P., Pruessner, J. C., Desrochers, A. B., Bourdon, O., Durand, N., Wan, N., Tourjman, V., Kouassi, E., Lesage, A., & Lupien, S. J. (2016). Sex and gender roles in relation to mental health and allostatic load. *Psychosomatic Medicine*, *78*(7), 788–804. https://doi.org/10.1097/PSY.0000000000000351

Kerr, P., Kheloui, S., Rossi, M., Désilets, M., & Juster, R.-P. (2020). Allostatic load and women's brain health: A systematic review. *Frontiers in Neuroendocrinology*, *59*, 100858. https://doi.org/10.1016/j.yfrne.2020.100858

Kwong, C. G., & Bacharier, L. B. (2019). Phenotypes of wheezing and asthma in preschool children. *Current Opinion in Allergy and Clinical Immunology*, *19*(2), 148–153. https://doi.org/10.1097/ACI.0000000000000516

Lam, P. H., Levine, C. S., Chiang, J. J., Shalowitz, M. U., Story, R. E., Hayen, R., Sinard, R. N., & Chen, E. (2018). Family obligations and asthma in youth: The moderating role of socioeconomic status. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *37*(10), 968–978. https://doi.org/10.1037/hea0000655

Lee, E., Lee, S. H., Kwon, J.-W., Kim, Y.-H., Yoon, J., Cho, H.-J., Yang, S.-I., Jung, Y.-H., Kim, H. Y., Seo, J.-H., Kim, H. B., Lee, S. Y., Kwon, H.-J., & Hong, S.-J. (2017). Persistent asthma phenotype related with late-onset, high atopy, and low socioeconomic status in school-aged Korean children. *BMC Pulmonary Medicine*, *17*(1), 45. https://doi.org/10.1186/s12890-017-0387-5

Lehman, B. J., David, D. M., & Gruber, J. A. (2017). Rethinking the biopsychosocial model of health: Understanding health as a dynamic system. *Social and Personality Psychology Compass*, *11*(8), e12328. https://doi.org/10.1111/spc3.12328

Levy, D. J., Heissel, J. A., Richeson, J. A., & Adam, E. K. (2016). Psychological and biological responses to race-based social stress as pathways to disparities in educational outcomes. *American Psychologist*, *71*(6), 455–473. https://doi.org/10.1037/a0040322

Logan, J. G., & Barksdale, D. J. (2008). Allostasis and allostatic load: Expanding the discourse on stress and cardiovascular disease. *Journal of Clinical Nursing*, *17*(7b), 201–208. https://doi.org/10.1111/j.1365-2702.2008.02347.x

Lunyera, J., Stanifer, J. W., Davenport, C. A., Mohottige, D., Bhavsar, N. A., Scialla, J. J., Pendergast, J., Boulware, L. E., & Diamantidis, C. J. (2020). Life course socioeconomic status, allostatic load, and kidney health in Black Americans. *Clinical Journal of the American Society of Nephrology*, *15*(3), 341–348. https://doi.org/10.2215/CJN.08430719

Mann, C. J. (2003). Observational research methods. Research design II: Cohort, cross sectional, and case-control studies. *Emergency Medicine Journal*, *20*(1), 54–60. https://doi.org/10.1136/emj.20.1.54

Martinez, F. D. (2019). The state of asthma research: Considerable advances, but still a long way to go. *American Journal of Respiratory and Critical Care Medicine*, *199*(4), 397–399. https://doi.org/10.1164/rccm.201901-0013ED

Matzer, F., Fazekas, C., Vajda, C., Pilz, S., Schwetz, V., Trummer, C., Pandis, M., Tomaschitz, A., Petsch, I., Obermayer-Pietsch, B., Pieber, T., & Kapfhammer, H.-P. (2018). Association of allostatic load with health-related quality of life in patients with arterial hypertension: A cross-sectional analysis. *Swiss Medical Weekly*, *148*(4950). https://doi.org/10.4414/smw.2018.14689

McCrory, C., Fiorito, G., Ni Cheallaigh, C., Polidoro, S., Karisola, P., Alenius, H., Layte, R., Seeman, T., Vineis, P., & Kenny, R. A. (2019). How does socio-economic position (SEP) get biologically embedded? A comparison of allostatic load and the epigenetic clock(s). *Psychoneuroendocrinology*, *104*, 64–73. https://doi.org/10.1016/j.psyneuen.2019.02.018

McEwen, B. S. (2015). Biomarkers for assessing population and individual health and disease related to stress and adaptation. *Metabolism: Clinical and Experimental*, *64*(3 Suppl 1), S2–S10. https://doi.org/10.1016/j.metabol.2014.10.029

McEwen, B. S. (2016). In pursuit of resilience: Stress, epigenetics, and brain plasticity. *Annals Of The New York Academy of Sciences*, *1373*(1), 56–64. https://doi.org/10.1111/nyas.13020

Mertens, D. M., & McLaughlin, J. A. (2004). *Research and evaluation methods in special education*. Corwin Press.

Millsap, R., & Maydeu-Olivares, A. (2009). *The SAGE Handbook of Quantitative Methods in Psychology*. SAGE Publications. https://doi.org/10.4135/9780857020994

Mims, J. W. (2015). Asthma: Definitions and pathophysiology. *International Forum of Allergy & Rhinology*, *5*(S1), S2-6. https://doi.org/10.1002/alr.21609

Mocayar Marón, F. J., Ferder, L., Saraví, F. D., & Manucha, W. (2019). Hypertension linked to allostatic load: From psychosocial stress to inflammation and mitochondrial dysfunction. *Stress*, *22*(2), 169–181. https://doi.org/10.1080/10253890.2018.1542683

Nobel, L., Roblin, D. W., Becker, E. R., Druss, B. G., Joski, P. I., & Allison, J. J. (2017). Index of cardiometabolic health: A new method of measuring allostatic load using electronic health records. *Biomarkers: Biochemical Indicators of Exposure, Response, and Susceptibility to Chemicals*, *22*(5), 394–402. https://doi.org/10.1080/1354750X.2016.1201535

Nurmagambetov, T., Kuwahara, R., & Garbe, P. (2018). The economic burden of asthma in the United States, 2008–2013. *Annals of the American Thoracic Society*, *15*(3), 348–356. https://doi.org/10.1513/AnnalsATS.201703-259OC

Oren, E., Gerald, L., Stern, D. A., Martinez, F. D., & Wright, A. L. (2017). Self-reported stressful life events during adolescence and subsequent asthma: A longitudinal study. *The Journal of Allergy and Clinical Immunology: In Practice*, *5*(2), 427-434.e2. https://doi.org/10.1016/j.jaip.2016.09.019

Osborne, J. W. (2015). *Best Practices in Logistic Regression*. SAGE Publications. https://doi.org/10.4135/9781483399041

Pfeiffer, C. M., Lacher, D. A., Schleicher, R. L., Johnson, C. L., & Yetley, E. A. (2017). Challenges and lessons learned in generating and interpreting NHANES nutritional biomarker data. *Advances in Nutrition*, *8*(2), 290–307. https://doi.org/10.3945/an.116.014076

Piazza, J. R., Stawski, R. S., & Sheffler, J. L. (2019). Age, daily stress processes, and allostatic load: A longitudinal study. *Journal of Aging & Health*, *31*(9), 1671–1691. https://doi.org/10.1177/0898264318788493

Picard, M., Juster, R.-P., Sloan, R. P., & McEwen, B. S. (2017). Mitochondrial nexus to allostatic load biomarkers. *Psychosomatic Medicine*, *79*(1), 114–117. https://doi.org/10.1097/PSY.0000000000000414

Rastogi, D., & Holguin, F. (2017). Metabolic dysregulation, systemic inflammation, and pediatric obesity-related asthma. *Annals of the American Thoracic Society*, *14*(Suppl 5), S363–S367. https://doi.org/10.1513/AnnalsATS.201703-231AW

Robertson, T., & Watts, E. (2016). The importance of age, sex and place in understanding socioeconomic inequalities in allostatic load: Evidence from the Scottish Health Survey (2008–2011). *BMC Public Health*, *16*(1), 126. https://doi.org/10.1186/s12889-016-2796-4

Robinette, J. W., Charles, S. T., Almeida, D. M., & Gruenewald, T. L. (2016). Neighborhood features and physiological risk: An examination of allostatic load. *Health & Place*, *41*, 110–118. https://doi.org/10.1016/j.healthplace.2016.08.003

Rodriguez, J. M., Karlamangla, A. S., Gruenewald, T. L., Miller-Martinez, D., Merkin, S. S., & Seeman, T. E. (2019). Social stratification and allostatic load: Shapes of health differences in the MIDUS study in the United States. *Journal of Biosocial Science*, *51*(5), 627–644. https://doi.org/10.1017/S0021932018000378

Rodriquez, E. J., Kim, E. N., Sumner, A. E., Nápoles, A. M., & Pérez-Stable, E. J. (2019). Allostatic load: Importance, markers, and score determination in minority and disparity populations. *Journal of Urban Health: Bulletin of the New York Academy of Medicine*, *96*(Suppl 1), 3–11. https://doi.org/10.1007/s11524-019-00345-5

Rosa, E. M., & Tudge, J. (2013). Urie bronfenbrenner's theory of human development: Its evolution from ecology to bioecology. *Journal of Family Theory & Review*, *5*(4), 243–258. https://doi.org/10.1111/jftr.12022

Salkind, N. (2010). *Encyclopedia of Research Design*. SAGE Publications. https://doi.org/10.4135/9781412961288

Shalowitz, M. U., Schetter, C. D., Hillemeier, M. M., Chinchilli, V. M., Adam, E. K., Hobel, C. J., Ramey, S. L., Vance, M. R., O'Campo, P., Thorp, J. M., Seeman, T. E., & Raju, T. N. K. (2019). Cardiovascular and metabolic risk in women in the first year postpartum: Allostatic load as a function of race, ethnicity and poverty status. *American Journal of Perinatology*, *36*(10), 1079–1089. https://doi.org/10.1055/s-0038-1675618

Slack, M. K., & Draugalis, J. R. (2001). Establishing the internal and external validity of experimental studies. *American Journal of Health-System Pharmacy : AJHP : Official Journal of the American Society of Health-System Pharmacists*, *58*(22), 2173–2181; quiz 2182–2183.

Steptoe, A., Hackett, R. A., Lazzarino, A. I., Bostock, S., La Marca, R., Carvalho, L. A., & Hamer, M. (2014). Disruption of multisystem responses to stress in type 2 diabetes: Investigating the dynamics of allostatic load. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(44), 15693–15698. https://doi.org/10.1073/pnas.1410401111

Sterling, P., & Eyer, J. (1988). Allostasis: A new paradigm to explain arousal pathology. In S. Fisher & J. Reason (Eds.), *Handbook of Life Stress, Cognition and Health* (pp. 629–649). Wiley.

Suvarna, B., Suvarna, A., Phillips, R., Juster, R.-P., McDermott, B., & Sarnyai, Z. (2020). Health risk behaviours and allostatic load: A systematic review. *Neuroscience & Biobehavioral Reviews*, *108*, 694–711. https://doi.org/10.1016/j.neubiorev.2019.12.020

Tampubolon, G., & Maharani, A. (2018). Trajectories of allostatic load among older Americans and Britons: Longitudinal cohort studies. *BMC Geriatrics*, *18*(1), 255. https://doi.org/10.1186/s12877-018-0947-4

Tomfohr, L. M., Pung, M. A., & Dimsdale, J. E. (2016). Mediators of the relationship between race and allostatic load in African and White Americans. *Health Psychology*, *35*(4), 322–332. https://doi.org/10.1037/hea0000251

Vaccarino, S. R., Rajji, T. K., Gildengers, A. G., Waters, S. E. S., Butters, M. A., Menon, M., Blumberger, D. M., Voineskos, A. N., Miranda, D., & Mulsant, B. H. (2018). Allostatic load but not medical burden predicts memory performance in late-life bipolar disorder. *International Journal of Geriatric Psychiatry*, *33*(3), 546–552. https://doi.org/10.1002/gps.4829

van Deurzen, I., & Vanhoutte, B. (2019). A longitudinal study of allostatic load in later life: The role of sex, birth cohorts, and risk accumulation. *Research on Aging*, *41*(5), 419–442. https://doi.org/10.1177/0164027518813839

Viljoen, M., & Claassen, N. (2017). Allostatic load and heart rate variability as health risk indicators. *African Health Sciences*, *17*(2), 428–435. https://doi.org/10.4314/ahs.v17i2.17

Warner, R. M. (2013). *Applied statistics: From bivariate through multivariate techniques* (2nd ed). SAGE Publications.

Wiley, J. F., Gruenewald, T. L., Karlamangla, A. S., & Seeman, T. E. (2016). Modeling multisystem physiological dysregulation. *Psychosomatic Medicine*, *78*(3), 290–301. https://doi.org/10.1097/PSY.0000000000000288

Zimmer Gembeck, M. J. (2016). Peer rejection, victimization, and relational self-system processes in adolescence: Toward a transactional model of stress, coping, and developing sensitivities. *Child Development Perspectives*, *10*(2), 122–127. https://doi.org/10.1111/cdep.12174

Zipf, G., Chiappa, M., & Porter, K. (2013). National Health and Nutrition Examination Survey: Plan and operations. *Vital Health Statistics*, *1*(56), 37.