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The Implications of Chronic Stress on Obesity: Allostatic Load on Body Mass Index (BMI) Classification in the United States, NHANES 2005-2006

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ABSTRACT

The Implications of Chronic Stress on Obesity: Allostatic Load on Body Mass Index (BMI) Classification in the United States, NHANES 2005-2006

By Sheila Grami

December 5th, 2016

INTRODUCTION: In this modern environment, our world is reflecting an exponential increase in not only population, but in body size. Obesity is an overwhelming public health concern among the United States population. Research has shown there is a positive correlation between adiposity and stress. Allostatic load (AL) has been presented to be a consistent measure of chronic stress damage on the body. Yet, there is few studies exemplifying the presence AL on classification of body mass index (BMI).

AIM: The aim of this study is to find a relationship between allostatic load (AL) and body mass index (BMI) classification in the United States adult population on a large national scale. This complex interaction can predetermine who among the US population will be at greater risk for excess adiposity following this psychoneuroendocrinology.

METHODS: A representative sample size of n=3826 was gathered using NHANES data (2005-2006). Criteria for sample included all United States adults that had numerical values for 10 biomarkers chosen to represent chronic stress damage (allostatic load) along with individual body mass index (BMI). Allostatic load (low, high) and BMI classification (underweight to class III obese) were further categorized on severity and computed in SPSS to find significance between gradients of each variable ($\alpha=.05$). Cross-sectional analysis and logistical regression (multivariate) were used to further decipher an association between allostatic load and BMI category.

RESULTS: A strong positive correlation between allostatic load risk and BMI category was found ($p<.001$). Also among the variables in the study, significance was found within the strata of age, gender, race, smoking status and poverty income ratio (PIR). Findings show a strong statistically significant relationship between allostatic load and BMI.

DISCUSSION: It is imperative to decipher the directional relationship between stress and obesity to provide effective treatment. Understanding the pathology of how stress affects adiposity could open the door for many clinical and public health interventions to eradicate a very preventable outcome. By addressing the effect of chronic stress, a new avenue of prevention can be developed to combat the growing obesity rates in the United States.

**The Implications of Chronic Stress on Obesity: Allostatic Load on Body Mass Index (BMI)
Classification in the United States, NHANES 2005-2006**

by

Sheila Grami

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The Implications of Chronic Stress on Obesity: The Implications of Allostatic Load on Body Mass Index (BMI) Classification in the United States, NHANES 2005-2006

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Author's Statement Page

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Sheila Grami

Signature of Author

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INTRODUCTION

Obesity and Stress

Humans have evolved throughout time to become well equipped with a complex interaction of chemicals, hormones and internal mechanisms to handle the given environment and maintain equilibrium throughout the body. Our built-in physiology has been able to fend starvation, propagate and handle threats to our survival. Yet since humanity, people have changed their surroundings drastically to accommodate themselves, averting the harsh extremities of the natural environment. Ironically, our survival mechanisms built to protect us such as an effective “fight or flight” response when faced with stress or an efficient energy saving system (fat tissue) have now become the dilemma of modern day man. Stress a common but yet often overlooked risk factor may be associated with obesity.

Obesity

Burden and Prevalence of Obesity

Obesity has gained public health and clinical interests in the last three decades due to its increasing rate. The World Health Organization has declared obesity a public health epidemic on a global scale (World Health Organization, 2000). In 2001, Surgeon General David Satcher called the nation’s attention on its growing trend in the United States, stating that obesity was comparable to poverty, smoking and drinking (Surgeon, 2001). Approximately one third of United States adults are obese and another third are considered overweight (Ogden et al., 2014). It is estimated that 13% of the global obese and overweight population live in the United States today (Ng et al., 2014). Greater amounts of excess fat are associated with high mortality

related chronic diseases and is considered the second leading cause of estimated 300,000 preventable deaths per year in America (Surgeon, 2001).

The medical costs of obesity in the United States account for \$147 billion dollars (2008) and obese individuals accrue over \$1,400 dollars more than their non-obese counterparts (Chronic Disease Overview, 2016). Many of these illnesses can be prevented or ameliorated by decreasing adiposity, in some instances by reducing fat tissue to only a few kilograms of body weight (Tremblay & Chaput, 2011). According to the US Surgeon General, “This burden manifests itself in premature death and disability, in health care costs, in lost productivity, and in social stigmatization. The burden is not trivial. Studies show that the risk of death rises with increasing weight” (Surgeon, 2001). The excess adiposity in the United States has a substantial footprint on the health care industry. Therefore, it is imperative to identify major causes in order to reduce and eliminate obesity-associated sequelae.

Current Intervention Strategies

To reverse adiposity, public health researchers and well-respected members of the scientific community have been persistently seeking a “cure” to fat for the last 30 years. Physicians, scientists, nutritionists and leading health advocates have approached the platform to explain the etiology of phenomenon. Countless recommendations of meal plans, physical activity routines, pharmacology intervention and even surgery have contributed to a multibillion dollar industry to combat expanding waistlines. For some, these can be effective avenues to losing weight, but for most, efforts to lose large amount of excess weight are not effective. In order to combat this outcome, it is crucial to determine the multifaceted dynamic of all factors that are leading to the obesity crisis.

Causes of Obesity

An outcome such as obesity typically does not occur from one source. Many environmental, biological and behavioral factors contribute to an individual's disproportionate weight gain. From a genetic perspective certain traits or genetic disease, such as polycystic ovarian syndrome, type I diabetes or Cushing's syndrome which can be explained by a possible endogenous factor (Kudo et al., 2014). Parental influences can impact activities through behavioral modeling and also sway the likelihood of obesity in children eventually leading into adulthood. Food, exercise and parental upbringing will all heavily influence a child's coping mechanisms, accepted form of stress management. From a societal and cultural standpoint, food availability, socioeconomic status, typically synonymous with race and ethnicity, affect an individual from childhood all the way to adulthood.

The changing environment can account for much of this variation compared to half a century before. Food availability in most modern cultures is not a public health concern, actually the contrary is now true. Greater access to calorically dense foods is more available due to their low cost and easy preservation. Nutrient rich food on the other hand such as produce, lean protein and fresh foods cost more money and require more funds to purchase.

Gaps in Current Obesity Interventions

Since obesity prevalence has continued to increase, some public health advocates are beginning to ponder if there are other risk factors not addressed in the current intervention available strategies. "In the last three decades, not one country has achieved success in reducing obesity rates, and we expect obesity to rise steadily as incomes rise in low- and middle-income countries in particular, unless urgent steps are taken to address this public

health crisis” (Murray & Ng, n.d.). Even after the national urgency the surgeon general placed on the obesity epidemic in 2001, David Satcher’s successor, Regina M. Benjamin, MD, MBA emphasizes the tight hold obesity continues to have on Americans almost one decade later (Surgeon, 2010). It is important to understand not only groups when considering life altering aspects of health, but how our individual physiology and choices interact and play upon each other to determine overall health (McEwen & Seeman, 1999).

Stress

Scientific research has revealed significant relationships between physiological chronic stress and adiposity (Sinha & Jastreboff, 2013). This may conceptualize what seems to be a protective factor for some individuals who maintain a relatively normal weight range regardless of similar lifestyles and choices. Variation in exercise and portion size nutrient dense diets contribute to overall health and excess fat tissue but stress may be an underlying factor (Tremblay & Chaput, 2011).

Stress simply defined is the resulting adaption, whether malignant or not, to an environmental, emotional or psychological encounter (Sinha & Jastreboff, 2013). Stress itself is not a harmful response within the body. This evolutionary adrenal reaction is a necessary neurobiological mechanism that responds to stimuli, actually causing chemical changes in the body to adapt and react to our environment. Stress was crucial to survival at times when humanity was small in size and lacking tools or technology for protection (McEwen & Seeman, 1999).

Typically present in first world countries, along with expanding waistlines, daily pressures are shown to increase cortisol and other stress related biomechanisms and plateau at

elevated levels chronically (McEwen & Seeman, 1999). Life stressors for modern day humans, such as financial struggles, family obligations and health concerns all attribute to a malignant stressful outcome that eventually causes obesity and cardiovascular disease (Rabasa & Dickson, 2016). This psychoneuroendocrinology is still innate within our biology, but in a modern environment our stress response is triggered incessantly by daily responsibilities and obligations that cycle day by day.

The complexity of stress pathology has many influences intertwined. Since the concept of stress is a subjective experience that each individual will encounter uniquely, one person can come across the exact same stimuli yet distinguish that interaction vastly different than another. Perception, environment and a multifaceted combination of other past experiences in a lifetime will influence the reaction to different types of stress (McEwen & Seeman, 1999). Some of these are coping mechanisms developed from the symphony of influences brought together; some are out of the individual's control.

Neurobiology and Physiological Reaction

The pathology of stress begins when stress mediators are released into the blood stream. It initiates the process of physiological and behavioral responses activating areas of the body tied to the adrenal glands, cardiovascular system, metabolic and other major homeostatic regulatory mechanisms (Logan & Barksdale, 2008). Stress mediators are typically comprised on cortisol and catecholamines (McEwen & Seeman, 1999). An individual perceives a stressful event; mechanisms within their biology (specifically the adrenal gland) begin the distribution of cortisol into circulation. Once in the bloodstream, the objective of the glucocorticoid is to initiate a catabolic response within the body. An effective tool for dangerous encounters with

predatory animals is now accessed and utilized for dealing with traffic, social status and utility bills.

Cortisol release is an essential anti-inflammatory response in human biology, but when chronic and long standing wreaks havoc on the body beginning atrophy of necessary components that regulate the human biosystem. “In light of this evidence, high prevalence of life stressors paired with an overactive cortisol response may in fact perpetuate obesity and HPA-related diseases” (Incollingo Rodriguez et al., 2015). Implications of this disharmony within the body may underlie weight gain and general balance within our bodies.

Allostatis

Luckily, human biology has evolved to be highly adaptive and well equipped to handle psychosocial reactions with a diverse group of hormones and chemicals to counter this dissonance. In order to comprehensively describe the effect of biological mediators involved in maintaining homeostasis within the body, Sterling and Eyer coined the term allostatis. Allostatis is the continual process that the body undergoes in order maintain homeostasis, the body's physiological equilibrium (McEwen & Seeman, 1999). This process is set in motion after the sympathetic nervous system releases the stress reaction into the bloodstream, calling to action various homeostatic systems within the body including metabolic, cardiovascular and immune. Similar to a compass pointing north, allostatis is the process of pulling and pushing these physiological mechanisms to maintain the balance within our body.

Allostatic Load

If the balancing act of allostatis is activated constantly by elevated physiological stress, the body experiences a transformation of a protective mechanism into a corrosive one.

Although stress is a necessary biological reaction, chronic stress creates “wear and tear” on the body and over time causing what endocrinologists define this as allostatic load (AL) (McEwen & Seeman, 1999). Allostatic load signifies a form of measurement on the severity of damage to tissue, organs and other components that are used to regulate allostatis.

Objective of Study

By identifying the pathway of allostatic load related physiological influences on the weight gain within the body, a foundation of public health intervention can pave a new avenue into addressing and resolving the national and global obesity crisis. Understanding the impact of the biological system on the body from neurobiological standpoint, a major component in the burgeoning obesity trend could be identified.

The objective of this study is to determine the relationship between allostatic load (AL) and body mass index (BMI) classification in the United States adult population on a large national scale. This complex interaction can predetermine who among the overweight and obese population will be at greater risk for the disease implications following this psychoneuroendocrinology.

LITERATURE REVIEW

Stress Behavior and Obesity

Empirical evidence has shown the interconnection between those who experience internal or environmental stress and their individual body weight. There has been emergent scientific literature linking stress, food choice and overeating in adults (Yin, Davis, Moore, & Treiber, 2005). Stress not only changes the chemistry within the body, it also affects our behavior. “Growing evidence supports weight-related biobehavioral adaptations in interacting

metabolic, neuroendocrine and neural (cortico-limbicstriatal) pathways, to potentiate food craving and intake under conditions of HP foods and related cues and with stress” (Sinha & Jastreboff, 2013).

Experiencing stress in the body creates a cascade of neurochemical reactions that influence our eating behavior. Aversive behavior linked to obesity could be attributed to secondary outcome such as abnormal metabolism, increased glucose fluctuations, insulin resistance within the body or taught coping mechanisms (Maloney et al., 2006). Obese and overweight individuals tend to increase their caloric intake and preference for high fat or sugary foods in these types of situations. Stress will not only influence maladaptive behaviors regarding food, but also physical activity. Previous studies have exemplified how the exhaustion from stress can actually prevent physical activity in individuals, which is found to be a strong protective factor (Yin et al., 2005).

Eating Behavior

Michels et al. (2013) explained how increased cortisol impacts individual food selection in unhealthy ways. Taking a sample of 323 children (5-19 years old) experimenters measured salivary cortisol levels for a total of two days. Along with lab tests, the researchers also collected information on the child’s dietary patterns via questionnaire. After controlling for covariates, results found a significantly higher correlation for greater affinity of sweet foods and salivary cortisol. Stress caused increase in appetite for high carb food, so behavioral changes in food selection followed the onset of stress. Cortisol levels in the body will also influence dietary choices and physical exertion in some cases, this hormonal change in the bloodstream can affect food choices to veer to larger intakes of macro nutrient foods (such as carbs or fat) over

micro nutrient varieties (Michels et al., 2013). Also within the findings, no associations of increase produce and fresh food intake were found.

Kim et al. (2013) argued if allostatic load could be used as a good marker for pathophysiological process in the adult metabolic syndrome patients (>20 years old) in a health promotion center located in Korea. They found a significant negative correlation in the male population for dietary fat preference and allostatic load with obese patients, also a negative association with salt preference for individuals in the overweight category. Strangely, a negative association between appetite control and allostatic load in normal and underweight categories was also found.

Aschbacher et al. (2014) sought to find an association found in previous literature regarding chronic stresses as the underlining component of fat distribution and weight. Using a sample size of 63 women (age 50 – 80), a case control study was conducted and women were segmented based upon “low stress” or chronic stress through food frequency survey. Lab measures were subsequently done to measure abdominal adipose tissue, truncal fat ultrasound (DEXA), oxidative stress and an oral glucose test. Results from this study further backed the behavioral effects of higher stress. Women in this study were found to consume greater amount of high palatable foods and higher risk lab measures were also found in these women.

This does not only affect post-menopausal women but pre-menopausal women as well. Epel et al. (2001) attempted to identify whether physiological and psychological stress impacted eating behaviors after provocation. A sample size of 59 women age (<50 years old) were exposed to stressor versus a non-stressor, high cortisol reactors were found to consume more calories than the low reactors. Surprisingly, they ate similar amounts of calories during days

exposed to the control session. Again, the significance of sweet foods was found among the high risk group. Negative mood also was found to increase the consumption of food.

Physical activity

Yin et al. (2005) theorized physical activity as a buffer for the effects of stress and weight gain in young adults. In this longitudinal study, 303 participants were given a survey to analyze their individual stress and community stress was set based on the monthly cost for shelter. BMI, skinfold adiposity and waist circumference were also measured. Using sweating a threshold, researchers also accounted for physical activity capabilities in this study. After adjusting for confounding variables, an independent association was found for individual stress and BMI and sum of skinfolds ($p < .05$). Interestingly, community stress and individual stress were found to influence waist circumference. Those found to have better physical activity were negatively associated skinfold ($p < .01$) and when considering personal stress it could predict all measures of adiposity.

PSYCHOSOCIAL STRESS ON OBESITY

Strong evidence has been presented linking the intricate relationship between psychological stress and obesity. Even when controlling for all other confounding variables, the perception of chronic stress alone can independently affect adiposity (Ortega-Montiel et al., 2015). Those experiencing mental health issues such as depression and anxiety typically suffer from elevated stress reactions leading to greater BMI than their peers (Jaremka, Lindgren & Kiecolt-Glaser, 2013). Social support, or lack thereof, can also contribute to stress reactivity within the body. Individuals found to feel disconnected or isolated from interpersonal relationships tend to have higher levels of perceived stress (Cho et al., 2014). Those found to

have strained or troubled adult relationships exemplify higher amount of stress that their peers as well (Jaremka et al., 2013). This can create a vicious cycle as the weight increases and depression, mental anguish and feelings of hopelessness can increase stress within the body. In general, a poorer quality of life overlap with obesity as the environmental and societal demands begins to wane on an individual's mental and physical stamina.

Mental Health

Pervanidou et al. (2013) examined the relationship of cortisol profiles with anxiety and depressive individuals on BMI. Previous studies have also found that these psychological dysregulations can actually exacerbate chronic illnesses associated with obese individuals (Pervanidou et al., 2013). The sample size included 128 children from a pediatric obesity clinic population. A questionnaire along with lab measurements including BMI, pubertal assessment and salivary cortisol were taken from the participants. Researchers found that children whose anxiety and depressive symptom displayed greater salivary cortisol concentrations than the control group. This study further finds the intricate association between mental stress and obesity.

Social Implications

Individuals suffering from obesity tend to have less social support than those who are of normal weight; this may contribute to the increase in body mass when social outlets are not available to an individual. Studies have shown individuals that are overweight or obese tend to societally be more stigmatized and socially isolated (Puhl & Brownell, 2001). "Weight stigma as a socially evaluative threat could be stressful and stimulate cortisol secretion, thereby

increasing weight, abdominal adiposity and consequently perpetuating stigma” (Himmelstein et al., 2015).

Cho et al. (2014) sought to discover the correlation between social support and women with greater adiposity around their midsection. Using a sample size of 126 women, a multiple regression analysis was used to understand the association between cases versus control groups. Former studies have shown that obese individuals have less support networks and social outlets than their peers. The data exemplified that those with greater amounts of social support and lower amounts of perceived stress were significantly associated with better health promoting behaviors.

In a research study conducted by Himmelstein et al., (2015) a psychological and physiological measurement of weight stigma was sought. Regardless of BMI category, research has shown weight stigma can decrease health promoting behaviors such as exercise, decreased calorie intake and increase disordered eating and cardiovascular ailments (Himmelstein et al., 2015). A sample size of 110 female participants in college were selected and put into either a control group or stigma condition. For this experiment, the stigma stimulus was participants being told by a confederate their weight were not ideal for the style of clothing in the shopping activity (experimental environment). Then researchers measured this negative interaction on HPA (hypothalamus-pituitary-adrenal) axis reactivity. Results found the individuals own perception of their perceived weight had a greater increase in the HPA response releasing cortisol in the blood stream. This further adds to the complex relationship between psychological stress and physiological reactions.

Chronic Adversity Stress

Within the current literature there has been a substantial link between social status, stress and obesity. Psychological stress appears before weight gain and those in lower brackets of SES continuously experience lack of resources and less than favorable life experiences (Yin et al., 2005). Similar patterns of status preceding chronic stress are found among disadvantaged minority groups. This can be attributed to many adverse circumstances minority group endure throughout their lifespan. "Stress responses caused by perceived racism cause allostasis that involves the sympathetic nervous system and HPA cortical axis" (Logan & Barksdale, 2008). Overtime the overexerted stress response system creates damage to the equilibrium in the body resulting in many negative health outcomes including obesity (Duru, Harawa, Kermah, & Norris, 2012). Some evidence has also shown exposure to disadvantageous environments set by institutions (such as foreign born vs. US born minorities) can also influence allostatic load severity (Doamekpor & Dinwiddie 2015).

PHYSIOLOGICAL STRESS ON OBESITY

True to the iteration "mind over matter" the weighted impact of cognitive thoughts actually provokes a physiological change within our bodies. It is important to identify HPA axis disequilibrium as a risk factor to physical and mental health. The HPA is one of the main regulatory components in the allostatis network. In previous research, both animal and human experiments have shown the correlation between cortisol and body fat (Incollingo Rodriguez et al., 2015). On a biological level, our bodies can alter chemically to create a catabolic environment prone to increasing fat tissue.

System Dyregulations

Incollingo Rodriguez et al. (2015) examined the relationship of obesity and hypothalamic-pituitary-adrenal (HPA) axis dysregulation through a literature review of the HPA axis and cortisol studies available from various peer reviewed resources. Scientific literature has shown that many chronic disease outcomes caused by obesity are parallel with stress coping mechanisms within the body. Although they found conflicting evidence of the relationship between cortisol and obesity, in most results found a substantial relationship between HPA over-reactivity and obesity.

George et al. (2010) sought to discover the HPA influence on stress and obesity. Seen as an underlying mechanism in the perceived threat to cortisol response pathway, George and colleagues sought to find the underlying relationship that may come into play after a stressful event. 14 adult subjects (18-42 years old) were given corticotropin-releasing hormone (CRH) injections to measure the subsequent reaction to physiological stress by the type of snack and quantity of snack they consumed. Findings illustrated that when compared to the placebo group, subjects that were injected with CRH consumed more and selected high caloric foods when cortisol peaked. These results showed that regardless of stress induced environmental or emotional stimuli, CRH stimulated cortisol (glucocorticoids) alone can create a chain reaction to greater adiposity.

Cortisol

If the human body was a computer, then hormones would be the hardware code. Hormones give direction and instructions on almost every facet of our bodies. Emotional reactions show physical and biological changes in our chemistry. Even feeling butterflies in the stomach is just an adrenal gland stimulation that released cortisol and adrenaline (epinephrine)

to create a “fluttering” feeling within the abdomen. From an evolutionary perspective, each of these biochemical reactions was once a necessity for survival, which is why these traits have been passed to modern day man. “Fight or flight” coined by Walter Cannon was a term to illustrate the pathology of these chemicals to ultimate action (McEwen & Seeman, 1999).

Cortisol is found to combine maladaptive health outcomes such as increased appetite and abdominal adiposity simultaneously (Himmelstein et al., 2015). This combination could contribute to a major fundamental component in global obesity today. “Physiologically, increased cortisol concentrations have been causally linked to fat accumulation and weight gain, as glucocorticoids promote conversion of preadipocytes to mature adipocytes” (Rebuffé-Scrive, Walsh, McEwen, & Rodin, 1992). Other studies have found when reducing or “normalizing” cortisol levels within the body has a direct negative correlation with BMI (Feelders, Pulgar, Kempel, & Pereira, 2012).

Schorr et al. (2015) found strong associations with cortisol and BMI, yet only in extreme ends of the BMI spectrum. A U-shape curve was found in the analysis implying a sweet spot of cortisol reactivity in the body present in larger amounts among significantly obese or underweight individuals (Schorr et al., 2015). Among the highest in the cortisol spectrum were women suffering from anorexia. One consideration for this bell shape is that although stress can affect BMI and waist circumference substantially, measuring cortisol can only give spectrum to that moment in time, not a long term measurement of damage due to chronic stress.

Abraham et al. (2013) also wanted to seek the connection between cortisol and obesity including another component, metabolic syndrome. Measuring subjects that displayed at least two features of Cushing’s syndrome, researchers attempted to decipher the relationship

between circulating cortisol and obesity, linking how psychosocial stress impacts weight gain. They were able to conclude that no significant association was found between UFC and dexamethasone responses to BMI or weight, yet they found a statistically significant association in salivary cortisol and BMI. Again, this may be due to the fact that cortisol is not a consistent hormone and varies greatly throughout the day. However, there was a statistically significant trend in salivary cortisol with increasing BMI values ($p < 0.001$).

Geliebter et al. (2013) studied the difference in cortisol levels between night eaters (NE) and non-night eaters when given a physical stressor (cold press). The cold pressor test was found to be a consistent and reliable instrument to arouse physiological stress (cortisol) among participants. A sample of overweight women ($n=28$) were segmented into those who have NE ($n=11$) and those who do not suffer from NE (controls). They found that when given a physical lab stressor (cold pressor) the NE group showed a greater but not significant baseline in cortisol than the controls. Yet all other measures including ghrelin, hunger and stress remained the same between the two before the stress stimuli. After the stimulus, NE were found to show their stress levels increase significantly higher than the control group. No difference in hunger was found between the groups in given measurements of stress including: ghrelin and cortisol. When asked to rate their stress and hunger, participants were found to have a significant increase in both (NE group). These findings further support evidence on regardless of the stress stimuli, an association can be made for the effects of obesity. One for instance is that cortisol fluctuates based on a circadian rhythm so it may need to be paired with other physiological reactions to show significance. These participants were not followed up and the intention for behavioral changes (increased eating, kind of food) was not measured. It is shown that the

perceived stress and cortisol increases do have a slightly stronger correlation, yet due to the sample size and lack of other measures; it may have not been able to fully give scope to the validity of this study. Although considering the limitations, this study was able to further decipher the correlation between stress and greater adiposity in individuals.

Pavlatou et al. (2013) examined if fluctuations of glucocorticoids reactivity have a strong influence on obesity and fat tissue. Glucocorticoids are a natural anti-inflammatory agent that is released during the stress response. In order to find this relationship, a sample size of 25 overweight and obese subjects were examined by their circadian cortisol patterns and 93 glucocorticoid-responsive genes in abdominal subcutaneous fat. "Through the genes identified in this study, glucocorticoids appear to influence intermediary metabolism, energy balance, inflammation, and local circadian rhythmicity in subcutaneous fat" (Pavlatou et al., 2013). Results illustrated that those night cortisol, cortisol night to morning ratios, and urinary free cortisol were associated with the 93 glucocorticoid-responsive genes.

Measuring Stress on Obesity

Maloney et al. (2006) examined if those suffering from chronic fatigue syndrome (CFS) have a relationship with allostatic load (AL). Using a case-control method, 43 CFS patients and 60 controls classified as "healthy" from Wichita, Kansas were compared using lab and clinical information and computed for allostatic load using previous studies' criteria. Among the variables selected to measure in this study, BMI was observed. After comparing the CFS patients to controls, results showed that those suffering from CFS exemplified a significant association between high AL and high BMI, but not for controls ($p < 0.01$) (Maloney et al., 2006).

This phenomenon can possibly account for those with chronic stress prone physiology have greater hurdles to overcome, ultimately interfering with their weight loss.

METHODS

Sample and Measures

The data for this study were extracted from National Health and Nutrition Examination Survey (NHANES) from 2005-2006. Funded by the National Center for Health Statistics (NHCS) NHANES is a cross-sectional cluster sampling research program collecting comprehensive data about the United States population through questionnaire survey data and clinical measurements within the home and mobile examination stations across the country.

Demographic and clinical data from this database were taken to include variables shown to influence allostatic load from previous data. Criteria for sample included all adults living in the United States (≥ 18 years old). The study population was also stratified by age, race, PIR, gender, smoking status for further insight on differences between subgroups. Inequalities among racial groups can influence chronic stress and allostatic load and were categorized for examination (Hispanic, Non-Hispanic white, Non-Hispanic black and Other). Previous studies have shown poverty income ratio (PIR) can facilitate chronic stress creating long term damage to the body (Tyrrell, Melzer, Henley, Galloway, & Osborne, 2013). Smoking status (“Do you smoke?”) was also considered since previous literature illustrates the association with elevated cortisol to combat the chemical effects of nicotine circulation in the body (Badrick et al., 2009). Among the sample, those who responded with “Yes” to pregnancy status were removed from the study due to possible skewed waist circumference. Within the data set, a total of four systolic and diastolic blood pressure measurements were collected at specified increments over

time. To increase validity, both SBP and DBP observations were averaged to create one lab measurement per biomarker, respectively. Gender-defined waist circumference thresholds (Female = 88 cm, Male = 103 cm) were set to delimit enlarged waist girth (Okosun et al., 2000).

Allostatic Load Biomarkers

Similar to HbA1C, a stable measurement of blood sugar damage over time, allostatic load does not fluctuate throughout the day like cortisol. Since allostatic load is essentially the damage created from chronic allostatis, it is a more reliable measurement in studying the implications of stress on the body. There are countless biomarkers that adequately represent damage of the homeostatic system (Juster, McEwen, & Lupien, 2010). This study will focus on the most widely used biomarkers that are available in NHANES (Read & Grundy, 2012). Eligibility criteria for analysis were a numerical value (no missing data) for all 10 allostatic load biomarkers selected for this study. The NHANES 2005-2006 timeframe was specifically selected as the lab measurements for each biomarker were available simultaneously. Biomarkers selected for this study used to illustrate the presence of elevated allostatic load included: Albumin (ug/mL), Creatinine (mg/dL), C-Reactive Protein (CRP) (mg/dL), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Homocystine (umol/L), Total Cholesterol (TC) (mg/dL), High Density Lipoprotein (HDL), Waist Circumference (WC) (cm) and Glycated Hemoglobin (HbA1C). These biomarkers exemplify organ and tissue damage within a variety of homeostatic systems: cardiovascular, atherosclerosis, inflammation, metabolic (anthropometric) and immune (Table 1.2).

Allostatic load measures the combination of chronic damage due to stress. Not one single component of this dysregulation can identify allostatic load, rather the summation of all

biomarkers can significantly recognize this theory (Maloney et al., 2006). This disharmony can range from moderate to large deviations when observing all homeostatic systems collectively (Karlman et al., 2002). Some studies define the cut off criteria for “high risk” at six “at risk” biomarkers. Other studies have shown combining these thresholds, some even tagging caution on “at risk” biomarker summations as little as three. Based on previous literature in order to make the estimation of this physiological impact, ten standard biomarkers were selected as indicators of allostatic load risk or not and stratified by severity into a dichotomous variable (low risk ≤ 4 and high risk > 4).

A criterion was set at the highest quartile (75%) for all biomarkers, except for albumin and HDL which were set at the lowest quartile (25%). Each biomarker was categorized as “high risk” or “low risk” based on their specific average percentage among the distribution (Table 1.3). If within the critical quartile (high risk), the biomarker received a value of one. Those within the “low risk” quartiles would be given a value “0”. As previous endocrinology experts have studied, regardless of the analysis, weighting each biomarker equally was scientifically sound approach regarding AL assessment (McEwen & Seeman, 1999).

BMI Classification

Body Mass Index (BMI) is a standardized estimation of the percentage of fat an individual carries on their body. Calculated by weight (kg) divided by height (m^2) a relatively robust assumption can be made about the amount of fat tissue in a body. Those found to be over 25% BMI are considered overweight and individuals greater or equal to a BMI of 30% are classified as obese (Defining Adult Overweight and Obesity, 2016).

Due to the dramatic increase of weight and girth among people over the years, public health organizations stratified body mass index to categorize the severity of excess weight, underweight (<18.5%) to class III obese ($\geq 40\%$) typically described as super obese (World Health Organization, 2000). For this analysis, BMI was stratified into six categories based on the WHO/CDC criteria (The Global Challenge). All biomarkers were tested for significance against BMI classification including underweight (< 18.5%), normal weight (18.5–24.9%), overweight (25.0–29.9%), class I obese (30.0–34.9%), class II obese (35.0–39.9%), and class III obese ($\geq 40.0\%$).

Statistical Analysis

Data were analyzed through IBM SPSS software. The association between BMI classification and allostatic load was presented using multiple logistic regression analysis (Table 3). Independent t-test was used to compare the continuous variables against prevalence of high allostatic load risk (age and PIR). To create a baseline of the data, descriptive statistics were calculated including the mean and standard deviation comparing high and low risk scores (Table 1.1). All biomarkers were tested through this method as well (Table 1.2). Crosstabulation was used to compare the means for categorical variables (gender, race, smoking and BMI category) using chi-squared for significance (Table 1.1).

RESULTS

Descriptive Statistics

Demographic characteristics of the study population are shown in Table 1.1. Those with low risk allostatic load tended to be younger (approximately by 10 years) and have higher family income as well (2.80 vs. 2.52). Among the race and ethnicity groups, Hispanic, non-

Hispanic white and Other had more “low risk” than “high risk” individuals (Non-Hispanic black were higher in high risk group). Compared to smokers, non-smokers had a slightly higher population with high allostatic load (79% vs. smokers 76%). Those subjects categorized as “low risk” also displayed biomarkers means less than the high risk category (with the exception of HDL and albumin, which showed an inverse result). Cardiovascular biomarkers DBP, SBP, homocystine and total cholesterol also had less averages than the high risk group. Glycated hemoglobin low (5.43) vs. high risk (6.28) and waist circumference low (95 cm) vs. high risk (110 cm) in the metabolic category both signified noteworthy differences as well. C-reactive protein, creatinine, albumin and HDL also showed significance between the allostatic load groups (Table 1.2). These differences are consistent with the expectation set in methods since cutoff criteria were defined to separate the high risk biomarkers from the low risk range.

Multivariate Analysis

Multivariate analysis was used to estimate the likelihood of association between allostatic load and BMI severity (Table 3). It was shown that among the 3826 selected subjects in this sample, poverty income ratio (PIR), race (Non-Hispanic black), smoking status, gender (male) and age were associated with increase odds of high allostatic load. Age was associated with 5% increase in allostatic load risk per additional year compared to those that were 18 years of age (OR 1.05, $p < .001$) and those with higher PIR had decreased odds of high allostatic load (OR 0.91, $p < .01$) after adjusting for other independent variables. Non-Hispanic blacks were shown to be 36% more likely to have high allostatic load over the other racial groups ($p < .03$). Subjects that smoked cigarettes “everyday” or “some days” were found to have a significant higher risk of allostatic load than the non-smoker group (OR 1.43). The sample showed a

statistically significant difference in allostatic load risk among gender. Males are 24% more likely to develop high risk allostatic load when compared to females.

There was a strong positive correlation between allostatic load risk and BMI category. Those who were overweight to class III obese had a statistically significant relationship with high risk allostatic load status ($p < .001$) (Table 3). When stratified by BMI level, the strength of association increased as BMI classification severity increased. Those in the normal weight were not statistically significant yet overweight (OR 13.15, $p < .01$), class I obese (OR 35.27, $p < .001$), class II obese (OR 50.84, $p < .001$), and class III obese (OR 76.95, $p < .01$) categories seem to have displayed a strong positive relationship when underweight was used as a reference point. Using odds ratio to estimate risk of high allostatic load as shown when compare to those underweight, subjects with normal weight, overweight, class I obese, class II obese and class III obese were associated with 3.17, 13.15, 35.27, 50.84, 76.95 increased odds of allostatic load, respectively (after adjusting for age, gender, PIR, race and smoking).

DISCUSSION AND CONCLUSION

Discussion

In this study we sought to determine if there was a relationship between chronic stress and obesity using allostatic load as the measurement for chronic stress damage within the body. This research found a strong positive correlation between those who physiologically displayed signs of stress damage and increased weight after adjusting for confounders (Figure 4). Also, relationships of allostatic load between demographic characteristics including age, gender, race, PIR and smoking were also found. Allostatic load in previous studies has been able to exemplify influence on other areas of disease and illnesses, such as aging, race and

socioeconomic status, yet very little research has been conducted illustrating the relationship between gradients of body fat and allostatic load. Based on these findings, we can conclude that allostatic load and BMI severity have a substantial positive correlation.

Strengths

NHANES data is nationally representative data and generalizable to the US population. Inferences made from this data can be assumed to be reliable and consistent. Since this secondary database is available to the public and easily accessed, it is a relatively effortless way to collect information on a large scale. Also, multiple outcomes and exposures can be analyzed simultaneously.

The nature of this data is quantitative in every respect, which leaves less room for errors due to subjectivity and participant bias. It is a solid source for descriptive data and creating scientific hypotheses that leave little to misinterpretation. The clinical measures are furthermore less wavering in outcome; giving dependable and consistent scope to participant's internal regulations.

Limitations

Although this study was able to show a strong relationship between allostatic load and BMI classification, there are limitations to this study. When considering BMI as a variable of interest, although reliable and generalizable, validity of this measure must be taken into account. "BMI has some limitations, in that it can overestimate body fat in persons who are very muscular, and it can underestimate body fat in persons who have lost muscle mass, such as many elderly" (Surgeon General, 2001). There are other more accurate measures of fat distribution (i.e. DEXA) that better identify visceral fat, a major contributor to chronic illnesses

that follow obesity (Okosun et al., 2015). Future studies will have to measure adiposity in more than one way to increase the validity of obesity classification.

Cross-sectional data cannot make direct inferences of which variable affects the other. Our results show a strong relationship between allostatic load (chronic stress) and BMI (obesity), but we cannot assume causation. In order to accurately find the direction of this relationship, a highly controlled longitudinal study will have to be conducted over time to decipher the cause and effect correlation. Also considering this secondary data, NHANES can be problematic in oversampling for certain cohorts among the population, possibly skewing the data (Odgen et al., 2014).

There is a vast array of biomarkers selection when defining allostatic load (Schnorpfeil, et al., 2003). This study used the most prevalent but not all biomarkers used in previous studies. Previous literature has shown the greater amount of biomarkers can determine more accurately mortality and other chronic illnesses and in that regard it may be held true for obesity as well (Seeman et al., 2001). BMI is considered a commonly used biomarker of allostatic load and will need to be carefully observed when used as a variable independent of allostatic load.

Implications

Based on these significant findings, further research on the association between allostatic load and BMI classification must be conducted to understand the directional “cause and effect” of this phenomenon. This may encompass behavior, biological and environmental scientific studies to highlight the most direct path between weight and stress. A retrospective study comparing “stressed” populations vs. “nonstressed” (controlling for confounders) could

provide information on BMI distribution between groups. To better hone in on what variables influence the other, a longitudinal study can provide a more comprehensive picture of the stress and obesity dynamic by measuring stress over time and subsequent adiposity among participants. By using more experimental or random control trial designs, have a higher probability of removing extraneous factors and bias that may influence the stress and obesity correlation. Understanding the causation of this link, very promising new approaches can be sought to address obesity on a clinical and population scale.

If scientific evidence can provide strong indication that stress does influence adiposity, a new paradigm will need to be developed when addressing obese and overweight individuals. To provide a holistic approach not only from a clinical perspective but from a population level, it is vital to consider common causes of stress, general coping mechanisms and other indicators of the stress to fat pathology. From a population standpoint public health educators will have to communicate the imperative nature of mental health care built into our current health care establishments. Within the medical and clinical organization, structural changes that emphasize better tactics for stress management. These may include physical activity, sleep guidelines, psychological coping mechanisms, even mindfulness and meditation.

The weighted implications of finding the effects of estimated perceived stress on adiposity can be applied to a diverse spectrum of other illnesses that affect the U.S. population today. “Other interventions to manage stress and allostatic load include helping individuals to change behaviors or lifestyles that are not conducive to health, improve sleep, enhance social networks, increase self-esteem and promote physical activity which is associated with improved cardiovascular function, memory and mood” (Logan, J., & Barksdale, D., 2008).

Studies have shown stress not only can increase BMI and waist circumference, but also increase chronic diseases that parallel obesity illness outcomes including: hypertension, cardiovascular disease and type 2 diabetes (Incollingo Rodriguez et al., 2015). This relationship can be found it may also explain those who experience obesity related health outcomes with normal weight status. Understanding stress on the physiological system can also target public health endeavors to address other stress related incidences that are macro level such as socioeconomic status, institutional racism or weight stigma.

If a directional relationship is found that stress does influence weight gain, an initiative for mental health integration into primary care as a protective factor for could be considered. Development of interventions to address behavioral changes influenced by stress such as food choices can also prevent some of the negative outcomes of this theory (George et al., 2010). From a behavioral standpoint, teaching healthy stress coping mechanisms can greatly improve weight status and quality of life in general. It is even found that mindfulness and meditation can actually positively influence mechanisms of the adrenal glands and significantly improve psychological wellbeing (Manzaneque et al., 2011).

By measuring the physiology and molecular level changes within the body may lead to synthetic pharmacology related interventions that can counteract the long term effects of cortisol and physiological stress hormones on the body. Future studies may also seek to find if stress could be “the smoking gun” for abdominal adiposity increase in post-menopausal woman and testosterone changes in men. Also, this research could approach oxidative stress, free radicals and the aging process from a different angle.

Conclusions

Although much scientific literature is found associating the relationship between stress and obesity, there is relatively little information on the relationship between allostatic load and BMI severity. Relationships found within this data can guide possible future studies that scope multilevel environmental, behavioral and mental influences on the human body. The significant findings within the strata of this sample (age, race, smoking, gender and PIR) public health advocates must consider the extraneous influences on stress, only then can effective intervention be implemented on a population scale. Future studies will have to decipher which of these variables influences the other to understand the role stress plays when addressing the obesity epidemic.

Results of this study have shed light on some possible new influences on the obesity epidemic from a clinical and public health standpoint. “Furthermore, it is important to better understand the implications of this new reality of living on metabolic allostasis, appetite control and ultimately body weight” (Tremblay & Chaput, 2011). Measuring allostatic load indicators as part of a primary care protocol can help decipher some of the dysregulation within an individual’s body, especially those in the obese to morbidly obese weight range. Due to the nature of this phenomenon coming from the psychoneuroendocrinology field, scientists and researchers must also be cognizant of psychological perception and stress when addressing weight gain and unhealthy weight status.

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APPENDICES

Tables

Table 1.1 Descriptive Statistics Demographic Measures

Survey	Allostatic Load		P-Value Sig.
	Low Risk (N=3108)	High Risk (N=718)	
Continuous Variables	<i>Mean ± SD</i>	<i>Mean ± SD</i>	
Age	47.35 ± 18.20	58.98 ± 15.49	<.001
PIR	2.80 ± 1.60	2.52 ± 1.56	0.025
Gender	<i>Percentages</i>	<i>Percentages</i>	
Men	51.40%	53.20%	0.371
Women	48.60%	46.80%	
Race and Ethnicity			
Hispanic	23.70%	18.90%	<.001
Non-Hispanic Black	20.60%	28.30%	
Non-Hispanic White	51.80%	49.90%	
Other	4.00%	2.90%	
Smoking Status			
Non-Smoker	76.40%	79.10%	0.127
Smoker	23.60%	20.90%	

Table 1.2 Descriptive Statistics Allostatic Load Biomarkers

Clinical Measures	Allostatic Load		P-Value Sig.
	Low Risk (N=3108)	High Risk (N=718)	
Cardiovascular	<i>Mean ± SD</i>	<i>Mean ± SD</i>	
Diastolic Blood Pressure	69.01 ± 12.69	72.77 ± 15.98	<.001
High Density Lipoprotein	55.27 ± 16.44	48.61 ± 13.71	<.001
Homocystine	10.31 ± 4.09	8.31 ± 4.56	<.001
Systolic Blood Pressure	138.64 ± 21.67	121.75 ± 17.23	<.001
Total Cholesterol	193.39 ± 39.04	213.05 ± 50.35	<.001
Metabolic			
Glycated Hemoglobin (HbA1C)	5.43 ± .86	6.28 ± 1.36	<.001
Waist Circumference	95.28 ± 14.52	109.89 ± 13.85	0.021
Inflammation			
Albumin*	31.14 ± 205.46	115.77 ± 741.57	<.001
C-reactive Protein (CRP)	.36 ± .76	.80 ± .95	<.001
Immune System			
Creatinine	128.58 ± 76.96	134.85 ± 84.13	<.001

Table 1.3 Allostatic Load Mean Distribution of Biomarkers and Cutoff Criteria

	Allostatic Load			Allostatic Load Cutoff Criteria
	Low Risk	High Risk	Total	
	<i>Mean</i>	<i>Mean</i>	<i>Mean ± SD</i>	
Albumin*	115.77	31.40	98.02 ± 15.48	≤4.30
C-Reactive Protein	0.36	0.80	0.44 ± 0.82	≥0.53
Creatinine	128.58	134.85	129.76 ± 78.38	≥172.00
Diastolic Blood Pressure	69.01	72.77	69.71 ± 13.45	≥76.67
Glycated Hemoglobin	5.43	6.28	5.59 ± 1.03	≥5.70
High Density Lipoprotein	55.27	48.61	54.02 ± 16.17	≤64.00
Homocystine	8.31	10.31	8.69 ± 4.55	≥9.58
Systolic Blood Pressure	121.75	138.64	124.92 ± 19.31	≥133.33
Total Cholesterol	193.39	213.05	197.08 ± 42.09	≥225.00
Waist Circumference <i>female</i>	95.28	109.89	98.02 ± 15.48	≥88.00
Waist Circumference <i>male</i>	95.28	109.89	98.02 ± 15.48	≥103.00

*Below 25% percentile to be considered at risk

Table 2. Chi-Squared Test Crosstabulation: Prevalence of Allostatic Load Risk by BMI Classification (%)

	Allostatic Load			P-Value Asymp. Sig. (2- tailed)
	Low Risk	High Risk	Total	
Underweight <i>< 18.5</i>	2.00%	0.10%	1.70%	<.001
Normal Weight <i>18.5–24.9</i>	34.20%	7.00%	29.10%	
Overweight <i>25.0–29.9</i>	35.80%	29.10%	34.60%	
Class I Obese <i>30.0–34.9</i>	17.20%	34.40%	20.40%	
Class II Obese <i>35.0–39.9</i>	7.10%	16.70%	8.90%	
Class III Obese <i>≥ 40.0</i>	3.70%	12.70%	5.40%	
Total	100.00%	100.00%	100.00%	

Table 3. Allostatic Load High Risk Multivariate Analysis

Variable	Odds Ratio	95% CI	P-Value
BMI Classification			
<i>Normal Weight</i>	3.17	(0.42; 24.00)	0.26
<i>Overweight</i>	13.15	(1.76; 98.16)	0.01*
<i>Class I Obese</i>	35.27	(4.72; 263.57)	<0.001*
<i>Class II Obese</i>	50.84	(6.75; 383.28)	<0.001*
<i>Class III Obese</i>	76.95	(10.13; 584.68)	<0.001*
Age	1.05	(1.04; 1.06)	<0.001*
Gender			
<i>Male</i>	1.24	(1.03;1.51)	0.03*
PIR	0.91	(0.85; 0.97)	<0.01*
Race*			
<i>Non-Hispanic Black</i>	1.36	(1.03; 1.80)	0.03*
<i>Non-Hispanic White</i>	0.92	(0.71;1.19)	0.51
<i>Other</i>	1.21	(0.69; 2.12)	0.50
Smoking Status	1.43	(1.13; 1.82)	0.003*
<i>*Significant</i>			

Figures

Figure 1.1 Distribution of BMI Category (Frequency)

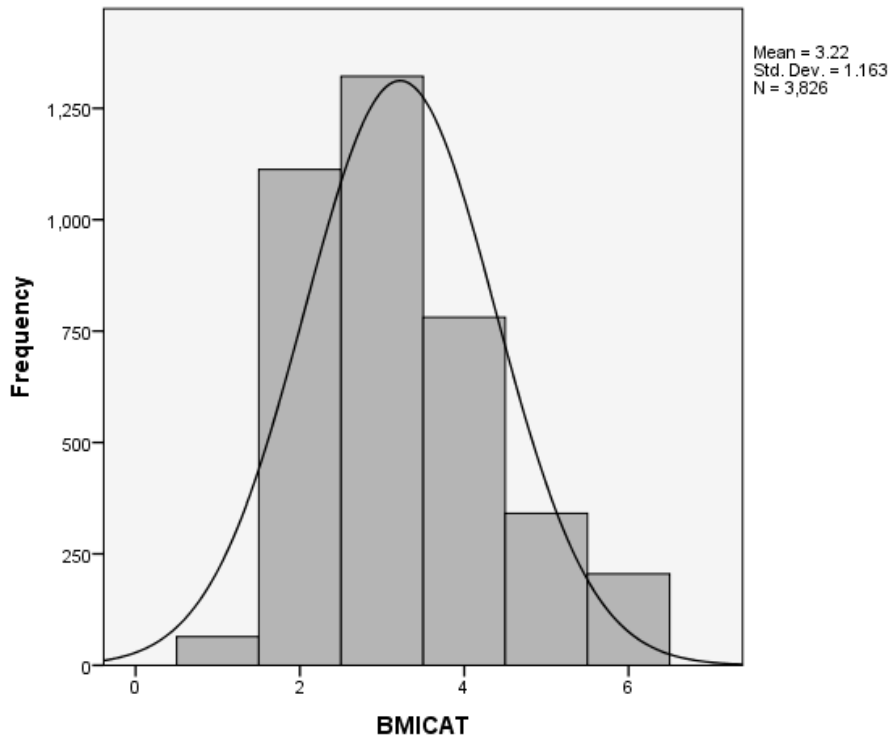


Figure 1.2 Distribution of Allostatic Load Risk (Frequency)

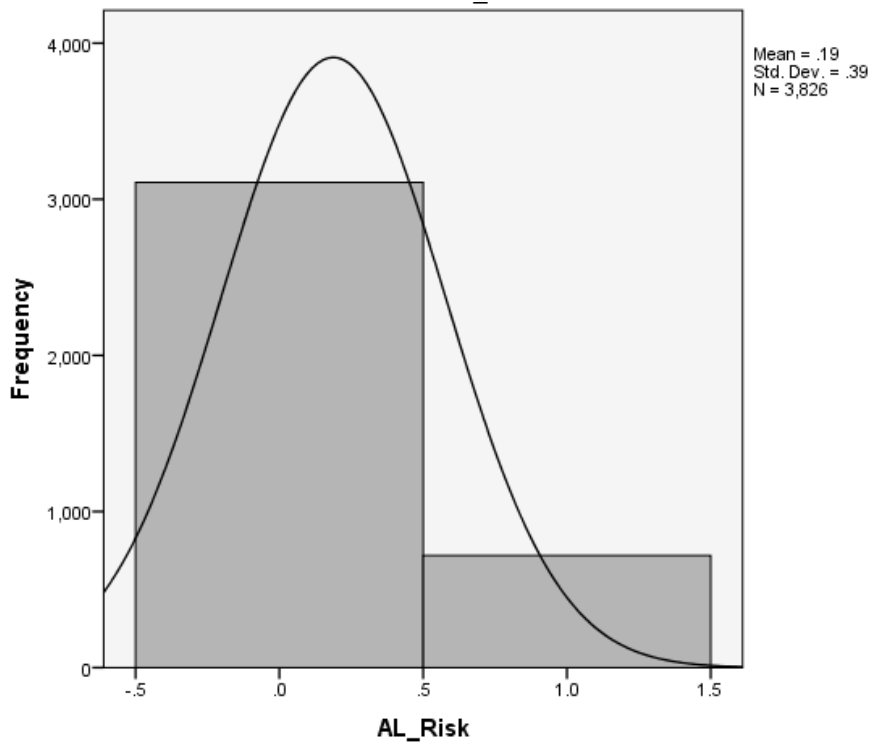


Figure 2.1 Distribution of High vs. Low Risk Allostatic Load Frequency by BMI (Category)

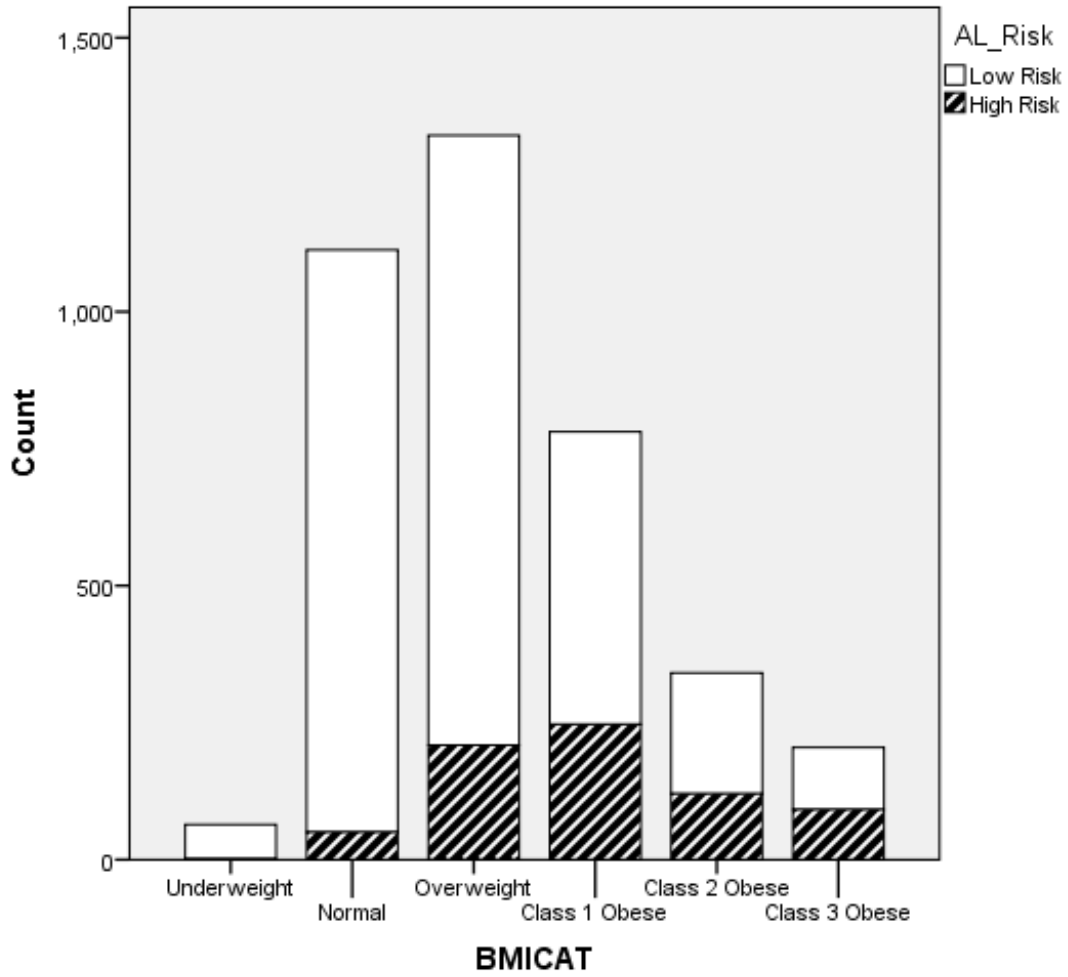


Figure 2.2 Distribution of High vs. Low Risk Allostatic Load Frequency by BMI (Continuous)

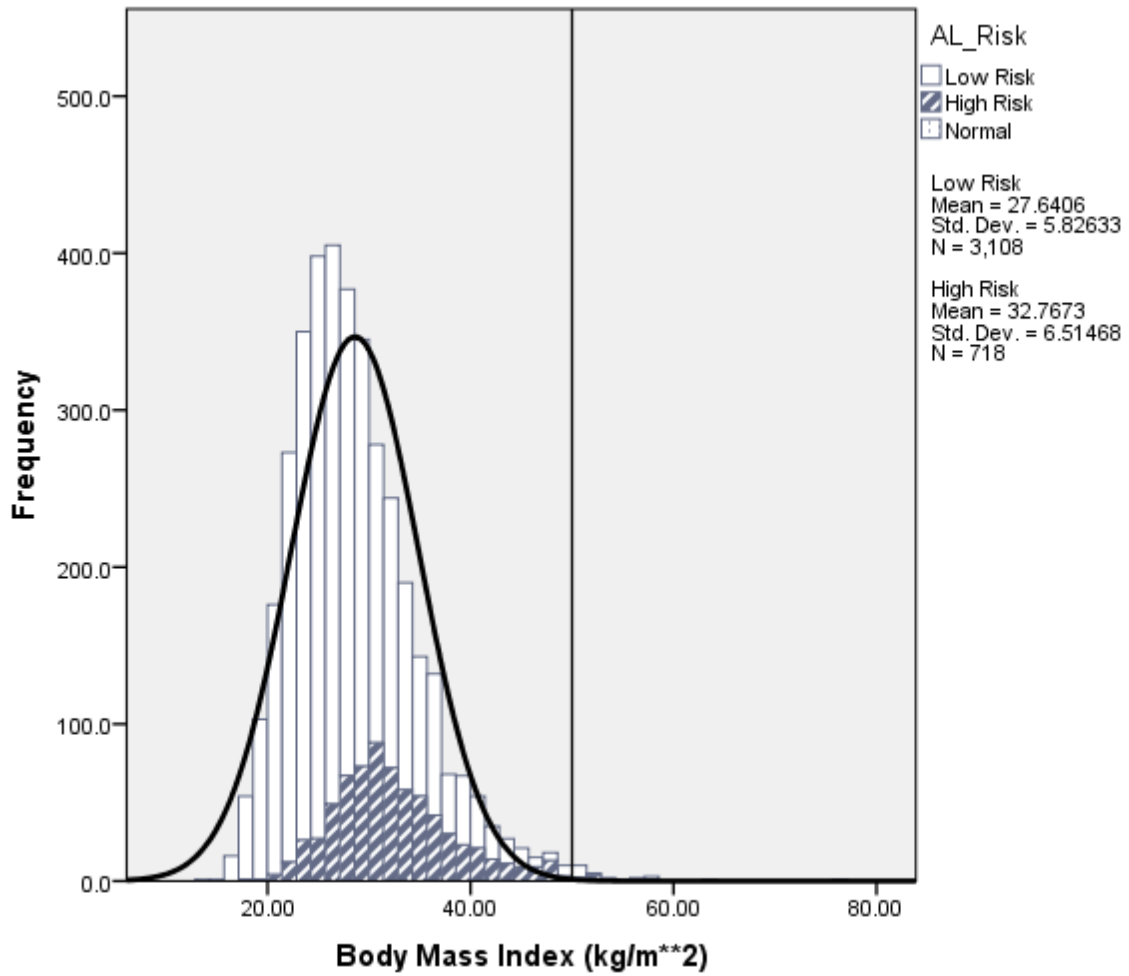


Figure 3. Subgroup Histogram: Distribution Comparison of Biomarkers by Allostatic Load Risk (High and Low)

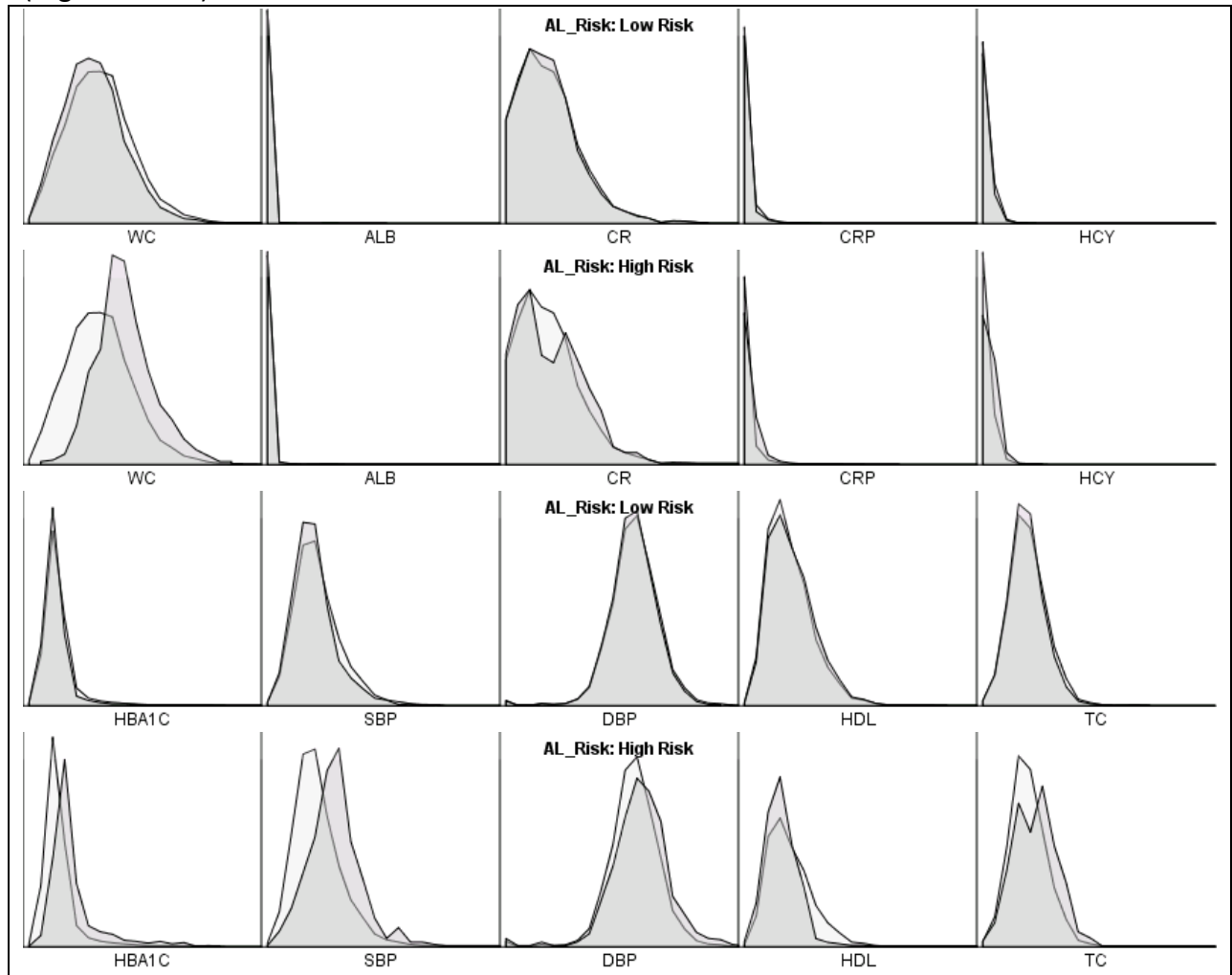


Figure 4. Scatterplot of Allostatic Load Score and BMI (Continuous)

