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The inflammatory consequences of stress and adiposity

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The Inflammatory Consequences of Stress and Adiposity

by

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ABSTRACT

The inflammatory process is important in protecting the body against the invasion of pathogens, but recent research has suggested that a long-term inflammatory response may lead to chronic diseases (e.g., Black, 2003; Wu, Dorn, Donahue, Sempos, & Trevisan, 2002). Two factors that have been implicated in the inflammatory and disease processes are stress and obesity (Black, 2003). While their individual lines of research continue to grow, few researchers have attempted to integrate these factors into one model to explain their effects on inflammation. This study aimed to replicate previous findings suggesting relationships between stress, obesity and inflammation and test an integrated model of stress and obesity by examining a possible interaction between the effects of stress and obesity on inflammation. Socioeconomic Status (SES) and depression were employed to examine the association between stress and the inflammatory marker, c-reactive protein (CRP). The study utilized the data resulting from the National Health and Nutrition Examination Survey (NHANES; National Center for Health Statistics, 2006). Included in the dataset are 4998 adults (2416 males and 2582 females) ranging in age from 18 years to over 85 years (M = 47.13, SD = 20.86). A subsample (N = 589) completed the Major Depression module of the Composite International Diagnostic Interview (CDCI). The results indicate that BMI, WC, income, education, and depression symptoms

significantly predict CRP. The data also suggest an interaction between the adiposity variables and the SES variables. This supports the hypothesis that the inflammatory effect of stress on an individual is moderated by adiposity.

The Inflammatory Consequences of Stress and Adiposity

The inflammatory process is important in protecting the body against the invasion of pathogens, but recent research has suggested that a long-term inflammatory response may lead to chronic diseases such as insulin resistance (Wu, Dorn, Donahue, Sempos, & Trevisan, 2002), atherosclerosis, type 2 diabetes, and metabolic syndrome (Black, 2003). The severity of these illnesses underscores the need to understand the mechanisms that lead to the prolonged inflammation with which they are associated. Two factors that have been implicated in the inflammatory and disease processes are stress and obesity (Black, 2003). Both factors have been associated with increased inflammatory markers (e.g. Brydon, Edwards, Mohamed-Ali, & Steptoe, 2004; Lemieux et al, 2001; McCarty, 1999; Owen, Poulton, Hay, Mohamed-Ali, & Steptoe, 2003) as well as increased risk for these inflammatory diseases (e.g. Burton, Foster, Hirsch & van Itallie, 1985; Wellen & Hotamisligil, 2005). While their individual lines of research continue to grow, few researchers have attempted to integrate stress and obesity into one model to explain their effects on inflammation. This paper will discuss the previous research in the distinct areas of stress and obesity and will then examine a model to explain possible interactions of the two factors.

The human body is equipped with a complex security system that is activated when faced with a threat due to injury or infection. Granulocytes are the major group of

cells that respond to most threats by migrating to the site of infection or injury, destroying the threat by secreting toxic chemicals, and then consuming the left-over particles and injured tissue. Some granulocytes also release cytokines which send out messages to the remainder of the body to prepare it for the impending attack (Segerstrom & Miller, 2004). The cytokines, particularly interluekin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α), initiate inflammation through the acute phase response (APR). The result is fever, a sickness response, and the production of acute phase proteins (APPs), such as c-reactive protein (CRP), which enable the body to defend itself against the threat (Black, 2003). The inflammatory response is intended to protect and heal the body. However, recent studies have begun to describe complications that can arise when this process occurs too frequently or persists for an extended period of time (Black, 2003; Wu et al., 2002). A better understanding of the factors that cause inflammation may lead to more effective remedies and prevention programs to decrease the incidence of inflammatory diseases.

Stress and the Inflammatory Response

The definition of stress is at the center of one of psychology's oldest debates. For many decades it has been unclear as to whether stress should be defined in terms of a stimulus or response. Hans Selye may be one of the most influential early stress researchers and his work, which focused on physiological reactions to a stimulus, shaped the field for many decades. He first used the term "stress" in 1946 to describe an outside influence that acts on an organism, a stimulus. He continued to use that definition until 1950, when he proposed that "stress" be defined in terms of an internal reaction to an outside influence, or "stressor" (Mason, 1975). Perhaps this surprising change in definitions by one of the great leaders in the field was the beginning of the confusion over

how to define stress. Today, researchers are forced to define stress for their own project, with some researchers studying the *stimulus*, some studying a *response*, and some studying an interaction of the two (Mason, 1975). Because of the vague nature of the term "stress" it can sometimes be unclear as to whether a particular outcome of stress is due to the stimulus or the response to the stimulus. For this reason, this paper examines both aspects of stress. The effects of stress will be measured in terms of the stimuli, or stressor, and in terms of the mental state that is the psychological reaction to a stressor or stressors.

From the early research of Selye and Cannon, scientists have acknowledged the physiological impact of stress (Mason, 1975). As researchers learn more about the biology of the human body and its responses to stress, it is becoming clearer that stressors and injury or infection result in the activation of the same pathways and the release of the same biochemicals. The body's response to stress is characterized by the release of corticosteroids and catecholamines, such as epinephrine and norepinephrine. These hormones, much like granulocytes, initiate the production of cytokines, commencing the APR. The connection between the two systems may be an evolutionary adaptation mechanism. When the body is faced with a threat the sympathetic nervous system is activated so that the person is ready to fight or flee the threat. In addition, the inflammatory system is activated so that the body is ready to battle any infection or injury that results from the fighting or fleeing (Black, 2002). This relationship between the two systems will be examined with a focus on the inflammatory results of stress (both as a stressor and a psychological reaction to a stressor).

Stress as a stressor. As previously mentioned, the first scientific definition of stress was that of a stimulus. This definition is still used in both science and everyday life. The field of physics refers to stress when referring to the force that is being placed on a material (Mason, 1975). In common language one talks about the stress of a deadline or the stress of school, with the focus on the stressor, not the reaction to the force or the deadline. Stress researchers employ this definition when they expose someone to "stress" by requiring them to give a speech, perform mental arithmetic, or to complete a difficult task, such as tracing a star in a mirror. Often it is understood that the force of the stimulus is the stress, and the focus is not on the individual's psychological reaction to the stress. It is assumed that a person has been exposed to stress when completing these tasks, although the individual is often not asked about his or her experience or reaction to the task. These studies benefit from the concrete definition of stress, it is much easier to measure how long a speech is than to have a person quantify his or her psychological reaction to a speech. Experimenters that employ the *stressor* definition of stress in laboratory experiments have more control over the stress than scientists that define stress in terms of an individual's reaction (Steptoe & Vogele, 1991).

Common laboratory stressors include mental arithmetic, giving a speech, and performing uncommon and difficult tasks (Steptoe & Vogele, 1991). Researchers have also studied common real-world stressors, such as caring for a chronically ill family member, death of a loved one and socioeconomic status (SES). It is important to point out that many researchers who study these concepts are looking for a specific reaction, such as increased heart rate or blood pressure. However, what they define as "stress" is the *stressor*. They may look for a reaction to stress but the reaction is not the stress. The

definition of stress that is being employed is based on a force outside the body. In order to distinguish between "stress" as a stimuli and "stress" as a reaction, the term "stressor" will be used to indicate a force outside the body, or a stimulus.

The study of inflammatory responses to stressors, in both animals and humans, has been growing exponentially in recent years. While the results are not always consistent (e.g., Goebel, Mills, Irwin, & Ziegler, 2000; Heinz et al., 2003; Lutgendorf, Logan, Costanzo, & Lubaroff, 2004; Owen & Steptoe, 2003), many experimenters have found a relationship between inflammatory markers, such as cytokines and APPs, and exposure to a stressor. Some of the first subjects to be studied were rats who demonstrated a relationship between IL-6 and stress. When rats were exposed to a physical stressor (e.g. electric foot-shock), a psychological stressor (e.g., a conditioned aversive stimulus) or a stressor that has both psychological and physical components (e.g., restraint), the rat's plasma level of IL-6 increased (Zhou, Kusnecov, Shurin, and DePaoli, 1993). This early animal research quickly led to the study of inflammation in response to stressors in humans. Increases in concentrations of the cytokines, such as IL-6 and TNF-α, have been observed following laboratory speech tasks (Ackerman, Martino, Heyman, Moyna, & Rabin, 1998), physical exercise (Goebel et al., 2000), color-word interference tasks, mirror tracing tasks (Owen and Steptoe, 2003) and academic examination (Maes et al., 1998).

In addition to an increase in IL-6 in response to an acute laboratory stressor, chronic naturalistic stressors also influence cytokine and APP production. One such stressor is socioeconomic status (SES), an indicator of social position. This construct describes types and amounts of resources to which a person has access, both tangible

(e.g. wealth) and intangible (e.g. knowledge and social support). The most common ways to measure SES is through highest level of education attained, amount of income, occupational status, or a combination of the three (Adler & Snibbe, 2003). Researchers have demonstrated that people of lower SES experience more life stressors, especially those stressors associated with a loss of income or ill health. In addition, those stressors have a greater impact on their emotional well-being, compared to individuals of higher SES (Kessler, 1979; McLeod & Kessler, 1990).

A substantial amount of research has demonstrated a strong negative relationship between SES and health, in prevalence of chronic diseases (including osteoarthritis, hypertension, cervical cancer and cardiovascular disease) as well as mortality rates (Adler et al., 1994). Lower SES has also been associated with higher levels of CRP. Owen et al. (2003) demonstrated an association between occupational status and CRP that was independent of age, sex, body mass, waist-to-hip ratio, smoking, alcohol use, and season of the year. A similar finding was recently reported when using education as a measure of SES (McDade, Hawkley, & Cacioppo, 2006). In addition, Brydon et al. (2004) found that individuals exposed to the chronic stressor of living at a low SES show greater increases in IL-6 production when they are exposed to a laboratory stressor, compared to those of a higher SES (Brydon et al., 2004).

The evidence that stress activates the inflammatory response is convincing when stress is defined as a stimulus. In this sense, when people are *exposed* to stress, their bodies respond by increasing chemicals such as cytokines and APPs, which are responsible for inflammation. However, as mentioned, defining stress as a stressor is

only one of the ways in which people have examined the construct. The psychological reaction or mental state that is the response to the stimulus must also be considered.

Stress as a psychological experience. The other definition of stress is that of the reaction to a stimulus. This implies that stress is an internal condition that may vary from person to person (Hobfoll, 1989). Again, the effects that this stress has on a person may be what are of interest in a particular study. However, this time it is the effect of the *mental state* that is the *result of the stimuli*. This form of stress is not as objective, making it more difficult to measure and understand. Researchers who study this form of stress focus on the psychological condition of a person during or after exposure to a stressor. In this sense stress is an *experience* that is due to a stimulus, or stressor. However, the stressor is not the stress, the experience is the stress. This type of stress is usually studied with the use of self-report questionnaires which question the participant about their state of mind and the psychological effects of a stimulus or stimuli. To make a clear distinction between this form of stress and *stressors*, stress that is the internal experience of a stimulus will be referred to as *psychological stress.*

Just as stressors have been associated with increases in the inflammatory response, studies examining psychological stress produce similar results. Research has shown that those who report severe psychological stress also have significantly higher levels of CRP (Hapuarachchi et al., 2003), TNF-α, and IL-6 (Maes et al., 1998) compared to those who report normal levels of psychological stress. Hapuarachchi, Chalmers, Winefiled, and Blake-Mortimer (2003) asked healthy volunteers to complete the General Health Questionnaire (GHQ) to indicate how much psychological stress they experienced over the previous two weeks. Within two days of the completion of the GHQ they

reported to the laboratory to allow for collection of a blood sample from which CRP concentrations were measured. Statistical analyses indicated that those who received GHQ scores of 0-1 (normal, little to no stress) had significantly lower CRP concentrations compared to those who received scores of 4 or greater (severely stressed). In a similar study, Maes et al. (1998) collected samples of blood and asked students to complete the Perceived Stress Scale (PSS) more than one month before and after an exam as well as one day before the exam. Their data indicate that when more psychological stress was perceived, higher concentrations of IL-6 and TNF-α were present (Maes et al., 1998). These results suggest a psychological component that is an important part of the inflammatory response.

Some researchers have explored specific conditions that result due to exposure to stressors. Burnout is a condition associated with emotional exhaustion, depersonalization and diminished personal accomplishment caused by long-term exposure to stress. This condition is associated with increased levels of TNF-α (Grossi, Perski, Evengard, Blomkvist, & Orth-Gomer, 2003) and CRP in women (Toker, Shirom, Shapira, Berliner, & Melamed, 2005). In addition, Tel Aviv women who report a state of fear induced by periodic terrorist attacks also show a positive relationship between the fear of terror (a type of psychological stress) and CRP level (Melamed, Shirom, Toker, Berliner, & Shapira, 2004). Also, individuals with post-traumatic stress disorder, a psychological state that is the result of a traumatic stressor, exhibit higher levels of IL-6 (Maes et al., 1999).

Depression can also be a mental state that results from exposure to a stressor, thus it can be considered a form of psychological stress. Depression is characterized by

episodes during which an individual experiences a depressed mood or loss of interest or pleasure in nearly all activities. Other depressive symptoms include a significant change in weight, sleep, psychomotor activity, or loss of energy, feelings of worthlessness, inability to concentrate, or recurrent thoughts of death. These symptoms often result in clinically significant distress or impairment in important areas of functioning (American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, IV – text revision, 2000).

Many studies have found that females who experience a stressful life event are more likely to have a depressive episode (Kendler, Karkowski, & Prescott, 1999). Kendler, Karkowski, & Prescott (1998) report that many stressful life events (11 of the 15 they studied) are associated with the onset of major depression (MD) in the month in which they occurred. This association indicates a link between the stimulus (stressor) and reaction to the stimulus (MD). They also found that the severity of the event was positively associated with onset of MD, indicating that the more stressful the person finds the event; the more likely they are to experience psychological stress.

A similar line of evidence suggests that a lack of resources creates stress in a person's life and also increases depressive symptoms. Hobfoll's (1989) Conservation of Resources model defines a resource as anything that is valued by an individual. A resource may be an object (e.g., car or house), condition (e.g., marriage or tenure), personal characteristic (e.g., self-esteem), or energy (e.g., time or knowledge). He goes on to explain stress as a reaction to the loss of resources, a threat to the loss of resources, or the inability to gain resources after they have been depleted. Researchers have studied this type of stress in relation to depressive symptoms. Resource loss has been associated

with an increase in depressive symptoms while resources gain has been associated with a decrease in depressive symptoms. It has also been observed that a change in resources mediates the relationship between negative life events and depressive symptoms (Holahan, Moos, Holahan, & Cronkite, 1999). Therefore, the lack of resources can be viewed as an experience of stress which is also manifested in depressive symptoms.

Depression has also been associated with increases in cytokines and APPs (e.g., Miller, Stetler, Carney, Freedland, & Banks, 2002; Owen & Steptoe, 2003; Suarez, Krishnan, & Lewis, 2003), although the results are not always consistent. One study did not find significantly higher CRP levels in depressed patients compared to non-depressed controls, although they did identify a difference in TNF-α levels (Tuglu, Kara, Caliyurt, Vardar, & Abay, 2003). Danner, Kasl, Abramson, and Vaccarino (2003) found that men with a history of a depressive episode were twice as likely to have high levels of CRP compared to men with no history of a depressive episode and that more recent episodes were associated with a greater likelihood of increased CRP levels. Interestingly this same relationship was not found in females, they hypothesize that this may be because of possible protective effects of estrogen or because CRP levels tend to be higher in even non-depressed women, making a difference difficult to observe.

Other studies have found that pharmacological treatment for depression resulted in significantly decreased inflammatory markers (Lanquillon, Krieg, Bening-Abu-Shach, & Vedder, 2000; Tuglu et al., 2003). Decreases in CRP levels after antidepressant treatment are consistently identified (Lanquillon et al., 2000; Tuglu et al., 2003). In addition, Tuglu et al. (2003) found decreases in TNF-α levels. However, Lanquillon et al. (2000) only found decreases in TNF-α levels in those patients who also exhibited less

depressive symptomatology. While IL-6 levels have not shown a significant post-treatment decrease, there is evidence that patients who will respond to treatment have significantly lower IL-6 levels pre-treatment compared to those who will not respond to treatment (Lanquillon et al., 2000). Perhaps this indicates that those who have more prolonged depression (or stress) show higher levels of this cytokine.

These data support the notion that the *psychological experience* of a stressor, manifested in conditions such as burnout and depression, is related to the inflammatory response. There is also evidence that when stress is defined in terms of the stressor, inflammatory cytokines and APPs are also increased. These inflammatory responses to stress may be the link between stress and diseases such as atherosclerosis, which is now thought to be an inflammatory disease (Heinz et al., 2003). Understanding the physiological repercussions of stress may allow for the prevention of such diseases.

Obesity and Inflammation

Another factor that influences the inflammatory system is adiposity, the accumulation of adipose, or fat, tissue. Obesity, an excess of adipose tissue, is associated with a number of diseases including hypertension, hypercholesterolemia, diabetes, coronary heart disease, and some types of cancer (Burton et al., 1985). Further, obesity is becoming an epidemic in the United States. Between the years 2001 and 2002, it was estimated that 65.7% of American adults were overweight or obese and that 30.6% were obese. In addition, overweight and obesity in children during that time period was estimated to be 31.5% (Hedley et al., 2004). The pervasiveness of obesity is dramatically increasing. Among American adults there has been a 50% increase in prevalence in each of the past two decades. A similar pattern is seen in the nation's children with the

prevalence of overweight tripling in just twenty years (Wyatt, Winters & Dubbert, 2006). Increased body fat has been associated with hyperinsulinemia, diabetes, increased lipid levels, hypertension, gallbladder disease, and some forms of cancer (Burton et al., 1985; Hartz, Rupley, & Rimm, 1984; Ohlson et al., 1985). The prevalence of obesity and its associated complications highlight the need for further research into the condition.

Historically, adipose tissue was considered to be only an energy store. In recent years, however, it is becoming apparent that adipose tissue is an active organ of the body (Kershaw & Flier, 2004). The endocrine properties of adipose tissue are becoming less ambiguous. Research indicates that it is capable of secreting many chemicals which have effects throughout the body, including proinflammatory cytokines and APPs (Calabro, Chang, Willerson, & Yeh, 2005; Lemieux et al., 2001; Mohamed-Ali et al., 1997; Mohamed-Ali, Pinkney, & Coppack, 1998; Owen & Steptoe, 2003; Visser, Bouter, McQuillan, Wener, & Harris, 1999; Yudkin, Stehouwer, Emeis, & Coppack, 1999). Understanding the actions of adipose tissue may provide insight into the connections between obesity and the diseases with which it is associated.

Numerous researchers have observed increased levels of cytokines and APPs with increased adiposity, measured by body mass index, waist-to-hip ratio, and similar procedures (Kern et al., 1995; Lemieux et al., 2001; Mohamed-Ali et al., 1997; Owen & Steptoe, 2003; Visser et al., 1999; Yudkin et al., 1999). One study found that obese women had significantly higher concentrations of IL-6 and TNF-α, compared to normal weight women. A weight-loss of at least 10% was also associated with a reduction in the cytokine levels (Ziccardi et al. 2002).

In addition to these correlational observations, in vivo and in vitro studies have been able to demonstrate the secretions of the tissue directly. For example, TNF-α production by adipose tissue and adipocytes has been demonstrated in vitro. Adipose tissue biopsies from the abdomens of 37 lean and obese premenopausal females and were tested for the presence of TNF-α mRNA and TNF-α protein. The results of this study, as well another that used a similar method, confirmed the presence of TNF-α mRNA in the adipose tissue of all volunteers (Hotamisligil, Arner, Caro, Atkinson, & Spiegleman, 1995; Kern et al., 1995). In addition, it was demonstrated that the adipose tissue of obese individuals expressed more than double the amount of TNF-α mRNA as lean controls. All tissue secreted the TNF-α protein and the tissue of obese individuals secreted more than that of lean individuals. Weight-loss resulted in a decrease of TNF-α (Hotamisligil et al., 1995) and TNF-α mRNA (Hotamisligil et al., 1995; Kern et al., 1995) in most of the obese individuals. This indication that adipose tissue of obese individuals produces excess TNF-α has increased our understanding of the role of obesity in health problems such as insulin resistance (Wellen & Hotamisligil, 2005).

Similar to the stress literature, studies of the production of cytokines by adipose tissue do not always result in consistent findings. One in vivo study measured the differences between artery and vein concentrations of IL-6 and TNF-α across subcutaneous adipose tissue. It was discovered that the concentration of IL-6 in venous samples, leaving the adipose tissue, were more than twice as high as the arterial samples, entering the adipose tissue. These results support the hypothesis that IL-6 is produced by adipose tissue. It was also estimated that approximately 30% of the IL-6 circulating in the body is secreted by adipose tissue. This same study found no arterio-venous

differences in TNF-α concentration (Mohamed-Ali et al., 1997). Although it is still believed that both IL-6 and TNF-α are produced by adipose tissue, these data indicate that they may be produced by different depots of adipose tissue at different locations in the body. IL-6 is produced by the abdominal subcutaneous fat depot that was examined in this particular experiment, however TNF-α may be produced by another depot (Mohamed-Ali et al., 1997).

The production of CRP by adipose tissue has also been demonstrated in vitro (Calabro et al., 2005; Ouchi et al., 2003). Human adipocytes incubated for 24 hours with IL-1-β and IL-6 produced about twice the amount of CRP as cells that were not stimulated. Cells incubated with adiponectin and leptin did not produce CRP. These data support the role of inflammatory cytokines in the initiation of production of CRP in human adipose tissue. Furthermore, treatment with anti-inflammatory drugs, such as aspirin, decreased the amount of CRP produced by the adipocytes, indicating a possible pharmacological modulator of CRP production (Calabro et al., 2005).

This evidence supports the concept that adipose tissue is not a passive energy storage center, but an active organ. Adipose tissue is responsible for the secretion of chemicals that influence the body's inflammatory process. There is substantial evidence that adipose tissue is a source of the proinflammatory cytokines, IL-6 and TNF-α, as well as the acute phase protein, CRP. However, studies have shown that not all fat depots secrete the same cytokines. The secretions of adipose tissue vary depending on the location of the tissue (Fried, Bunkin, & Greenburg, 1998; Mohamed-Ali et al., 1997). The differing secretions of the tissue help to explain why central adiposity has been shown to be a better predictor of cardiovascular disease, premature death, stroke, and

ovarian cancer than overall obesity (Bjorntorp, 1988). One study even suggested that visceral adipose tissue is detrimental to health whereas adipose tissue stored on the hips may be beneficial to health (Yusef et al., 2005). The strong associations between central adiposity and illness make it likely that more inflammatory markers are produced in central adipose tissue than in adiposity tissue located in other regions. Continuing to study the function of adiposity and its location with respect to inflammation is important in understanding the role of obesity in inflammatory disease.

An Integrated Model of Stress and Obesity's Effect on Inflammation

There is a significant amount of research to suggest that psychological stress contributes to the inflammatory process. The result of this relationship is the increased levels of cytokines and acute phase proteins during times of stress. This is evident in that IL-6, TNF-α, and CRP are all associated with both the acute phase response and reactions to stress. These chemicals serve to protect and heal the body when faced with an infection. However, in excess they result in chronic diseases such as type 2 diabetes (Pradhan, Manson, Rifai, Buring, & Ridker, 2001), metabolic syndrome X (Black, 2003), atherosclerosis (Libby, Ridker, & Maseri, 2002), and cardiovascular disease (Black & Garbutt, 2002).

Obesity is a growing epidemic in the United States and it is important to understand both the causes and effects of obesity (Wyatt et al., 2006). The implications of obesity are becoming greater as we learn more about the role of adipose tissue as an active endocrine organ, secreting chemicals that influence all parts of the body. There is sufficient evidence that adipose tissue is responsible for some of the body's production of

cytokines and acute phase proteins (e.g., Calabro et al., 2005; Mohamed-Ali et al., 1997; Ouchi et al., 2003).

The relationships between stress and cytokine/APP increases and adipose tissue and cytokine/APP production have led to the proposal of a new model. It is known that stress is associated with the release of cytokines and APPs and that adipose tissue is one source of these chemicals. The proposed model combines this information to suggest that stress acts at the level of the adipose tissue to increase the secretion of these chemicals. The new model suggests that stress promotes the release of inflammatory markers from adipose tissue. Stress may act on or interact with the adipose tissue to result in the release of more cytokines and APPs than are produced under normal circumstances.

The proposed model is based on the research indicating that adipose tissue produces cytokines and APPs. The body needs a certain level of these chemicals to protect itself from injury and infection, so the adipose tissue may be constantly secreting the inflammatory markers. However, if there is too much adipose tissue, there are more secretion sites, which lead to an abundance of the markers. Another line of research suggests that stress is associated with an increase in inflammatory markers. The proposed model suggests that this increase in inflammatory markers may be due to stress causing the adipose tissue to secrete more cytokines and APPs than it would under normal circumstances. Therefore, the new model posits that the relationship between stress and inflammation is moderated by adiposity. Stress increases the release of cytokines and APPs from adipose tissue, when there is a lot of adipose tissue there will be many secretion sites and more cytokines will be released. Thus, the effect that stress has on inflammation is dependent on the amount of adipose tissue that is present. This

interaction between stress and adipose tissue may help to explain their relationships to disease.

This model proposes a potential mechanism through which obesity and stress lead to diabetes, atherosclerosis, and other cardiovascular diseases. If the mechanism can be better understood, more treatment options may become available. Reducing the body's supply of cytokines and APPs is complicated because there is a level that is necessary to fight infection. Researchers have begun to focus on the possibility that drugs may be used to control levels of inflammatory cytokines. Studies indicate that non-steroidal anti-inflammatory drugs, such as ibuprofen, can prevent monocytes from producing inflammatory cytokines (Jiang, Ting, & Seed, 1998). However, it is possible that these drugs may decrease the cytokines to a dangerously low level which will inhibit the body's ability to fight infection (Yudkin, Kumari, Humphries, & Mohamed-Ali, 2000). The proposed model suggests that the body is at homeostasis when the correct amount of adipose tissue is present and there is no stress. Therefore, when inflammation is at a high level, decreasing the amount of adipose tissue or stress may enable an individual to achieve homeostasis safely.

Previous studies have focused on the differences between obese and non-obese participants or the impact of stress compared to lack of stress in participants. A study that combines these two areas of research will aid in the determination of the validity of this model. The model predicts that because lean people have less adipose tissue to secrete cytokines and APPs, they will not produce as many of these chemicals, even when faced with stress. Conversely, those that are obese have more adipose tissue to secrete the inflammatory cytokines and APPs. When obese people are faced with stress

they will show a more dramatic increase in cytokines and APPs due to their greater number of production sites (adipose cells). These explorations would help to determine the legitimacy of this model as well as further our understanding of the effects of stress and obesity on health.

While limited experimental information is available concerning the direct relationships between stress, adiposity and inflammation, there is some evidence of the interactions. For example, some researchers have found that measures of adiposity reduce or negate the association between stress (and depression) and cytokines and/or APPs. The indication that significant associations between stress and inflammation become insignificant after adjusting for adiposity may indicate that adiposity moderates the stress/inflammation relationship (Douglas, Taylor, & O'Malley, 2004; Miller et al., 2002). These data have led Miller and colleagues to demonstrate a mediator model in which depression promotes accumulation of adipose tissue and the adipose tissue causes inflammation directly by releasing cytokines as well as indirectly through the release of leptin which stimulates the production of cytokines (Miller, Freedland, Carney, Stetler, & Banks, 2003). This type of model does not account for the inflammatory effects of depression that are independent of adiposity. A moderator model may be able to better explain this relationship. It is also limited to the effects of depression and not stress in general.

A similar model was tested by Ladwig, Marten-Mittag, Lowel, Doring, and Koenig (2003) in a German, population-based sample of 3205 men ages 45-74. They found increased CRP concentrations in obese, compared to non-obese men. Also, CRP and BMI were significantly correlated. They also found that depressive mood was

associated with high CRP concentrations in obese, but not non-obese, participants. An ANOVA revealed significant main effects for BMI and a depressive mood as well as a depressed mood x BMI interaction. This study indicates the importance of examining the combined effects of adiposity and depression on inflammation. Interestingly, there have been very few studies to examine the interactions between stress and adiposity on inflammation, producing no strong conclusions (McDade et al., 2006).

Present Study

The goal of this study is to replicate previous findings of the relationships between stress, obesity and inflammation. In addition, this study will test the integrated model by examining a possible interaction between the effects of stress and obesity on inflammation. The APP, CRP will be used as a measure of inflammation. This protein has been identified as one of the most useful in predicting future cardiovascular disease (Albert, Ma, Rifai, Stampfer, & Ridker, 2002; Pearson et al., 2003; Ridker, Cushman, Stampfer, Tracy, & Hennekens, 1997; Ridker, Hennekens, Buring, & Rifai, 2000). High levels of CRP are associated with risk for coronary heart disease that is 1.7 times the risk for those with lower levels of CRP (Danesh, Collins, Appleby, & Peto, 1998). Therefore, it is important to gain better understanding of the factors that increase the levels of the APP. CRP has also been associated with both stress (e.g. Hapuarachchi et al., 2003; Melamed et al., 2004; Owen et al., 2003) and obesity (e.g. Lemieux et al., 2001; Visser et al., 1999; Yudkin et al., 1999).

To gain a comprehensive understanding of the effects of stress, measures of stressors and psychological stress will be examined. Socioeconomic Status (SES) will be used to examine the effect that this type of *stressor* has on the inflammatory marker,

CRP. In addition, depression will be employed to examine the role that *psychological reactions* to stressors have on CRP. This will add to the evidence that Ladwig et al. (2003) and Miller et al. (2003) presented with regard to only depression. A review of the literature has not resulted in a study that has examined the interactions of SES and adiposity on inflammation.

This study will also examine the association between adiposity and inflammation. A previous study on the interaction of obesity and depression focused only on BMI (Ladwig et al., 2003). However, recent literature has indicated that the location of adiposity may be more important than how much there is (Yusef et al., 2005). In addition, in Miller et al.'s (2002) study of depressed and non-depressed participants, they did not identify an association of waist-to-hip ratio and CRP but did find an association between BMI and CRP. More research is needed to provide a better understanding the effects of adiposity and distribution of adiposity. Therefore, in addition to looking at the relationship between BMI and inflammation, this study will also examine the effects of central adiposity, measured via waist circumference (WC), which will provide a more complete picture of the types of adiposity that are associated with the detrimental effects of stress and inflammation.

In addition, this study will include both men and women from a population-based sample in the United States. Ladwig et al.'s (2003) study of German men may not be generalizable to the entire US population. In addition, Danner et al. (2003) found that depression in men, but not women, was associated with increased levels of CRP. This indicates that the interactions of adiposity and stress may be different in men and women.

Both genders will be studied in order to develop a more complete understanding of this model.

Recent research has dramatically changed our understanding of the physiology of the body. We are now aware of the relationship between the stress response and the inflammatory process. It is becoming clear that stress causes an increase in the concentrations of cytokines and acute phase proteins associated with inflammation. We are also learning more about the endocrine properties of adipose tissue and there is evidence to support the production of cytokines and APPs by adipose tissue. The proposed model joins these two quickly progressing areas of research. It suggests that if stress causes the increase in certain biochemicals, and those biochemicals are produced by adipose tissue, stress may cause an increase in the adipose tissue's production of those chemicals. This model may provide a better understanding of how stress and obesity interact and cause serious, often deadly, diseases.

This study will test three main hypotheses in order to demonstrate the relationships between stress, adiposity, and inflammation. The first hypothesis is that stress will be positively related to inflammation. Stress will be defined as both a stressor (SES) and as psychological stress (depression). An increase in stress is expected to be associated with an increase in inflammatory markers (CRP). The second hypothesis is that adiposity will be positively related to inflammation. Total body mass (BMI) as well as central adiposity (WC) will be used to measure adiposity. An increase in adiposity is expected to be associated with an increase in inflammation (CRP concentration). The third hypothesis states that there will be an interaction between stress and adiposity. Adiposity is expected to moderate the association between stress and inflammation.

Method

This study utilized the data resulting from the National Health and Nutrition Examination Survey (NHANES). The survey was conducted by the National Center for Health Statistics division of the Centers for Disease Control (CDC) to obtain health, diet and nutrition information from a nationally representative sample. The current version of the NHANES survey began in 1999. The data were compiled and released in two-year increments; this study involved the analysis of the 2003-2004 data release. The data are available to the public and are accessed via the CDC's website (National Center for Health Statistics, 2006).

Participants

NHANES utilized a complex, stratified random sampling procedure to obtain a sample of participants that is representative of the civilian, non-institutionalized population of the United States. The sampling procedure first sampled counties (or groups of small counties) in the United States. Within the counties, segments (blocks or clusters of households) were sampled and from each segment, households were selected. One or more member of each household sampled was asked to participate in the study. Participants were compensated for their time and reimbursed for the cost of transportation and childcare (National Center for Health Statistics, 2006).

Included in the dataset were 4998 adults who participated in the household interview and medical examination. The sample was comprised of 48% (N = 2416)

males and 52% (N = 2582) females ranging in age from 18 years to over 85 years (*M* = 47.13, *SD* = 20.86). Mexican Americans, African Americans, low-income individuals, and the elderly were over-sampled. However, the CDC provided sampling weights which were used to correct for the over-sampling and ensure that the data can be generalized to the U.S. population (National Center for Health Statistics, 2006).

A subsample was chosen to participate in the Major Depression module of the Composite International Diagnostic Interview (CDCI)[1]. Participants eligible for this subsample were those who spoke English or Spanish and were between the ages of 20 and 39 (*M* = 28.97, *SD* = 5.74). The depression subsample consisted of 589 participants (294 male and 295 female). Analysis of the subsample utilized sampling weights to ensure that the subsample is also representative of the U.S. population (National Center for Health Statistics, 2006).

Materials

Stressor. The stressor that was measured was socioeconomic status (SES). As previously mentioned, this is an indicator of social position, which is often quantified through education, income, and occupation. Because occupational status is subjective and hard to quantify in the U.S., studies examining the relationship between SES and health often rely on measures of income and/or education to assess SES (Gallo &

[1] This small subsample allowed for the analysis of psychological stress, operationalized as depression. However, there was a concern that the restricted age range may limit the external validity of the study and may not allow for enough variability in CRP to demonstrate a clear relationship. Therefore, the larger sample was the primary sample used for the analyses not requiring the measurement of depression or depressive symptoms.

Matthews, 2003). Therefore, the effects of income and education on inflammation were each explored.

The income variable was based on the participant's annual household income. There were 13 categories from which the participants was asked to select which best describes his/her household income. The categories were divided into five $5,000 ranges between $0 and $24,999 and five $10,000 ranges between $25,000 and $74,999. They were also given the options of "$75,000 and over," "Over $20,000," and "Under $20,000" (National Center for Health Statistics, 2006). There is an inverse relationship between income level and the amount of stressors in a person's life (Kessler, 1979; McLeod & Kessler, 1990).

Participants were also asked to indicate the highest grade or level of school that they have completed or the highest degree that they have received. The answers were then coded as "Less than High School," "High School Diploma (including GED)," or "More than High School" (National Center for Health Statistics, 2006). There is an inverse relationship between the amount of education received and the amount of stressors a person experiences (Kessler, 1979; McLeod & Kessler, 1990).

Psychological stress. Depressive symptoms were measured to indicate the level of psychological stress. The Depression Module of an automated version of the Composite International Diagnostic Interview (CIDI) was used to assess depressive symptoms and to provide a diagnosis of Major Depressive Disorder (MDD). The CIDI was designed by the World Health Organization to diagnose mental illness according to the criteria of the 10th edition of the International Classification of Diseases (ICD-10) and the 4th edition of the Diagnostic and Statistics Manual of Mental Disorders (DSM-IV).

The CIDI is a structured interview designed to be used by lay people collecting data in epidemiological studies. The items assess the presence of each of the criteria for MDD over the past 12 months. The participant was asked if there was a period of two weeks or longer during which they felt "sad or depressed or empty" or during which they "lost interest in most things." The items also addressed symptoms of MDD, such as appetite change, insomnia/hypersomnia, reduced psychomotor activity, feelings of worthlessness, inability to concentrate, or recurrent thoughts of death. The interview resulted in a diagnosis as well as information to assess the severity of the disorder. The module was administered during a face-to-face interview at the Mobile Examination Center (MEC) during which the interviewer asked each question (in either Spanish or English) as it appeared on a computer screen and entered the answers into a personal computer. The scores were provided as a quantity of depressive symptoms (0-9) as well as a dichotomous variable indicating whether or not criteria for Major Depressive Disorder were met (National Center for Health Statistics, 2006).

Adiposity. Adiposity was measured using both body mass index (BMI) and waist circumference (WC). BMI is a measure of total body mass that is calculated by dividing the total body weight (in kilograms) by height (in meters) squared. These measurements were conducted by a health technician at the MEC. Weight was measured and recorded when the participant stepped onto a digital scale that was connected to the Integrated Survey Information System (ISIS system), which automatically stored the data. Participants were weighed wearing only underwear, a disposable paper gown, and foam slippers. Height was measured with an electronic stadiometer that was also connected to the ISIS system. The participant was instructed to stand straight against a vertical board,

with relaxed arms and shoulders, both feet together and toes pointed out at an angle of approximately 60°. The headboard was then lowered to the top of the participant's head and the height was sent to the ISIS (National Center for Health Statistics, 2006).

WC is a measure of central adiposity and was measured with a metal tape which is placed around the participant's torso at the level of the right ilium. This measurement was also conducted at the MEC by a trained health technician. All measurements were made to the nearest 0.1 cm (National Center for Health Statistics, 2006).

Inflammation. Blood CRP concentration was used to measure inflammation. Venipuncture was performed by a certified phlebotomist at the MEC. The phlebotomist collected 89 to 92 ml of blood from the participant's arm. The blood was processed, stored and shipped to the University of Washington to be processed using latex-enhanced nephelometry. A Behring Nephelometer was used to obtain the concentration of CRP in the sample of blood (National Center for Health Statistics, 2006).

Procedure

Households that were selected to participate in the study were sent a brochure describing the study's purpose and procedures. A trained interviewer then visited each household and conducted a screening interview to determine if any occupants of the household were eligible for the study. Once the eligible occupants were identified, they were asked to participate and provided informed consent. Each participant then completed the household interview to obtain demographic information, including information regarding SES. At the conclusion of the home interview the interviewer scheduled an appointment for the participant at the MEC (National Center for Health Statistics, 2006).

The MEC is comprised of four large trailers that were designed for the NHANES survey and are equipped to perform extensive medical testing. When the participant reported to the MEC, the measures of adiposity were performed and blood was drawn to determine CRP level. The subset of participants who were selected to undergo mental health testing also completed the CIDI during this visit to the MEC (National Center for Health Statistics, 2006).

The data were then compiled and posted on the CDC's website to be made available to the public (National Center for Health Statistics, 2006).

Data Analysis

The NHANES survey used a complex, stratified sampling procedure to produce a sample that is representative of the non-institutionalized civilian population of the United States. To achieve this representation, each participant's data was weighted. Analyses that incorporate these weights allow for an estimate of the data that would result if the entire non-institutionalized civilian population of the U.S. were sampled (National Center for Health Statistics, 2006). The data were analyzed with and without the sample weights and the results were similar. The unweighted analyses will be presented in the results section (see Appendix A for summaries of the weighted analyses).

The primary goal of the study was to test the proposed model which suggests that stress interacts with adipose tissue to increase the production of inflammatory cytokines and APPs. There were three primary hypotheses: (1) stress variables (income/education/depression diagnosis/depression symptoms) will be positively related to the inflammatory marker, CRP, (2) adiposity variables (BMI/WC) will be positively

related to CRP, and (3) there will be an interaction between stress variables and adiposity variables.

To test the hypotheses, eight (4 stress variables x 2 adiposity variables) hierarchical multiple regression analyses were conducted. Other factors which affect CRP levels, including gender, age, race, use of blood pressure medication, use of cholesterol medication, and smoking status, were statistically controlled to eliminate these constructs as possible confounding variables, increasing confidence in the conclusion that stress and adiposity are related to increased CRP levels[2].

The covariates were entered into the model in step one. To test Hypotheses 1 and 2, the stress variable (income or education or depression measure) and adiposity variable (WC or BMI) were entered at step two. Hypothesis 3 was tested at step three when the interaction between the adiposity and stress variable was added to the model. When a statistically significant interaction between a stress variable and an adiposity variable was detected, regression lines were plotted as described by Preacher (2003) to demonstrate the nature of the interaction.

Previous research has indicated that the relationship between depression and inflammation may differ by gender (Danner et al., 2003). Therefore, further analyses were conducted to test the moderating effect of gender on the relationships between stress and adiposity and inflammation. To explore this possibility, hierarchical regressions were conducted in which the covariates (age, race, use of blood pressure medication, use

[2] Because race and SES may be related, there was a concern that controlling for race would restrict the range of the SES variable. Therefore, the analyses were also conducted excluding race as a covariate. However, the exclusion of race variables produced a similar pattern of results. Race is included in all analyses reported.

of cholesterol medication, and smoking status) were entered in step one, the stress variable, adiposity variable, and gender were entered at step two, the two way interactions were added to the model in step three and in step four a three way interaction between gender, stress, and adiposity was entered.

To further examine the two-way interactions between gender and stress variables and gender and adiposity variables, specific analyses were conducted to examine the role of gender. To explore the moderating effect of gender on the relationship between the stress variables and CRP, a hierarchical regression was conducted in which all of the covariates mentioned above and the adiposity variables were entered into step one. In step two, gender and the stress variable were entered and in step three the interaction between gender and the stress variable was entered into the model. Similarly, to explore the moderating effect of gender on the relationship between adiposity and CRP, a hierarchical regression was conducted in which the covariates and stress variables were entered into step 1, the gender and adiposity variable was entered into step two and the gender x adiposity interaction was entered into step 3. When a statistically significant interaction was detected, regression lines were plotted as described by Preacher (2003).

A concentration of CRP that is greater than 1 mg/dL (i.e., 10 mg/L) is indicative of an inflammatory response to an infection (Pearson et al., 2003). Therefore, participants with a concentration of CRP that was greater than or equal to 1 mg/dL were excluded from the analysis (n = 538; 10.78%). In addition, the distribution of CRP concentrations in the sample was positively skewed, necessitating a logarithmic transformation of the data, which resulted in a normal distribution. Therefore, logCRP was used in all analyses.

The distribution of number of depressive symptoms was also positively skewed, with 87.44% of the sample reporting no depression symptoms. Logarithmic and square root transformations were unsuccessful at normalizing the data; therefore raw data were used in all analyses.

Due to the design of NHANES (see above), the sample of participants used for the "stressor" (education and income) analyses was not the same as the sample of participants used for the "psychological stress" (depression diagnosis and number of depression symptoms) analyses. The sample that was used in the stressor analyses is referred to as the *SES Sample* and the sample that was used in the psychological stress analyses is referred to as the *Depression Sample*.

Results

SES Variables and Adiposity Variables as Predictors of CRP

Descriptive statistics. Means and standard deviations of logCRP, BMI, and WC for the SES sample are presented in Table 1. The participants were distributed across the three levels of education: 1348 (30.26%) reported less than a high school education, 1141 (25.61%) reported having a high school education and 1966 (44.13%) reported having received more than a high school education. They were also distributed across the income brackets (see Table 2).

Table 1

Mean Values of Variables in the SES Analyses

Variable	*M*	*SD*
logCRP	-1.86	1.09
BMI	27.57	5.72
WC	95.86	14.80

Note. logCRP = logarithmic transformation of C-reactive protein (mg/dL), BMI = body mass index (kg/m^2), WC = waist circumference (cm)

Table 2

Distribution of Participants Across the Levels of Household Income

Income Bracket	Frequency	Percent
$0 to $4, 999	96	2.32
$5,000 to $9,999	240	5.81
$10,000 to $14,999	410	9.92
$15,000 to $19,999	354	8.57
$20,000 to $24,999	372	9.01
$25,000 to $34,999	580	10.94
$35,000 to $44,999	452	10.94
$45,000 to $54,999	364	8.81
$55,000 to $64,999	235	5.69
$65,000 to $74,999	203	4.91
$75, 000 and over	825	19.97

Note. 329 participants did not have data regarding household income

Correlations. Pearson correlation coefficients indicate significant positive relationships between logCRP and the adiposity variables and negative relationships between logCRP and the stress variables (i.e., higher CRP is associated with lower SES). In addition, the two adiposity variables and the two stress variables were significantly correlated. However, the stress and adiposity variables were not related to each other (See Table 3).

Table 3

Correlations Between Variables in the Socioeconomic Status Analyses

	Log CRP	BMI	WC	Education	Income
logCRP	1.00	0.420***	0.438***	-0.059***	-0.076***
BMI		1.00	0.879***	-0.027	-0.011
WC			1.00	-0.028	-0.020
Education				1.00	0.334***
Income					1.00

Note. logCRP = logarithmic transformation of C-reactive protein (mg/dL), BMI = body mass index (kg/m^2), WC = waist circumference (cm). ***$p < 0.001$

Hierarchical linear regression analyses. Hierarchical linear regressions were conducted to determine the ability of the stress variables (education and income) and the adiposity variables (BMI and WC) to predict logCRP. Tables 4 through 7 summarize the results of the four analyses that were conducted.

The models that included education and BMI, education and WC, income and BMI, and income and WC were all statistically significant predictors of logCRP (see Tables 4 through 7). All models supported the first and second hypotheses, indicating significant main effects for education, income, BMI, and WC. In addition, the analyses suggested an interaction between education and BMI, education and WC, and income and BMI. All models that included the main effects (i.e., step 2) accounted for a significant amount of variance. Adding significant interaction terms resulted in statistically significant increases in R^2, though the changes were small (see Tables 4 through 7).

Table 4

Summary of Hierarchical Regression Analysis for Education and BMI Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3681)	*p*
Step 2				0.137***	93.50	<0.001
Education	- 0.028	0.020	- 0.023			
BMI	0.069	0.003	0.381***			
Step 3				0.001*	85.52	<0.001
Education	- 0.225	0.092	- 0.183*			
BMI	0.054	0.008	0.296***			
Education x BMI	0.007	0.003	0.179*			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.066$, F (8,3683) = 32.25, $p < 0.001$ for Step 1; $R^2 = 0.203$ for Step 2; $R^2 = 0.204$ for Step 3.

*$p < .05$, ***$p < .001$

Table 5

Summary of Hierarchical Regression Analysis for Education and WC Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3621)	*p*
Step 2				0.161***	105.36	<0.001
Education	- 0.025	0.020	- 0.020			
WC	0.031	0.001	0.426***			
Step 3				0.001*	96.36	<0.001
Education	- 0.308	0.127	- 0.250*			
WC	0.024	0.003	0.337***			
Education x WC	0.003	0.001	0.243*			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = waist circumference (cm). $R^2 = 0.065$, F (8, 3623) = 31.38, $p < 0.001$ for Step 1; $R^2 = 0.225$ for Step 2; $R^2 = 0.227$ for Step 3. *$p < .05$, ***$p < .001$

Table 6

Summary of Hierarchical Regression Analysis for Income and BMI Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3434)	*p*
Step 2				0.136***	86.53	<0.001
Income	-0.021	0.006	-0.060***			
BMI	0.069	0.003	0.377***			
Step 3				0.002**	79.75	<0.001
Income	-0.102	0.027	-0.293***			
BMI	0.050	0.007	0.272***			
Income x BMI	0.003	0.001	0.256**			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.065$, $F(8, 3436) = 29.85$, $p < 0.001$ for Step 1; $R^2 = .201$ for Step 2; $R^2 = .204$ for Step 3.

**$p < .01$, ***$p < .001$

Table 7

Summary of Hierarchical Regression Analysis for Income and WC Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3378)	*p*
Step 2				0.158***	96.96	<0.001
Income	-0.018	0.006	-0.050**			
WC	0.031	0.002	0.421***			
Step 3				0.001	88.51	<0.001
Income	-0.083	0.037	-0.240*			
WC	0.026	0.003	0.357***			
Income x WC	0.001	0.000	0.199			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = waist circumference (cm). $R^2 = 0.065$, $F(8, 3380) = 29.18$, $p < 0.001$ for Step 1; $R^2 = 0.223$ for Step 2; $R^2 = 0.224$ for Step 3. *$p < .05$, ***$p < .001$

Regression lines were plotted to gain a better understanding of the nature of the interactions. Figures 1 and 2 demonstrate the effect of education and income on logCRP moderated by BMI. The regression lines illustrate the simple slopes and simple intercepts for normal (BMI = 21.70), overweight (BMI = 27.45), and obese (BMI = 35) individuals. The BMI chosen to represent each group is the median BMI value for each category. Figure 3 illustrates the effect of education on logCRP moderated by WC. The regression lines illustrate the simple slopes and simple intercepts for individuals with high (106.7 cm) and low (86.0 cm) WC. The values of WC chosen represent the 75^{th} and 25^{th} percentile of WC in the SES sample, respectively. They are also above/below the recommended maximum WC for males (101.6 cm) and females (88.9 cm).

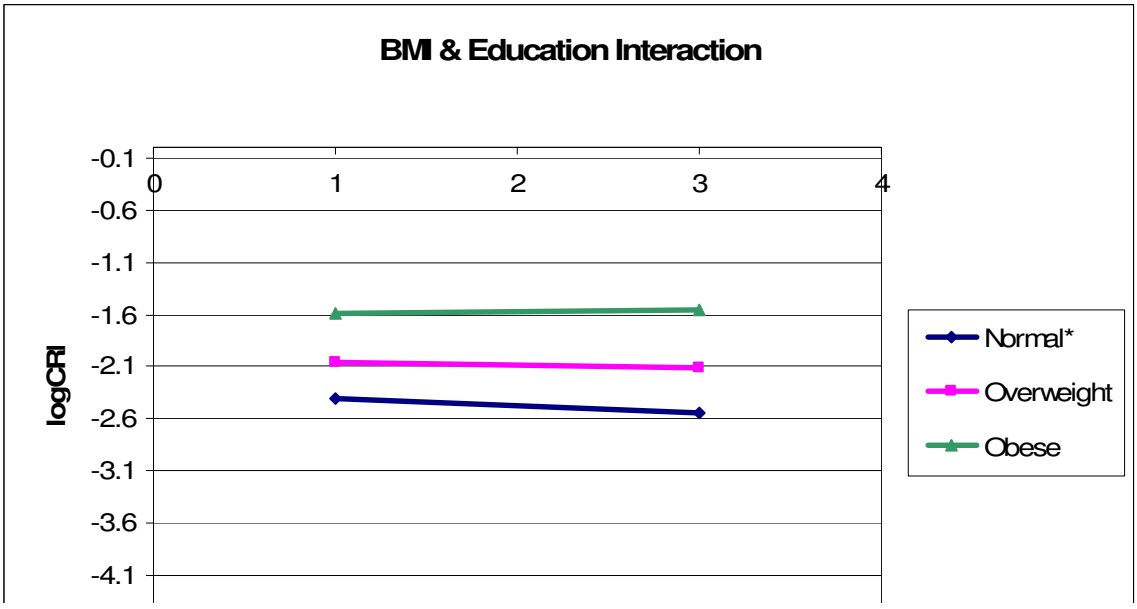

Figure 1. BMI moderates the effect of education on logCRP concentrations. Values for Education: 1 = less than high school; 2 = high school or GED; 3 = more than high school. Follow-up analyses indicated that the slope for the normal BMI group was significantly different from zero (B = -0.072, $t(3680)$ = -2.540, $p < 0.05$). However the slopes for the overweight and obese groups were not significantly different from zero (B = -0.032, $t(3680)$ = -1.586, $p > 0.05$; B = 0.021, $t(3680)$ = 0.704, $p > 0.05$, respectively).
*slope is significantly different than zero.

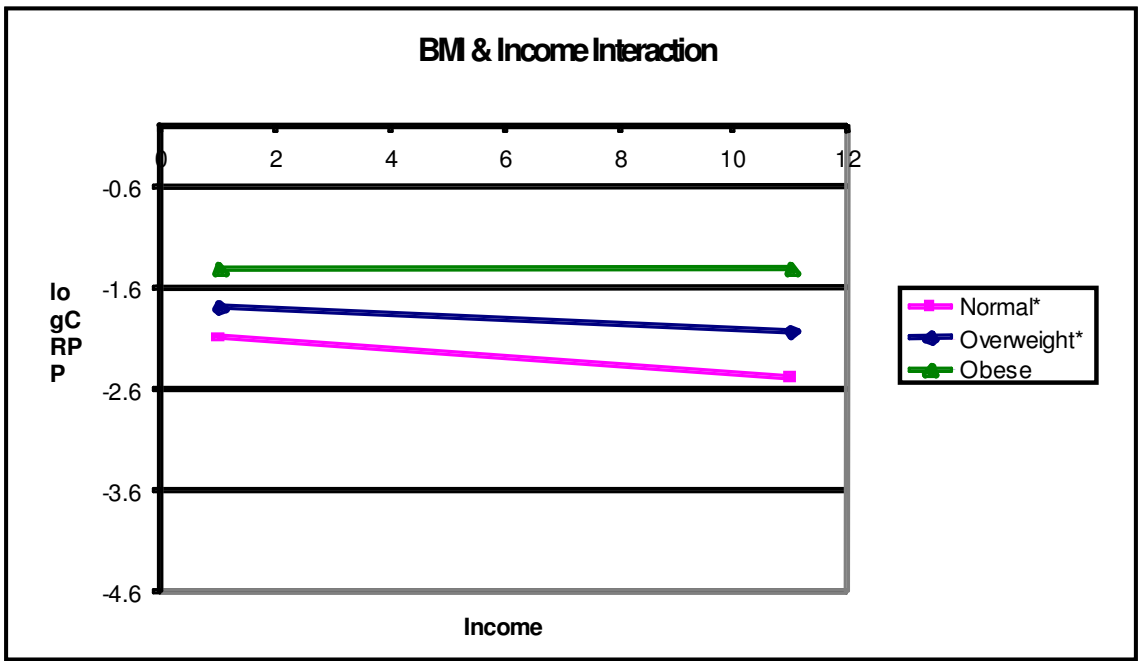

Figure 2. BMI moderates the effect of income and BMI on logCRP concentrations. Values for Income represent the income brackets described in the methods section: 1 = $0 to $4, 999; 2 = $5,000 to $9,999; 3 = $10,000 to $14,999; 4 = $15,000 to $19,999; 5 = $20,000 to $24,999; 6 = $25,000 to $34,999; 7 = $35,000 to $44,999; 8 = $45,000 to $54,999; 9 = $55,000 to $64,999; 10 = $65,000 to $74,999; 11 = $75, 000 and over. Follow-up analyses indicated that the slopes for the normal BMI and overweight groups were significantly different from zero (B = -0.039, $t(3433)$ = -4.857, $p < 0.01$; B = -0.023, $t(3433)$ = -4.047, $p < 0.01$, respectively). However the slope for the obese group was not significantly different from zero (B = -0.001, $t(3433)$ = -0.095, $p > 0.05$).
*slope is significantly different than zero.

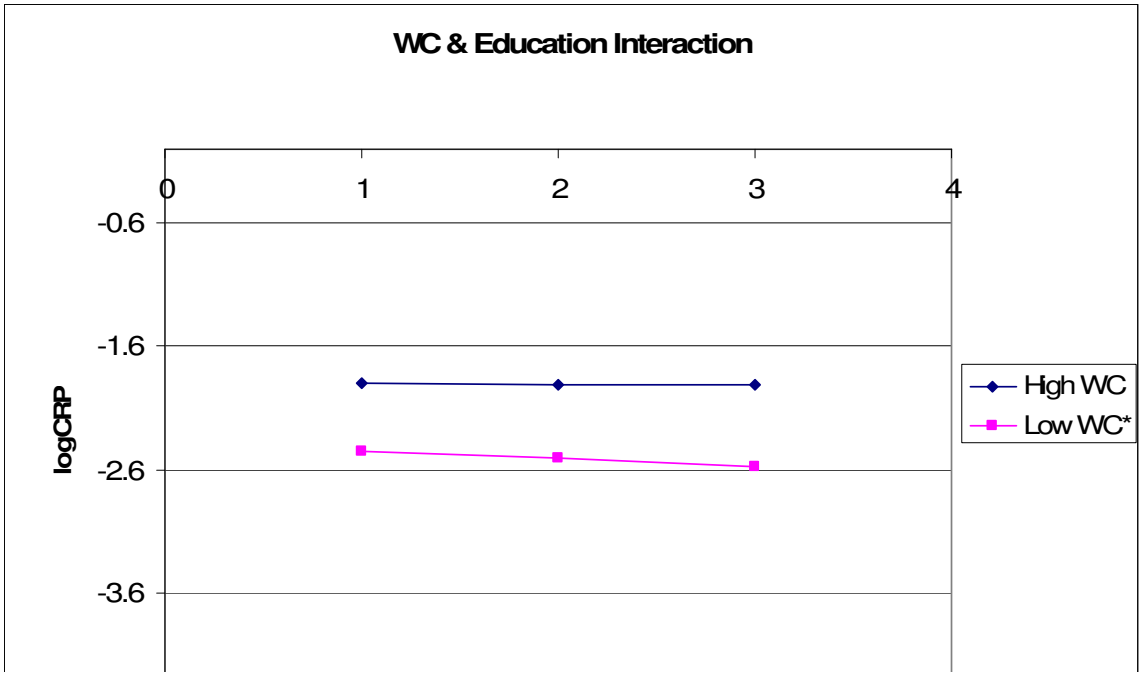

Figure 3. WC moderates the effect of education on logCRP concentrations. Education Values: 1 = less than high school; 2 = high school or GED; 3 = more than high school. Follow-up analyses indicated that the slope for the low WC group was significantly different from zero (B = -0.061, t(3620) = -2.386, $p < 0.05$). However, the slope for high WC group was not significantly different from zero (B = -0.002, t(3620) = -0.103, $p >$ 0.05).

*slope is significantly different than zero.

It was hypothesized that, when faced with more stress (i.e, lower SES), those with more adiposity would demonstrate a greater increase in concentrations of CRP than those with less adiposity. Interestingly, this is not the pattern present in the data (see Figures 1 – 3). Across all analyses of the SES sample, the simple slope of the regression line for those with the highest adiposity is not significantly different from zero, suggesting no effect of education or income on logCRP for this group. Conversely, those with lower adiposity demonstrate the expected negative relationship between education, income and logCRP. Thus, the inflammatory marker, CRP, in those with less adiposity appears to be more strongly related to the SES variables.

Depression Variables and Adiposity Variables as Predictors of CRP

Descriptive statistics. Means and standard deviations of logCRP, BMI, WC, and number of depression symptoms for the Depression sample are presented in Table 8. As previously mentioned, 87.44% of the participants in this sample reported no symptoms of depression. In addition, 550 (93.38%) of the participants did not meet criteria for major depressive disorder.

Table 8

Mean Values of Variables in the Depression Analyses

Variable	*M*	*SD*
logCRP	-2.00	1.18
BMI	27.25	6.04
WC	93.52	15.36
Depression Symptoms	0.78	2.15

Note. logCRP = logarithmic transformation of C-reactive protein, BMI = body mass index (kg/m^2), WC = waist circumference (cm)

Correlations. Pearson correlation coefficients indicate significant positive relationships between logCRP and the adiposity variables. Further, the two adiposity variables (BMI and WC) were related to each other as were the two psychological stress variables (depression diagnosis and number of depression symptoms). In addition, there was a small positive correlation between number of depression symptoms and BMI (See Table 9).

Table 9

Correlations between Variables in the Depression Analyses

	Log CRP	BMI	WC	Income	Education	Depression Diagnosis	Depression Symptoms
logCRP	1.00	0.438***	0.428***	-0.079	-0.031	0.061	0.080
BMI		1.00	0.909***	-0.120**	-0.113**	0.048	0.088*
WC			1.00	-0.064	-0.073	0.024	0.063
Income				1.00	0.338***	-0.077	-0.079
Education					1.00	-0.022	-0.003
Depression Diagnosis						1.00	0.767***
Depression Symptoms							1.00

Note. CRP = logarithmic transformation of C-reactive protein, BMI = body mass index (kg/m^2), WC = waist circumference (cm). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Hierarchical linear regression analyses. Hierarchical linear regressions were conducted to determine the ability of the depression indices (depression diagnosis and depression symptoms) and the adiposity variables (BMI and WC) to predict logCRP. Tables 10 through 13 summarize the results of the four analyses that were conducted (depression diagnosis and BMI, depression diagnosis and WC, depression symptoms and BMI, and depression symptoms and WC). These analyses indicate that both BMI and WC are significantly related to logCRP. However, neither depression symptoms nor depression diagnosis not significantly predicted logCRP in any analysis. There were also no significant interactions between the depression and adiposity variables.

Table 10

Summary of Hierarchical Regression Analysis for Depression Diagnosis and BMI Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 572)	*p*
Step 2				0.189***	21.79	<0.001
Depression Diagnosis	0.175	0.171	0.037			
BMI	0.087	0.007	0.444***			
Step 3				0.000	19.80	<0.001
Depression Diagnosis	0.443	0.626	0.094			
BMI	0.088	0.008	0.450***			
Depression Diagnosis x BMI	-0.010	0.021	-0.060			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.087$, F (8, 574) = 6.80, $p < 0.001$ for Step 1; $R^2 = 0.276$ for Step 2; $R^2 = 0.276$ for Step 3. ***$p < .001$

Table 11

Summary of Hierarchical Regression Analysis for Depression Diagnosis and WC Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 568)	*p*
Step 2				0.201***	22.72	<0.001
Depression Diagnosis	0.206	0.172	0.043			
WC	0.036	0.003	0.463***			
Step 3				0.000	20.64	<0.001
Depression Diagnosis	0.569	0.966	0.119			
WC	0.036	0.003	0.467***			
Depression Diagnosis x WC	-0.004	0.010	-0.077			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC=Waist Circumference (cm). $R^2 = 0.085$, F (8, 570) = 6.65, $p < 0.001$ for Step 1; $R^2 = 0.286$ for Step 2; $R^2 = 0.286$ for Step 3. ***$p < .001$

Table 12

Summary of Hierarchical Regression Analysis for Depression Symptoms and BMI Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 572)	*p*
Step 2				0.189***	21.79	<0.001
Depression Symptoms	0.020	0.020	0.037			
BMI	0.087	0.007	0.443***			
Step 3				0.000	19.78	<0.001
Depression Symptoms	0.010	0.079	0.019			
BMI	0.086	0.008	0.441***			
Depression Symptoms x BMI	0.0003	0.003	0.019			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.087$, F (8, 574) = 6.80, $p < 0.001$ for Step 1; $R^2 = 0.276$ for Step 2; $R^2 = 0.276$ for Step 3. ***$p < .001$

Table 13

Summary of Hierarchical Regression Analysis for Depression Symptoms and WC Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 548)	*p*
Step 2				0.207***	22.04	<0.001
Depression Symptoms	0.022	0.020	0.041			
WC	0.036	0.003	0.466***			
Step 3				0.000	20.00	<0.001
Depression Symptoms	0.001	0.118	0.002			
WC	0.035	0.003	0.463***			
Depression Symptoms x WC	0.0002	0.001	0.039			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = Waist Circumference (cm). $R^2 = 0.080$, $F(7, 551) = 6.84$, $p < .0001$ for Step 1; $R^2 = .287$ for Step 2; $R^2 = .287$ for Step 3. ***$p < .001$.

Gender as a Moderator of the relationship between Stress Variables and CRP

Analyses were conducted to test the moderating effect of gender on the relationships between stress and adiposity and inflammation. Hierarchical regressions were conducted to determine whether there were interactions between the stress variables, adiposity variables, and CRP. The results did not suggest a three-way interaction between gender, stress, and adiposity. However, they did indicate that gender moderates the effects of the stress variables on levels of CRP and adiposity on levels of CRP (see Appendix B).

Hierarchical linear regressions were conducted to further examine the moderating effect of gender on the relationship between the stress variables and CRP, controlling for adiposity. Tables 14 through 17 summarize the four analyses (gender and education, gender and income, gender and depression diagnosis, and gender and depression symptoms). All analyses indicate significant main effects for gender, with females having higher logCRP values than males. In addition, there was a significant main effect for income ($t(1) = -3.37$, $p < 0.01$) in the hypothesized directions. There was also a significant interaction between gender and income ($t(1) = 2.42$, $p < 0.05$). The addition of this interaction resulted in a small, yet statistically significant, increase in variance accounted for ($\Delta R^2 = 0.001$; $t(3380) = 6.087$, $p < 0.05$).

Table 14

Summary of Hierarchical Regression Analysis for Gender and Education Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,3611)	*p*
Step 2				0.037***	96.31	<0.001
Gender	0.448	0.034	0.215***			
Education	-0.027	0.020	-0.022			
Step 3				0.000	41.73	<0.001
Gender	0.351	0.086	0.169***			
Education	-0.092	0.057	-0.075			
Education x Gender	0.044	0.036	0.074			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.190$ for Step 1, $F(9,3613) = 93.94$, $p < .0001$; $R^2 = .227$ for Step 2; $R^2 = .227$ for Step 3. ***$p < .001$.

Table 15

Summary of Hierarchical Regression Analysis for Gender and Income Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,3368)	*p*
Step 2				0.038***	88.51	<0.001
Gender	0.429	0.036	0.206***			
Income	-0.018	0.006	- 0.053***			
Step 3				0.002*	81.74	<0.001
Gender	0.252	0.081	0.121**			
Income	-0.057	0.017	- 0.164***			
Gender x Income	0.026	0.011	0.141*			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.186$ for Step 1, $F(9,3370) = 85.56$, $p < .0001$; $R^2 = .224$ for Step 2; $R^2 = .226$ for Step 3. *$p < .05$, **$p < .01$, ***$p < .001$.

Table 16

Summary of Hierarchical Regression Analysis for Gender and Depression Diagnosis Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,567)	*p*
Step 2				0.069***	21.01	<0.001
Gender	0.647	0.089	0.273***			
Depression Diagnosis	0.193	0.172	0.040			
Step 3				0.001	19.35	<0.001
Gender	0.670	0.092	0.282***			
Depression Diagnosis	0.757	0.568	0.158			
Gender x Depression Diagnosis	-0.360	0.345	-0.125			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.221$, $F(9, 569) = 17.93$, $p < .001$ for Step 1; $R^2 = 0.290$ for Step 2; $R^2 = 0.291$ for Step 3. ***$p < .001$.

Table 17

Summary of Hierarchical Regression Analysis for Gender and Depression Symptoms Predicting LogCRP

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,567)	*p*
Step 2				0.068***	20.97	<0.001
Gender	0.645	0.089	0.272***			
Depression Symptoms	0.019	0.020	0.035			
Step 3				0.002	19.33	<0.001
Gender	0.678	0.094	0.286***			
Depression Symptoms	0.090	0.067	0.163			
Gender x Depression Symptoms	-0.045	0.040	-0.135			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.221$, $F(9, 569) = 17.93$, $p < .001$ for Step 1; $R^2 = 0.289$ for Step 2; $R^2 = 0.291$ for Step 3. ***$p < .001$.

Regression lines were plotted to gain a better understanding of the nature of the interaction between gender and income (see Figure 4). The slope of the regression line for females did not significantly differ from zero (B = -0.006; $t(3367)$ = -0.722, $p > 0.05$), suggesting no effect of income on logCRP for this group. Conversely, males demonstrate the expected positive relationship between income and logCRP (B = -0.031, $t(3367)$ = -4.067, $p < 0.01$).

Figure 4. Gender moderates the relationship between income and concentration of logCRP. Values for Income represent the income brackets described in the methods section: 1 = $0 to $4, 999; 2 = $5,000 to $9,999; 3 = $10,000 to $14,999; 4 = $15,000 to $19,999; 5 = $20,000 to $24,999; 6 = $25,000 to $34,999; 7 = $35,000 to $44,999; 8 = $45,000 to $54,999; 9 = $55,000 to $64,999; 10 = $65,000 to $74,999; 11 = $75, 000 and over.

*slope is significantly different than zero.

Gender as a Moderator of the Relationship between Adiposity and CRP

Hierarchical linear regressions were conducted to determine whether gender moderates the relationship between adiposity and CRP, controlling for stress variables (i.e., education, income, depression diagnosis, and depression symptoms). Analyses in both the SES and depression samples indicate significant main effects for gender and BMI in step 2. However, the interaction term is not significant when entered into the model in step 3 (see Appendix C, Tables C1 and C2). The analyses that examine the interaction between gender and WC also show significant main effects of gender and WC in step 2. In addition, the results indicate a significant, but small, interaction between gender and WC ($t(1) = 1.98$, $p < 0.05$) in the depression sample and an effect that approached significance ($t(1) = 1.91$, $p = 0.056$) in the SES sample. However, the addition of the gender by WC interaction does not significantly increase the R^2 in any model (see Appendix C, Tables C3 and C4).

The Relationship of BMI versus WC to CRP

It has been suggested that BMI and WC may have different effects on health and inflammation (Bjorntorp, 1988). Therefore, the effects of BMI and WC on CRP were compared. In the SES sample, the correlation between WC and logCRP was slightly higher than the correlation between BMI and logCRP (see Table 3). However, in the Depression sample the correlation between BMI and logCRP was slightly higher than between WC and logCRP (see Table 9). In both cases the differences are very small. To further explore this question, regression analyses were conducted. The analyses controlled for all other variables in step one. In step two BMI or WC was added to the model and in step three the other adiposity measure was included (i.e., WC or BMI). In

the SES sample, each measure of adiposity accounted for significantly more variance when entered in to the equation. The addition of WC to a model including BMI resulted in $\Delta R^2 = 0.0194$ ($F(1,3611) = 90.30$, $p < 0.01$). The addition of BMI to a model containing WC resulted in $\Delta R^2 = 0.0012$ ($F(1,3611) = 5.59$, $p = 0.018$). In the Depression sample the addition of WC resulted in a significantly higher amount of variance accounted for ($\Delta R^2 = 0.017$; $F(1,527) = 13.01$, $p < 0.01$) but the addition of BMI did not ($\Delta R^2 = 0.003$; $F(1,527) = 1.96$, $p = 0.163$). This suggests that WC, a measure of central adiposity as opposed to overall adiposity, may have a slightly stronger relationship with CRP.

Discussion

Stress and Inflammation

The first goal of the study was to determine the relationship between stress and inflammation. Low SES has been identified as a chronic stressor (e.g., Kessler, 1979; Turner, Wheaton, & Lloyd, 1995) and has been associated with increased rates of morbidity and mortality (Adler et al., 1994). Two major components of SES, educational attainment and income level, were examined as proxies for stress in this study. Results indicated that those with lower SES had higher concentrations of CRP. These findings are consistent with previous studies that found higher levels of CRP in individuals in lower social classes compared to their more affluent counterparts (e.g., McDade et al., 2006; Owen et al., 2003; Panagiotakos et al., 2004).

Stress has also been conceptualized as a psychological reaction to a stressor (Mason, 1975). Further, depressive symptoms and major depressive disorder have been associated with the occurrence of stressors (Holahan et al., 1999; Kendler et al., 1998; Kendler et al., 1999). Thus, these constructs were employed to gain a better understanding of the inflammatory responses to such psychological responses. These analyses did not suggest a relationship between depression and CRP; this is contrary to previous research that has identified relationships between these variables (e.g., Danner et al., 2004; Miller et al., 2002, Owen & Steptoe, 2003; Suarez, et al., 2003).

There are multiple explanations for the difference in findings between previous studies and the current one. For example, in a sample of well-functioning elderly

individuals (70 – 79 years of age, *M* = 73.6 years, *SD* = 2.8), Penninx et al. (2003) found a significant difference in CRP, IL-6, and TNF-α between those who scored above the clinical cut-off (i.e., 16) on the Center for Epidemiological Studies Depression (CES-D) scale and those with scores below the cut-off. Similarly, Vetta et al. (2001) found differences in a number of biological markers, including TNF-α and CRP concentrations, in depressed compared to control participants in a sample of individuals ranging in age from 65 to 94 years (*M* = 80.1, *SD* = 12.4). Conversely, the depression sample in the current study consisted of those 20 to 39 years of age, with a mean age of 28.97 years (*SD* = 5.74). Age is positively associated with inflammation (Suarez, 2004), therefore the disparity in ages between the samples may account for the difference in findings. These data, along with the findings of the present study, suggest that the relationship between CRP and depression may only be present in the elderly.

The lack of a relationship between the measures of depression and CRP may also be due to the measure of depression that was employed in this study. The CIDI asked participants about their depressive episodes over the previous year. The data did not indicate how recently the depressive episode occurred, therefore it is possible that participants were recalling depressive episodes that they experienced months before and had since recovered. Danner et al. (2003) reported that participants who experienced a depressive episode more than six months before measurement of CRP exhibited levels that are similar to those who have never had a depressive episode. Thus, it is possible that the participants in this study had previously experienced a depressive episode accompanied by increased levels of CRP, which returned to normal following recovery from the episode.

Although this study did not find a relationship between CRP and depression, one cannot rule out the possibility that inflammation is related to depression. The inflammatory response is very complex and involves many cytokines, proteins, and catecholamines. Therefore, the lack of a relationship between depression and CRP in this sample may not be generalizable to the entire inflammatory process. That is, inflammation may still be increased in those with depression, through mechanisms other than CRP. In fact, other studies that have examined multiple biomarkers have failed to find a relationship between depression and CRP, though they have found relationships with other inflammatory markers (Joyce et al., 1992; Tuglu et al., 2003).

Adiposity and Inflammation

A second goal of this study was to explore the relationship between adiposity and inflammation. Previous studies have suggested that adipose tissue is involved in secretion of inflammatory markers such as IL-6, TNF-α, and CRP (Calabro et al., 2005; Lemieux et al., 2001; Mohamed-Ali et al., 1997; Mohamed-Ali et al., 1998; Owen & Steptoe, 2003; Visser et al., 1999; Yudkin et al., 1999). Therefore it was expected that those with more adipose tissue would have higher levels of such inflammatory markers. Indeed, across all analyses there were significant associations between measures of adiposity (both BMI and WC) and CRP concentration, which is consistent with the findings of other researchers (e.g., Owen & Steptoe, 2003; Kern et al., 1995; Lemieux et al., 2001; McDade et al., 2006; Mohamed-Ali et al., 1997; Visser et al., 1999; Yudkin et al., 1999).

Further, it has been suggested that central adiposity is a better predictor of obesity-related diseases than overall adiposity (Bjorntorp, 1988). Likewise, some

researchers have found that WC is better at predicting CRP than BMI and total body fat percentage (McDade et al., 2006). However, others have found a relationship between CRP and BMI, but not waist-to-hip ratio, particularly in samples of depressed participants (Miller et al., 2002). While the data from the current study suggest that WC may be a slightly better predictor of CRP, the differences were very small. Thus, they did not provide convincing evidence that WC is more influential than BMI. Both measures were related to inflammation and appear to be useful predictors of the inflammatory response.

Interactions between the Stress and Adiposity Variables

The third goal of this study was to investigate the proposed model, which integrates the effects of stress and the effects of obesity on the inflammatory system. Given that adipose tissue secretes pro-inflammatory cytokines and CRP and that stress is related to increases in inflammation, it was hypothesized that adiposity would moderate the effect of stress on inflammation. The proposed model suggested that individuals with more adiposity would be more affected by stress, demonstrating greater changes in levels of CRP under stress than those with less adiposity.

Analysis of the data revealed interactions between the SES variables and adiposity but no interactions between the depression variables and adiposity. Interestingly, the nature of the interactions differed from the expected pattern (see Figures 1 – 3). The plots of the regression lines indicated that adiposity was positively related to higher CRP. However, while CRP was not related to income or education levels among those with higher levels of adiposity, individuals with lower levels of adiposity demonstrated the expected relationship. That is, they had lower levels of inflammation than those with more adiposity and their level of CRP was positively

related to the amount of stress they were experiencing, as measured by two indices of SES, income and education.

These findings may suggest that under less stress (i.e., higher SES), inflammation in those with more adiposity remains at levels that are similar to those observed in high stress situations. This is consistent with research that shows that having too much adiposity is detrimental to health. That is, even in non-stressful situations, those with high levels of adiposity exhibit levels of inflammation that are similar to those seen in people living in stressful conditions. This explanation lends credence to theories that suggest that physiological factors may be more important than psychosocial factors in determining health. Accordingly, if a person has an abundance of adipose tissue, stress may not dramatically impact the level of inflammation. In terms of the proposed model it may suggest that adipose tissue is constantly secreting inflammatory markers to the point where a ceiling is reached, preventing stress from further influencing the levels of these markers. This interpretation highlights the importance of successful weight management before stress management can be productive at reducing inflammation because a high level of adiposity may overshadow any effect of stress management on inflammation. However, having low levels of adiposity is not enough to ensure healthy levels of CRP. Those with less adiposity are affected by chronic stress, making stress management more important once weight is at healthy levels.

An alternative explanation emphasizes the psychological factors that are associated with obesity. Some have suggested that the state of being obese is itself a stressor. In a national sample of adults, Carr and Friedman (2005) found that compared to participants who were in the normal weight range, very obese subjects (BMI $\geq$ 35)

reported less self-acceptance, more discrimination, and poorer overall health. The obese and very obese participants were 40 to 50% more likely to report experiences of major discrimination than normal weight participants. It is possible that the stress of being obese may be more detrimental than the stress of living at low SES. It may be that the level of inflammation is higher across all obese participants regardless of their SES because they are all faced with equal stressors that because of their weight. The stress of living at low SES may not add a significant amount of stress on top of being obese. This interpretation also suggests the utility of weight management as a way to manage stress, improve psychological well-being and lower levels of inflammation.

Unfortunately the validity of this explanation is not clear. In this sample there were no significant correlations between the measures of adiposity and depression diagnosis and there was only a small correlation between depression symptoms and BMI. Thus, those with more adiposity did not appear to be more depressed. Further, there were no correlations between the SES variables and the adiposity variables. The lack of relationships between the adiposity and stress variables suggests that those with more adiposity may not be experiencing more stress. Future research would benefit from measuring and controlling for these types of stress and stigmatization to determine the pure effect of SES.

Gender

A secondary goal of this study was to examine the relationship of gender to inflammation. The only previous study that examined the interaction between obesity and depression on inflammation studied only men (Ladwig et al., 2003). Therefore, it was not clear that the results could be generalized to women. In addition, other studies

have suggested that depression is related to increased levels of CRP in men but not women (Danner et al., 2003; Ford & Erlinger, 2004; Liukkonen et al., 2006). However, others have not found gender differences in the effect of SES on CRP (Owen et al., 2003).

Given the conflicting data regarding the effects of gender and stress on CRP, analyses were conducted to determine the role of gender in these data. All analyses that included gender demonstrate a main effect of gender, indicating that females have higher levels of CRP than males, which is consistent with previous research (McDade, 2006). There were no significant gender x stress x adiposity interactions, suggesting that the relationships between stress and adiposity do not differ across genders.

However, there was a small but significant two-way interaction between gender and income, indicating that the relationship between income and CRP is negative for males, but not females. This is contrary to the findings of Owen et al. (2003) but consistent with previously reported data on the effect of depression on CRP concentrations (Danner et al., 2003; Ford & Erlinger, 2004; Liukkonen et al., 2006). Interestingly, the interactions between depression variables and gender were not significant. This analysis suggests that CRP levels in males and females may be differentially affected by stress, underscoring the need to examine inflammatory responses in males and females separately rather than simply controlling for gender. It also suggests that care should be taken when generalizing results, as the relationships seen in males may not be present in females.

Strengths of the Study

This study had several important strengths. The size of the sample indicates a high degree of external validity. The analyses were conducted using a large, nationally-representative sample, making the results generalizable to the population of the United States. The analyses that are discussed are those that did not utilize the sampling weights. However, the results were similar when the sample weights were used, demonstrating the generalizability of the data even without the use of the weights. The size of the sample also allows for adequate representation of minorities and individuals at all levels of SES.

Another strength of this study is that it included measures of two types of stress: SES (including education and income) and depression (including symptoms and diagnosis). The ability to look at multiple stressors and psychological factors allowed for more specific knowledge of how stress affects CRP levels and interacts with adiposity. In addition, the variables were treated as continuous. Researchers often split SES variables into high and low groups, losing important information about the gradation of the effect. By using continuous variables in the current analysis, it was possible to determine the effects of stress and adiposity on CRP at all values of the variables.

These analyses also statistically controlled for factors that are known to be associated with CRP, SES, and adiposity. By controlling for race, smoking, age, gender and use of medications, the effects of stress and adiposity on CRP independent of these confounds could be identified. In addition, those who had levels of CRP that are indicative of active infections were eliminated from the analyses. This ensured that the

effects that were seen in these data are common in normal conditions and are not accounted for by another infection or acute inflammatory reaction.

Limitations of the Study

Unfortunately, there were also a number of limitations to this study. Due to the correlational nature of this study, one cannot rule out the presence of an unknown third variable influencing the stress or adiposity variables and CRP. These variables, and CRP in particular, are known to be affected by many factors. While this study statistically controlled for the effects of race, age, gender (where appropriate), use of blood pressure and cholesterol medication, and smoking there are other factors that may have influenced the relationship between CRP, adiposity and stress. For example, other researchers have controlled for alcohol intake, history of coronary heart disease, cancer, psychological illnesses, endocrinological illnesses, use of other anti-inflammatory drugs, and season (e.g., Owen et al., 2003). While, the elimination of individuals with high concentrations of CRP (>1 mg/dL) should have reduced the effects that other illnesses had on the data, we did not have access to information on these factors, so their influence could not be directly controlled.

The nature of the study also introduced some limitations to the analyses. This study was conducted on data obtained from a national epidemiological study. The primary goal of the larger study was to gain a better understanding of Americans' health and nutritional status and there were no direct measures of stress available in the dataset. Therefore, two proxies for stress were used (SES and depression). It is possible that a direct measure of stress would have provided different information than those measures that were available. Regardless, this study provided valuable insight into the effects of

SES and depression on CRP levels. Both of these factors have been associated with increased risk for cardiovascular disease (eg., Adler & Snibbe, 2003; Frasure-Smith & Lespérance, 2005). Given the relationship between CRP and cardiovascular disease (e.g., Albert, Ma, Rifai, Stampfer, & Ridker, 2002; Danesh et al., 1998; Mendall et al., 2000; Ridker et al., 2000), it is important to understand how SES and depression affect CRP.

Similarly, only one measure of inflammation was available in the dataset. CRP is only one of a number of elements involved in the inflammatory process. It is possible that a more comprehensive examination of multiple inflammatory markers would have provided more information about the effect of adiposity and stress on inflammation. Also, some researchers have found relationships between stress and other markers of inflammation, such as haptogloblin, α-l-antichymotrypsin, IL-6 and TNF-α, but not with CRP (e.g., Grossi et al., 2003; Joyce et al., 1992; Sutherland et al., 2003; Tuglu et al., 2003). However, CRP is believed to be one of the best markers of risk for cardiovascular disease (Albert et al., 2002; Cushman, Stampfer, Tracy, & Hennekens, 1997; Danesh, Collins, Appleby, & Peto, 1998; Pearson et al., 2003; Ridker et al., 2000), therefore, it is important that we understand the influences on this inflammatory marker in particular.

Another constraint on the current analysis was that the raw SES data was not made available to the public. Only information regarding general level of education was provided, i.e. if the individual had less than a high school education, a high school education, or more than a high school education. In addition, the income data was also only available in income brackets. Use of categories may have masked the effects of SES on CRP. If this data could have been analyzed in its more detailed form (i.e., exact income or number of years of education), it may have provided better information about

the relationships between education, income and CRP. However, these multiple categories provide a more continuous variable than analyses in which the SES data was divided into only high and low groups. Therefore, though not ideal, this type of data was useful in illustrating the gradation of CRP concentrations across levels of SES.

The depression analyses also suffered due to the design of the study. Some studies that have found CRP and depression relationships have sampled equal groups of depressed and non-depressed, whereas the current study was population-based. While this increased external validity, it also decreased the proportion of depressed participants. Only 6.62% (n = 39) of the sample met the criteria for major depression. In addition, only 12.56% (n = 74) of the participants reported one or more symptoms of depression. If a sample of depressed participants were specifically selected for this study a more normal distribution of symptom frequency may have been obtained, which may have affected the results.

The scope of the CIDI may have also affected the data. The questionnaire asked about symptoms of depression over the previous year. The participants' responses may have been subject to retrospective memory bias which may have affected their ability to accurately recall the events of a major depressive episode that occurred months ago. As previously discussed, only a subsample of participants ages 20 to 39 years were asked to complete the CIDI. This reduced sample of relatively young participants may have had a substantial impact on the findings. There was also no way to know if the participants were currently taking antidepressant medications. Lanquillon et al.'s (2000) study suggested that these medications impact levels of CRP. It is possible that those who had

experienced depressive symptoms had been taking medication that affected the relationship between the symptoms and the CRP level.

The correlational and cross-sectional nature of the analyses does not allow for conclusions regarding causality. One cannot be sure if low SES causes changes in CRP or if high CRP levels affect SES. There are multiple hypotheses regarding the direction of the relationship between SES and health. There is a possibility that an increase in inflammation could inhibit an individual's ability to achieve higher education or income. However, the consensus in the literature seems to be that low SES leads to poorer health (Adler et al., 1994).

The directionality of the relationship between depression and inflammation has raised even more questions and hypotheses. It is possible that the presence of depression symptoms results in an increase in inflammation. Indeed, researchers have demonstrated that alleviating depression lowers levels of inflammatory markers (Lanquillon et al., 2000; Tuglu et al., 2003). However, others have found that increased inflammation can lead to depressed mood. Wright, Strike, Brydon and Steptoe (2005) injected participants with a low dose of *S. typhi* capsular polysaccharide vaccine or saline solution in the morning. The vaccination contained a level of antigen that was sufficient to cause an inflammatory response (increase in IL-6) but not cause physical symptoms in the participants. They found that the participants who had been injected with the antigen reported a more negative mood throughout the day, compared to those who received saline. There was also a correlation between the amount of increase of IL-6 and the change in mood, with those who had more IL-6 production showing an increase in measures of negative mood. It is likely that the relationship between depression and

inflammation is even more complex. Miller and Blackwell (2006) present a model in which chronic stressors elicit an increase in inflammation. In response to the increased inflammation, people may develop depressive symptoms and cardiovascular disease. The depressive symptoms and cardiovascular disease then participate in perpetuating the heightened inflammation, creating a positive feedback loop (Miller & Blackwell, 2006). These contradictory studies and models that suggest bidirectional effects make it difficult to interpret the results of this study. There is obviously a need for more experimental and longitudinal studies to tease apart the cause and effect or bidirectional relationships between stress, adiposity, and CRP.

There were also some statistical limitations to the analyses. While a large sample increases reliability and external validity, one must keep in mind that it also has its drawbacks. The large sample size may have overpowered the analyses such that even small effects could be statistically significant. In addition, multiple statistical tests were conducted, which may have inflated the alpha, resulting in an increase in type 1 errors. Another statistical difficulty was the non-normality of the depression data. The data was skewed due to the fact that many participants reported no symptoms of depression. Transformations of the data were unsuccessful at normalizing, causing the researcher to conduct the analyses on non-normal data. This may have reduced the confidence that one has in the results and conclusions.

Conclusions

The purpose of this study was to integrate two lines of research. There is substantial evidence suggesting that psychological stress is related to inflammation (e.g. Hapuarachchi et al., 2003; Melamed et al., 2004; Owen et al., 2003) and that adiposity is

also related to inflammation (e.g. Lemieux et al., 2001; Visser et al., 1999; Yudkin et al., 1999). The proposed model led to the hypothesis that stress would cause adipose tissue to secrete more cytokines and APPs than it would under normal circumstances. Therefore, the relationship between stress and inflammation was expected to be moderated by adiposity. Indeed, adiposity did moderate the relationship between stress and inflammation; however, not in the hypothesized direction. The obese participants in this sample exhibited higher levels of inflammation than the normal weight participants, regardless of income and education. In contrast, among normal weight individuals, income and education were related to CRP levels. While the relationship between SES and CRP is different for obese and normal weight individuals, the reason for these differences is still unclear.

Epidemiological data suggest that obesity is reaching epidemic proportions in the United States in both children and adults (Hedley et al., 2004; Wyatt, Winters & Dubbert, 2006). Further, high levels of adiposity have been linked to a number of chronic diseases (e.g., Burton et al., 1985; Hartz, Rupley, & Rimm, 1984; Ohlson et al., 1985). In addition, stress (specifically SES and depression) is known to be a risk factor for cardiovascular disease. It has been suggested that inflammation may be one pathway through which adiposity and stress lead to these health complications. This study demonstrates the relationship between these variables and especially highlights the dramatic impact of adiposity on inflammation. While lowering stress may be beneficial at reducing CRP in individuals at healthy weights, it does not appear to be enough in those with high levels of adiposity. This is probably due to both the biological and psychological factors that are associated with obesity. Adipose cells release

inflammatory materials. Therefore, those with larger or a greater number of adipose cells may be releasing more of these dangerous substances. Further, obesity is associated with psychological distress such as low self-acceptance and experiences of discrimination (Carr & Friedman, 2005). These psychological factors possibly increase inflammatory markers on top of any other stress with which these people are faced. This highlights the importance of successful weight management to improve both physiological and psychological health.

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Appendix A

Hierarchical Linear Regressions that Utilize Sampling Weights: Tables

Table A1

Summary of Hierarchical Regression Analysis for Education and BMI Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.156***	123.33	<0.001
Education	- 0.015	0.027			
BMI	0.076***	0.003			
Step 3			0.000	168.40	<0.001
Education	- 0.157	0.102			
BMI	0.064***	0.010			
Education x BMI	0.005	0.003			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.067$, F (8,15) = 48.58, $p < 0.001$ for Step 1; $R^2 = 0.223$ for Step 2; $R^2 = 0.223$ for Step 3. ***$p < .001$

Table A2

Summary of Hierarchical Regression Analysis for Education and WC Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.164***	125.65	<0.001
Education	- 0.014	0.027			
WC	0.032***	0.001			
Step 3			0.000	147.22	<0.001
Education	- 0.138	0.168			
WC	0.029***	0.005			
Education x WC	0.001	0.002			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = waist circumference (cm). $R^2 = 0.067$, F (8, 15) = 48.58, $p < 0.001$ for Step 1; $R^2 = 0.232$ for Step 2; $R^2 = 0.232$ for Step 3. *$p < .05$, ***$p < .001$

Table A3

Summary of Hierarchical Regression Analysis for Income and BMI Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.159***	230.58	<0.001
Income	- 0.023***	0.006			
BMI	0.077***	0.003			
Step 3			0.002*	285.22	<0.001
Income	- 0.106**	0.030			
BMI	0.055***	0.009			
Income x BMI	0.003**	0.001			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.067$, $F(8, 15) = 48.58$, $p < 0.001$ for Step 1; $R^2 = .226$for Step 2; $R^2 = .228$ for Step 3. $^{**}p < .01$, $^{***}p < .001$

Table A4

Summary of Hierarchical Regression Analysis for Income and WC Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.167***	132.26	<0.001
Income	- 0.021**	0.006			
WC	0.032***	0.001			
Step 3			0.001	144.39	<0.001
Income	- 0.078	0.049			
WC	0.028***	0.004			
Income x WC	0.001	0.000			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = waist circumference (cm). $R^2 = 0.067$, $F(8, 15) = 48.58$, $p < 0.001$ for Step 1; $R^2 = 0.234$ for Step 2; $R^2 = 0.235$ for Step 3. $^{**}p < .01$, $^{***}p < .001$

Table A5

Summary of Hierarchical Regression Analysis for Depression Diagnosis and BMI Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.181***	498.77	<0.001
Depression Diagnosis	0.090	0.156			
BMI	0.085***	0.006			
Step 3			0.000	666.85	<0.001
Depression Diagnosis	0.472	0.529			
BMI	0.087***	0.006			
Depression Diagnosis x BMI	-0.014	0.014			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.077$, F (8, 15) = 83.84, $p < 0.001$ for Step 1; $R^2 = 0.258$ for Step 2; $R^2 = 0.2581$ for Step 3. ***$p < .001$

Table A6

Summary of Hierarchical Regression Analysis for Depression Diagnosis and WC Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.167***	214.67	<0.001
Depression Diagnosis	0.093	0.189			
WC	0.032	0.003			
Step 3			0.000	311.30	<0.001
Depression Diagnosis	0.564	0.596			
WC	0.033***	0.003			
Depression Diagnosis x WC	0.005	0.005			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC=Waist Circumference (cm). $R^2 = 0.077$, F (8, 15) = 83.84, $p < 0.001$ for Step 1; $R^2 = 0.244$ for Step 2; $R^2 = 0.244$ for Step 3. ***$p < .001$

Table A7

Summary of Hierarchical Regression Analysis for Depression Symptoms and BMI Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.180***	834.67	<0.001
Depression Symptoms	0.007	0.011			
BMI	0.085***	0.005			
Step 3			0.000	1017.33	<0.001
Depression Symptoms	-0.002	0.081			
BMI	0.084***	0.007			
Depression Symptoms x BMI	0.000	0.002			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.077$, F (8, 15) = 83.84, $p < 0.001$ for Step 1; $R^2 = 0.257$ for Step 2; $R^2 = 0.257$ for Step 3. ***$p < .001$

Table A8

Summary of Hierarchical Regression Analysis for Depression Symptoms and WC Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.161***	272.21	<0.001
Depression Symptoms	0.007	0.013			
WC	0.033***	0.003			
Step 3			0.000	356.19	<0.001
Depression Symptoms	-0.001	0.107			
WC	0.032***	0.003			
Depression Symptoms x WC	0.000	0.001			

Note. All steps contain the covariates (gender, age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = Waist Circumference (cm). $R^2 = 0.077$, $F(8,15) = 83.84$, $p < .0001$ for Step 1; $R^2 = .238$ for Step 2; $R^2 = .238$ for Step 3. ***$p < .001$.

Table A9

Summary of Hierarchical Regression Analysis for Education, BMI, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.167***	123.33	<0.001
Education	-0.015	0.027			
BMI	0.076***	0.003			
Gender	0.276***	0.037			
Step 3			0.001	195.75	<0.001
Education	-0.245	0.126			
BMI	0.057**	0.015			
Gender	- 0.014	0.239			
Education x BMI	0.005	0.003			
Education x Gender	0.064	0.049			
BMI x Gender	0.005	0.007			
Step 4			0.000	204.13	<0.001
Education	-0.546	0.502			
BMI	0.032	0.042			
Gender	-0.467	0.771			
Education x BMI	0.016	0.016			
Education x Gender	0.255	0.307			
BMI x Gender	0.021	0.025			
Education x BMI x Gender	-0.007	0.010			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.056$, F (7, 15) = 46.44, $p < 0.001$ for Step 1; $R^2 = 0.223$ for Step 2; $R^2 = 0.224$for Step 3; $R^2 = 0.224$ for Step 4. $^{**}p < .01$, $^{***}p < .001$.

Table A10

Summary of Hierarchical Regression Analysis for Education, WC, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.176***	125.65	<0.001
Education	-0.014	0.027			
WC	0.032***	0.001			
Gender	0.476***	0.042			
Step 3			0.002**	186.40	<0.001
Education	-0.311	0.206			
WC	0.019*	0.007			
Gender	0.002	0.002			
Education x WC	-0.016	0.015			
Education x Gender	0.096	0.051			
WC x Gender	0.006*	0.003			
Step 4			0.000	181.71	<0.001
Education	-0.228	0.726			
WC	0.021	0.017			
Gender	-0.207	1.152			
Education x WC	0.001	0.007			
Education x Gender	0.040	0.471			
WC x Gender	0.005	0.011			
Education x WC x Gender	0.001	0.005			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = waist circumference (cm). $R^2 = 0.056$, F (7, 15) = 46.44, $p < 0.001$ for Step 1; $R^2 = 0.232$ for Step 2; $R^2 = 0.234$ for Step 3; $R^2 = 0.234$ for Step 4. ***$p < .001$, **$p < .01$, *$p < .05$

Table A11

Summary of Hierarchical Regression Analysis for Income, BMI, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.170***	230.58	<0.001
Income	-0.023***	0.006			
BMI	0.077***	0.003			
Gender	0.251***	0.035			
Step 3			0.004**	293.17	<0.001
Income	-0.140**	0.036			
BMI	0.043**	0.012			
Gender	-0.096	0.227			
Income x BMI	0.003**	0.001			
Income x Gender	0.021	0.012			
BMI x Gender	0.007	0.006			
Step 4			0.000	921.96	<0.001
Income	-0.133	0.111			
BMI	0.045	0.027			
Gender	-0.064	0.480			
Income x BMI	0.002	0.004			
Income x Gender	0.016	0.065			
BMI x Gender	0.006	0.015			
Income x BMI x Gender	0.0001	0.002			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.056$, F (7, 15) = 46.44, $p < 0.001$ for Step 1; $R^2 = 0.226$ for Step 2; $R^2 = 0.230$ for Step 3; $R^2 = 0.230$ for Step 4. $^{**}p < .01$, $^{***}p < .001$.

Table A12

Summary of Hierarchical Regression Analysis for Income, WC, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.178***	132.26	<0.001
Income	-0.021**	0.006			
WC	0.032***	0.001			
Gender	0.454***	0.041			
Step 3			0.005**	233.75	<0.001
Income	-0.157*	0.062			
WC	0.016*	0.006			
Gender	-0.440	0.254			
Income x WC	0.001	0.0005			
Income x Gender	0.033*	0.012			
WC x Gender	0.007**	0.002			
Step 4			0.000	276.35	<0.001
Income	-0.105	0.128			
WC	0.020*	0.009			
Gender	-0.189	0.545			
Income x WC	0.0003	0.001			
Income x Gender	-0.001	0.074			
WC x Gender	0.004	0.005			
Income x WC x Gender	0.0003	0.00			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = Waist Circumference (cm). $R^2 = 0.056$, $F(7, 15) = 46.44$, $p < 0.001$ for Step 1; $R^2 = 0.234$ for Step 2; $R^2 = 0.239$ for Step 3; $R^2 = 0.239$ for Step 4. $^*p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Table A13

Summary of Hierarchical Regression Analysis for Depression Diagnosis, BMI, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.219***	498.77	<0.001
Depression Diagnosis	0.090	0.156			
BMI	0.085***	0.006			
Gender	0.548***	0.094			
Step 3			0.002	591.49	<0.001
Depression Diagnosis	0.991*	0.461			
BMI	0.074**	0.020			
Gender	0.347	0.339			
Depression Diagnosis x BMI	-0.016	0.015			
Depression Diagnosis x Gender	-0.297	0.322			
BMI x Gender	-0.008	0.012			
Step 4			0.000	869.54	<0.001
Depression Diagnosis	0.623	2.024			
BMI	0.073**	0.022			
Gender	0.329	0.376			
Depression Diagnosis x BMI	-0.002	0.070			
Depression Diagnosis x Gender	-0.094	1.153			
BMI x Gender	0.009	0.014			
Depression Diagnosis x BMI x Gender	-0.008	0.037			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.039$, F (7, 15) = 105.87, $p < 0.001$ for Step 1; $R^2 = 0.258$ for Step 2; $R^2 = 0.260$ for Step 3; $R^2 = 0.260$ for Step 4. ***$p < .001$, **$p < .01$, *$p < .05$

Table A14

Summary of Hierarchical Regression Analysis for Depression Diagnosis, WC, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.205***	214.67	<0.001
Depression Diagnosis	0.093	0.189			
WC	0.032	0.003			
Gender	0.685***	0.095			
Step 3			0.004	604.34	<0.001
Depression Diagnosis	1.377*	0.588			
WC	0.021	0.010			
Gender	-0.078	0.629			
Depression Diagnosis x WC	-0.009*	0.004			
Depression Diagnosis x Gender	-0.286	0.317			
WC x Gender	0.009	0.007			
Step 4			0.000	419.16	<0.001
Depression Diagnosis	2.538	2.704			
WC	0.022	0.011			
Gender	-0.029	0.664			
Depression Diagnosis x WC	-0.021	0.028			
Depression Diagnosis x Gender	-0.945	1.514			
WC x Gender	0.008	0.007			
Depression Diagnosis x WC x Gender	0.007	0.016			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC=Waist Circumference (cm). $R^2 = 0.039$, F (7, 15) = 105.87, $p < 0.001$ for Step 1; $R^2 = 0.244$ for Step 2; $R^2 = 0.248$ for Step 3, $R^2 = 0.248$ for Step 4. *$p < .05$, ***$p < .001$

Table A15

Summary of Hierarchical Regression Analysis for Depression Symptoms, BMI, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.218***	834.67	<0.001
Depression Symptoms	0.007	0.011			
BMI	0.085***	0.005			
Gender	0.549***	0.094			
Step 3			0.001	1680.61	<0.001
Depression Symptoms	0.042	0.083			
BMI	0.076**	0.020			
Gender	0.417	0.324			
Depression Symptoms x BMI	0.0002	0.003			
Depression Symptoms x Gender	-0.027	0.043			
BMI x Gender	0.006	0.012			
Step 4			0.001	1681.86	<0.001
Depression Symptoms	0.192	0.266			
BMI	0.080**	0.023			
Gender	0.488	0.385			
Depression Symptoms x BMI	-0.005	0.009			
Depression Symptoms x Gender	-0.111	0.154			
BMI x Gender	0.003	0.014			
Depression Symptoms x BMI x Gender	0.003	0.005			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.039$, F (7, 15) = 105.87, $p < 0.001$ for Step 1; $R^2 = 0.257$ for Step 2; $R^2 = 0.258$ for Step 3; $R^2 = 0.259$ for Step 4. **$p < .01$, ***$p < .001$

Table A16

Summary of Hierarchical Regression Analysis for Depression Symptoms, WC, and Gender Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(10, 15)	*p*
Step 2			0.199***	272.21	<0.001
Depression Symptoms	0.007	0.013			
WC	0.033***	0.003			
Gender	0.673***	0.098			
Step 3			0.008	133.82	<0.001
Depression Symptoms	0.020	0.080			
WC	0.022*	0.010			
Gender	0.014	0.609			
Depression Symptoms x WC	0.00003	0.001			
Depression Symptoms x Gender	-0.011	0.040			
WC x Gender	0.007	0.007			
Step 4			0.001	375.69	<0.001
Depression Symptoms	0.444	0.350			
WC	0.025*	0.012			
Gender	0.238	0.698			
Depression Symptoms x WC	-0.004	0.004			
Depression Symptoms x Gender	-0.266	0.193			
WC x Gender	0.005	0.008			
Depression Symptoms x WC x Gender	0.003	0.002			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = Waist Circumference (cm). $R^2 = 0.039$, F (7, 15) = 105.87, $p < 0.001$ for Step 1; $R^2 = .238$ for Step 2; $R^2 = .246$ for Step 3; $R^2 = .247$ for Step 4. $^*p < .05$, $^{***}p < .001$.

Table A17

Summary of Hierarchical Regression Analysis for Gender and Education Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.026***	122.18	<0.001
Gender	0.398***	0.049			
Education	-0.015	0.028			
Step 3			0.001	132.23	<0.001
Gender	0.217	0.120			
Education	-0.128	0.089			
Education x Gender	0.076	0.051			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.211$, $F(9,15) = 134.60$, $p < .001$ for Step 1; $R^2 = .237$ for Step 2; $R^2 = .238$ for Step 3. ***$p < .001$.

Table A18

Summary of Hierarchical Regression Analysis for Gender and Income Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.028***	157.15	<0.001
Gender	0.377***	0.051			
Income	-0.022**	0.006			
Step 3			0.002*	155.17	<0.001
Gender	0.186	0.096			
Income	-0.060**	0.019			
Gender x Income	0.025*	0.011			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.211$, $F(9,15) = 134.60$, $p < .0001$ for Step 1; $R^2 = .239$ for Step 2; $R^2 = .241$ for Step 3. *$p < .05$, **$p < .01$, ***$p < .001$.

Table A19

Summary of Hierarchical Regression Analysis for Gender and Depression Diagnosis Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.055***	836.16	<0.001
Gender	0.592***	0.088			
Depression Diagnosis	0.089	0.166			
Step 3			0.001	910.08	<0.001
Gender	0.614***	0.087			
Depression Diagnosis	0.550	0.518			
Gender x Depression Diagnosis	-0.294	0.348			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.203$ $F(9, 15) = 219.63$, $p < .001$ for Step 1; $R^2 = 0.258$ for Step 2; $R^2 = 0.259$ for Step 3. ***$p < .001$.

Table A20

Summary of Hierarchical Regression Analysis for Gender and Depression Symptoms Predicting LogCRP: Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.055***	1265.33	<0.001
Gender	0.593***	0.089			
Depression Symptoms	0.007	0.012			
Step 3			0.000	1062.00	<0.001
Gender	0.611***	0.090			
Depression Symptoms	0.040	0.058			
Gender x Depression Symptoms	-0.021	0.042			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, body mass index, and waist circumference) variables presented are those that are relevant to the hypotheses. $R^2 = 0.203$ $F(9, 15) = 219.63$, $p < .001$ for Step 1; $R^2 = 0.258$ for Step 2; $R^2 = 0.258$ for Step 3. ***$p < .001$.

Table A21

Summary of Hierarchical Regression Analysis for Gender and BMI Predicting LogCRP (The SES Sample): Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.164***	207.45	<0.001
Gender	0.251***	0.035			
BMI	0.077***	0.003			
Step 3			0.000	217.57	<0.001
Gender	0.098	0.183			
BMI	0.068***	0.010			
Gender x BMI	0.005	0.006			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, education, and income) variables presented are those that are relevant to the hypotheses. These analyses utilized the sampling weights. BMI = body mass index. $R^2 = 0.063$, $F(9, 15) = 33.41$, $p < .0001$ for Step 1; $R^2 = 0.227$ for Step 2; $R^2 = 0.227$ for Step 3. ***$p < .001$

Table A22

Summary of Hierarchical Regression Analysis for Gender and BMI Predicting LogCRP (The Depression Sample): Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,583)	*p*
Step 2			0.215***	811.48	<0.001
Gender	0.548***	0.094			
BMI	0.085***	0.006			
Step 3			0.000	719.22	<0.001
Gender	0.401	0.312			
BMI	0.076**	0.021			
Gender x BMI	0.005	0.013			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, depression diagnosis, and depression symptoms) variables presented are those that are relevant to the hypotheses. These analyses utilized sampling weights. BMI = body mass index. $R^2 = 0.043$, $F(9, 15) = 94.82$, $p < .001$ for Step 1; $R^2 = 0.258$ for Step 2; $R^2 = 0.258$ for Step 3. **$p < .01$, ***$p < .001$.

Table A23

Summary of Hierarchical Regression Analysis for Gender and WC Predicting LogCRP (the SES sample): Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.172***	119.08	<0.001
Gender	0.453***	0.041			
WC	0.032***	0.001			
Step 3			0.001**	190.49	<0.001
Gender	-0.139	0.224			
WC	0.023***	0.004			
Gender x WC	0.006*	0.002			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, education, and income) variables presented are those that are relevant to the hypotheses. These analyses utilized sampling weights. WC = waist circumference (cm). $R^2 = 0.063$, $F(9, 15) = 33.41$, $p < .001$ for Step 1; $R^2 = .235$ for Step 2; $R^2 = 0.236$ for Step 3. **$p < .01$, ***$p < .001$.

Table A24

Summary of Hierarchical Regression Analysis for Gender and WC Predicting LogCRP (the Depression Sample): Weighted Data

Variable	*B*	*SE B*	ΔR^2	*F*(11,15)	*p*
Step 2			0.201***	554.23	<0.001
Gender	0.685***	0.095			
WC	0.032***	0.003			
Step 3			0.002	1600.32	<0.001
Gender	0.015	0.022			
WC	0.022	0.010			
Gender x WC	0.007	0.007			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, depression diagnosis, and depression symptoms) variables presented are those that are relevant to the hypotheses. These analyses utilized sampling weights. WC = waist circumference (cm). $R^2 = 0.043$, $F(9, 15) = 94.82$, $p < .001$ for Step 1; $R^2 = 0.244$ for Step 2; $R^2 = 0.246$ for Step 3. ***$p < .001$.

Appendix B

3-way Hierarchical Linear Regressions (Unweighted Data)

Table B1

Summary of Hierarchical Regression Analysis for Education, BMI, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3681)	*p*
Step 2				0.159***	93.50	<0.001
Education	-0.028	0.020	-0.023			
BMI	0.069	0.003	0.381***			
Gender	0.304	0.031	0.146***			
Step 3				0.001	72.40	<0.001
Education	-0.266	0.104	-0.217*			
BMI	0.055	0.011	0.303***			
Gender	0.256	0.180	0.123			
Education x BMI	0.007	0.003	0.176*			
Education x Gender	0.031	0.037	0.051			
BMI x Gender	-0.001	0.006	-0.009			
Step 4				0.000	67.46	<0.001
Education	-0.750	0.304	-0.611*			
BMI	0.017	0.025	0.095			
Gender	-0.422	0.438	-0.203			
Education x BMI	-0.024	0.011	0.621*			
Education x Gender	0.339	0.185	0.564			
BMI x Gender	0.024	0.015	0.386			
Education x BMI x Gender	-0.011	0.007	-0.550			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.044$, F (7, 3684) = 24.33, $p < 0.001$ for Step 1; $R^2 = 0.203$ for Step 2; $R^2 = 0.204$ for Step 3; $R^2 = 0.204$ for Step 4. *$p < .05$, **$p < .01$, ***$p < .001$.

Table B2

Summary of Hierarchical Regression Analysis for Education, WC, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3621)	*p*
Step 2				0.181***	105.36	<0.001
Education	-0.025	0.020	-0.020			
WC	0.031	0.001	0.426***			
Gender	0.482	0.032	0.231***			
Step 3				0.003**	82.01	<0.001
Education	-0.417	0.145	-0.339**			
WC	0.019	0.004	0.257***			
Gender	-0.0002	0.234	-0.0001			
Education x WC	0.003	0.001	0.261*			
Education x Gender	0.062	0.037	0.103			
WC x Gender	0.004	0.002	0.174			
Step 4				0.000	76.15	<0.001
Education	-0.587	0.405	-0.477			
WC	0.015	0.010	0.205			
Gender	-0.252	0.607	-0.121			
Education x WC	0.005	0.004	0.406			
Education x Gender	0.175	0.254	0.291			
WC x Gender	0.006	0.006	0.297			
Education x WC x Gender	-0.001	0.003	-0.184			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = waist circumference (cm). $R^2 = 0.044$, F (7, 3684) = 24.33, $p < 0.001$ for Step 1; $R^2 = 0.225$ for Step 2; $R^2 = 0.228$ for Step 3; $R^2 = 0.228$ for Step 4. ***$p < .001$, **$p < .01$, *$p < .05$

Table B3

Summary of Hierarchical Regression Analysis for Income, BMI, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10,3434)	*p*
Step 2				0.157***	86.53	<0.001
Income	-0.021	0.006	-0.060***			
BMI	0.069	0.003	0.377***			
Gender	0.280	0.032	0.135***			
Step 3				0.004**	67.84	<0.001
Income	-0.134	0.031	-0.384***			
BMI	0.046	0.012	0.253***			
Gender	0.072	0.179	0.035			
Income x BMI	0.003	0.001	0.256**			
Income x Gender	0.021	0.011	0.253*			
BMI x Gender	0.003	0.006	0.117			
Step 4				0.000	62.98	<0.001
Income	-0.155	0.092	-0.446			
BMI	0.041	0.024	0.225			
Gender	-0.017	0.399	-0.008			
Income x BMI	0.004	0.003	0.325			
Income x Gender	0.035	0.055	0.190			
BMI x Gender	0.006	0.014	0.093			
Income x BMI x Gender	0.0004	0.002	-0.077			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.044$, F (7, 3684) = 24.33, $p < 0.001$ for Step 1; $R^2 = 0.201$ for Step 2; $R^2 = 0.205$ for Step 3; $R^2 = 0.205$ for Step 4. ***$p < .001$, **$p < .01$, *$p < .05$

Table B4

Summary of Hierarchical Regression Analysis for Income, WC, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 3378)	*p*
Step 2				0.179***	96.96	<0.001
Income	-0.018	0.006	-0.050**			
WC	0.031	0.001	0.421***			
Gender	0.459	0.033	0.221***			
Step 3				0.004**	76.09	<0.001
Income	-0.151	0.043	-0.433***			
WC	0.017	0.004	0.238***			
Gender	-0.233	0.240	-0.112			
Income x WC	0.001	0.0004	0.263*			
Income x Gender	0.032	0.011	0.173**			
WC x Gender	0.005	0.002	0.239*			
Step 4				0.000	70.64	<0.001
Income	-0.159	0.121	-0.456			
WC	0.017	0.009	0.231			
Gender	-0.268	0.553	-0.129			
Income x WC	0.001	0.001	0.287			
Income x Gender	0.037	0.074	0.200			
WC x Gender	0.005	0.006	0.256			
Income x WC x Gender	-0.0001	0.001	-0.027			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC=Waist Circumference (cm). $R^2 = 0.044$, F (7, 3684) = 24.33, $p < 0.001$ for Step 1; $R^2 = 0.223$ for Step 2; $R^2 = 0.227$ for Step 3; $R^2 = 0.227$ for Step 4. ***$p < .001$, **$p < .01$, *$p < .05$

Table B5

Summary of Hierarchical Regression Analysis for Depression Diagnosis, BMI, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 572)	*p*
Step 2				0.239***	21.79	<0.001
Depression Diagnosis	0.175	0.171	0.037			
BMI	0.087	0.007	0.444***			
Gender	0.569	0.087	0.241***			
Step 3				0.002	16.87	<0.001
Depression Diagnosis	1.133	0.821	0.239			
BMI	0.080	0.023	0.407***			
Gender	0.447	0.406	0.189			
Depression Diagnosis x BMI	-0.010	0.022	-0.062			
Depression Diagnosis x Gender	-0.432	0.345	-0.152			
BMI x Gender	-0.006	0.015	0.079			
Step 4				0.000	15.65	<0.001
Depression Diagnosis	0.297	2.833	0.063			
BMI	0.078	0.024	0.397**			
Gender	0.409	0.424	0.173			
Depression Diagnosis x BMI	0.020	0.100	0.126			
Depression Diagnosis x Gender	0.034	1.551	0.012			
BMI x Gender	0.007	0.015	0.098			
Depression Diagnosis x BMI x Gender	-0.017	0.054	-0.178			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI= body mass index (kg/m^2). $R^2 = 0.037$, F (7, 575) = 3.17, $p < 0.01$ for Step 1; $R^2 = 0.276$ for Step 2; $R^2 = 0.278$ for Step 3; $R^2 = 0.278$ for Step 4. ***$p < .001$, **$p < .01$, *$p < .05$

Table B6

Summary of Hierarchical Regression Analysis for Depression Diagnosis, WC, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 568)	*p*
Step 2				0.249***	22.72	<0.001
Depression Diagnosis	0.206	0.172	0.043			
WC	0.036	0.003	0.463***			
Gender	0.679	0.087	0.287***			
Step 3				0.005	17.81	<0.001
Depression Diagnosis	1.551	1.191	0.324			
WC	0.022	0.009	0.284*			
Gender	-0.197	0.537	-0.083			
Depression Diagnosis x WC	-0.008	0.010	-0.162			
Depression Diagnosis x Gender	-0.371	0.348	-0.129			
WC x Gender	0.010	0.006	0.406			
Step 4				0.000	16.51	<0.001
Depression Diagnosis	1.113	4.263	0.233			
WC	0.022	0.009	0.281*			
Gender	-0.212	0.556	-0.090			
Depression Diagnosis x WC	-0.004	0.043	-0.071			
Depression Diagnosis x Gender	-0.124	2.339	-0.043			
WC x Gender	0.010	0.006	0.413			
Depression Diagnosis x WC x Gender	-0.003	0.024	-0.085			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC=Waist Circumference (cm). $R^2 = 0.037$, F (7, 571) = 3.11, $p < 0.01$ for Step 1; $R^2 = 0.286$ for Step 2; $R^2 = 0.291$ for Step 3, $R^2 = 0.291$ for Step 4. *$p < .05$, ***$p < .001$

Table B7

Summary of Hierarchical Regression Analysis for Depression Symptoms, BMI, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 572)	*p*
Step 2				0.239***	21.79	<0.001
Depression Symptoms	0.020	0.020	0.037			
BMI	0.087	0.007	0.443***			
Gender	0.568	0.087	0.244***			
Step 3				0.003	16.94	<0.001
Depression Symptoms	0.103	0.099	0.189			
BMI	0.080	0.023	0.407***			
Gender	0.497	0.406	0.210			
Depression Symptoms x BMI	0.001	0.003	0.030			
Depression Symptoms x Gender	-0.063	0.040	-0.193			
BMI x Gender	0.005	0.015	0.062			
Step 4				0.001	15.74	<0.001
Depression Symptoms	0.302	0.346	0.551			
BMI	0.085	0.025	0.434***			
Gender	0.590	0.435	0.249			
Depression Symptoms x BMI	-0.007	0.012	-0.358			
Depression Symptoms x Gender	-0.175	0.191	-0.534			
BMI x Gender	0.002	0.016	0.015			
Depression Symptoms x BMI x Gender	0.004	0.007	0.373			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. BMI = body mass index (kg/m^2). $R^2 = 0.037$, F (7, 575) = 3.17, $p < 0.01$ for Step 1; $R^2 = 0.276$ for Step 2; $R^2 = 0.279$ for Step 3; $R^2 = 0.280$ for Step 4. ***$p < .001$

Table B8

Summary of Hierarchical Regression Analysis for Depression Symptoms, WC, and Gender Predicting LogCRP: Unweighted Data

Variable	*B*	*SE B*	β	ΔR^2	*F*(10, 568)	*p*
Step 2				0.248***	22.68	<0.001
Depression Symptoms	0.021	0.020	0.039			
WC	0.036	0.003	0.461***			
Gender	0.677	0.088	0.286***			
Step 3				0.005	17.73	<0.001
Depression Symptoms	0.098	0.143	0.178			
WC	0.022	0.009	0.282*			
Gender	-0.153	0.538	-0.065			
Depression Symptoms x WC	-0.0001	0.001	-0.020			
Depression Symptoms x Gender	-0.042	0.041	-0.127			
WC x Gender	0.009	0.006	0.389			
Step 4				0.001	16.49	<0.001
Depression Symptoms	0.453	0.480	0.817			
WC	0.024	0.009	0.314*			
Gender	-0.003	0.573	-0.001			
Depression Symptoms x WC	-0.004	0.005	-0.662			
Depression Symptoms x Gender	-0.248	0.270	-0.750			
WC x Gender	0.008	0.006	0.321			
Depression Symptoms x WC x Gender	0.002	0.003	0.624			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication and smoking) variables presented are those that are relevant to the hypotheses. WC = Waist Circumference (cm). $R^2 = 0.037$, F (7, 571) = 3.11, $p < 0.01$ for Step 1; $R^2 = .285$ for Step 2; $R^2 = .290$ for Step 3; $R^2 = .291$ for Step 4. *$p < .05$, ***$p < .001$.

Appendix C

Gender as a Moderator of the Relationship between Adiposity and CRP (Unweighted Data): Tables

Table C1

Summary of Hierarchical Regression Analysis for Gender and BMI Predicting LogCRP (The SES Sample)

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,3430)	*p*
Step 2				0.151***	78.69	<0.001
Gender	0.282	0.032	0.136***			
BMI	0.069	0.003	0.377***			
Step 3				0.000	72.12	<0.001
Gender	0.249	0.163	0.120			
BMI	0.067	0.010	0.366***			
Gender x BMI	0.001	0.006	0.019			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, education, and income) variables presented are those that are relevant to the hypotheses. These analyses did not utilize the sampling weights. BMI = body mass index. $R^2 = 0.051$, $F(9, 3432) = 20.48$,
$p < .0001$ for Step 1; $R^2 = 0.202$ for Step 2; $R^2 = 0.202$ for Step 3. ***$p < .001$

Table C2

Summary of Hierarchical Regression Analysis for Gender and BMI Predicting LogCRP (The Depression Sample)

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,571)	*p*
Step 2				0.231***	19.79	<0.001
Gender	0.568	0.087	0.240***			
BMI	0.087	0.007	0.443***			
Step 3				0.000	18.12	<0.001
Gender	0.479	0.398	0.203			
BMI	0.082	0.023	0.418***			
Gender x BMI	0.003	0.014	0.045			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, depression diagnosis, and depression symptoms) variables presented are those that are relevant to the hypotheses. These analyses did not utilize sampling weights. BMI = body mass index. $R^2 = 0.045$, $F(9, 573) = 3.01$, $p < 0.01$ for Step 1; $R^2 = 0.276$ for Step 2; $R^2 = 0.276$ for Step 3.

Table C3

Summary of Hierarchical Regression Analysis for Gender and WC Predicting LogCRP (the SES sample)

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,3374)	*p*
Step 2				0.174***	87.97	<0.001
Gender	0.461	0.033	0.222***			
WC	0.030	0.001	0.420***			
Step 3				0.001	81.01	<0.001
Gender	0.037	0.224	0.018			
WC	0.024	0.004	0.330***			
Gender x WC	0.004	0.002	0.209			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, education, and income) variables presented are those that are relevant to the hypotheses. These analyses did not utilize sampling weights. WC = waist circumference (cm). $R^2 = 0.049$, $F(9, 3376) = 19.50$, $p < .001$ for Step 1; $R^2 = .223$ for Step 2; $R^2 = 0.224$ for Step 3. ***$p < .001$.

Table C4

Summary of Hierarchical Regression Analysis for Gender and WC Predicting LogCRP (the Depression Sample)

Variable	*B*	*SE B*	β	ΔR^2	*F*(11,567)	*p*
Step 2				0.242***	20.63	<0.001
Gender	0.677	0.086	0.286***			
WC	0.036	0.003	0.462***			
Step 3				0.003	19.16	<0.001
Gender	-0.134	0.531	-0.057			
WC	0.023	0.009	0.293*			
Gender x WC	0.009	0.006	0.366			

Note. All steps contain the covariates (age, ethnicity, use of blood pressure medication, use of cholesterol medication, smoking, depression diagnosis, and depression symptoms) variables presented are those that are relevant to the hypotheses. These analyses did not utilize sampling weights. WC = waist circumference. $R^2 = 0.044$, $F(9,569) = 2.90$, $p< 0.01$ for Step 1; $R^2 = 0.286$ for Step 2; $R^2 = 0.289$ for Step 3.