DIET COMPOSITION AS A CANDIDATE MECHANISM UNDERLYING THE DEPRESSION-TO-OBESITY ASSOCIATION: THE CARDIA STUDY

by

Elizabeth A. Vrany

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STATEMENT OF COMMITTEE APPROVAL

Dr. Jesse C. Stewart
Department of Psychology
Dr. Adam T. Hirsh
Department of Psychology
Dr. Melissa A. Cyders
Department of Psychology
Dr. Daniel O. Clark
Indiana University, School of Medicine
Dr. Karen A. Matthews
University of Pittsburgh, Department of Psychiatry

Approved by:

Dr. Nicholas J. Grahame
Head of the Graduate Program

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ABSTRACT

Author: Vrany, Elizabeth A. PhD
Institution: Purdue University
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Major Professor: Jesse C. Stewart

People with depression are at elevated risk for future obesity; however, little is known about the potential mechanistic role of diet composition in this association. The aims of the present study were: (1) to examine depressive symptom severity as a predictor of 13-year change in seven diet composition factors over time, (2) to test 13-year change in diet composition factors as mediators of the association between depressive symptom severity and 13-year change in adiposity, and (3) to explore whether the Aim 2 mediation models are moderated by sex and race.

Participants were 2,449 non-Hispanic Black and White adults who participated in the 1990, 1992, and 2005 years of the CARDIA study (mean baseline age = 35 years, 54% women, 56% non-Hispanic Black, mean baseline waist circumference = 84.0 cm, mean change in waist circumference = 8.3 cm). Depressive symptoms were assessed in 1990 using the Center for Epidemiologic Studies-Depression Scale (CES-D). Waist circumference and seven diet composition factors were assessed in 1992 and 2005. Diet composition factors included intake of total energy, saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, fiber, sugar, and protein. PROCESS bootstrapping analyses were used to test for mediation and moderated mediation (see Figure 1 for the conceptual model). All models included adjustment for age; sex; race; education; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; and 13-year change in physical activity.

Greater baseline CES-D Total predicted greater 13-year increases in waist circumference (path *c* β = 0.032, *p* = .006). In separate models, there was a trend for greater baseline depressive symptoms predicting 13-year increases in total energy intake (path *a* β = 0.040, *p* = .054), and greater baseline depressive symptoms predicted 13-year increases in protein intake (path *a* β = 0.059, *p* = .004) and fiber intake (path *a* β = 0.040, *p* = .0496). Depressive symptoms were unrelated to 13-year changes in intake of the other diet composition factors of saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, and sugar (all *p*s ≥ .129). Mediation models revealed that 13-year change in total energy intake and protein intake partially mediated the association between baseline depressive symptoms and 13-year change in waist circumference (total energy intake indirect effect = 0.001, *95% CI*=0.0001-0.004; protein intake indirect effect = 0.002, *95% CI*=0.0004-0.005); mediation was not observed for the other diet composition factors. Exploratory moderated mediation models detected a significant interaction for CES-D Total by sex predicting 13-year change protein intake only (Index of moderated mediation=0.004, 95%CI=0.001-0.010). All other tests of moderated mediation were non-significant (95% CIs included zero). Analyses stratified by sex revealed that CES-D Total was more strongly associated with 13-year increases protein intake in men (β = 0.011, p=.004) than in women (*β* = 0.027, *p* = .246).

Findings from this larger, longitudinal, epidemiologic study suggest that the prospective relationship between depression and future obesity risk may be explained, in part, by intake of certain diet composition factors. Advancing the understanding of the relationship between depression and diet changes will inform clinical efforts to prevent or manage depression-related obesity.

INTRODUCTION

Overview

Obesity is an important public health problem that affects over one third of adults in the U.S. In addition to traditional risk factors, depression has been identified as a novel psychological risk factor for obesity. Mechanisms linking depression to future obesity risk include a variety of biological and psychosocial factors, one of which is dietary behavior. Although dietary behavior is commonly mentioned as a potential mechanism linking depression to chronic disease risk, relatively few investigations have prospectively examined (a) depression as a predictor of change in dietary behavior over time or (b) dietary behavior as a candidate mechanism underlying the depression-to-obesity relationship.

Several topics will be discussed to provide context for the present study. First, obesity will be introduced, including a review of its definition, measurement, pathophysiology, and traditional risk factors. Second, depression will be discussed as a novel risk factor for obesity. Third, dietary behavior – specifically, diet composition – will be discussed as a candidate mechanism underlying the depression-to-obesity association. In this section, I will define diet composition, discuss its association with obesity, and summarize and evaluate the empirical evidence linking depression to each diet composition factor. Fourth, I will present the conceptual model and aims for the present study. The aims of the present study were: (1) to examine depressive symptom severity as a predictor of 13-year change in seven diet composition factors over time, (2) to test 13-year change in diet composition factors as mediators of the association between depressive symptom severity and 13-year change in adiposity, and (3) to explore whether the Aim 2 mediation models are moderated by sex and race.

The Obesity Problem

Obesity is defined as an excess accumulation of body fat, or adiposity, in proportion to lean body mass (Straub, 2014) that elevates health risk (World Health Organization, 2016). Obesity is commonly measured using body mass index (BMI), which is calculated as a person's weight in kilograms divided by their height in meters squared (kg/m^2) (Centers for Disease Control and Prevention, 2016). According to the Centers for Disease Control and Prevention (2016), BMI values are classified into the following categories: < 18.5 kg/m^2 is considered underweight, 18.5-24.9 kg/m^2 is considered normal weight, 25.0-29.9 kg/m^2 is considered overweight, and ≥ 30.0 kg/m^2 is indicates obesity.

Although BMI is the internationally accepted measure of overweight and obesity (World Health Organization, 2016), alternative measures are available. One such measure is waist circumference (Straub, 2014). Waist circumference is an index of central adiposity, or fat distributed near the abdominal region, whereas BMI is an index of total body adiposity (Straub, 2014). Based on data from NHANES from 1999-2004, waist circumference and BMI have a strong positive correlation (r = 0.90-0.94 in men; r = 0.85-0.92 in women) (Flegal et al., 2009). According to the National Institutes of Health, waist circumference values > 102 cm (40.2 inches) in men and > 88 cm (34.6 inches) in women are indicative of high risk for the development of obesity-related health problems (Janssen, Katzmarzyk, & Ross, 2004; National Institutes of Health, 1998). Waist circumference has been found to be a stronger predictor of future cardiometabolic disease (i.e., cardiovascular disease and type 2 diabetes) than BMI (Klein et al., 2007). In addition, waist circumference is associated with cardiometabolic disease above and beyond BMI (Janssen et al., 2004; Klein et al., 2007). Collectively, these findings suggest that waist circumference is a more health-relevant measure of adiposity than BMI.

Since 1980, the prevalence of obesity has more than doubled worldwide (World Health Organization, 2016) and in the U.S. (Ogden, Carroll, Kit, & Flegal, 2013). Data from the National Health and Nutrition Examination Survey (NHANES) indicates that the prevalence of obesity among U.S. adults has increased from 14.5% in 1976-1980 (Flegal, Carroll, Kuczmarski, & Johnson, 1998) to 34.9% in 2011-2012 (Ogden et al., 2013). Some demographic groups have disproportionately high rates of obesity. To illustrate, 47.8% of non-Hispanic Blacks and 42.5% of Hispanics have obesity, compared to 32.6% of non-Hispanic Whites. Although obesity rates do not significantly differ by sex, the highest rates of obesity are observed among non-Hispanic Black women (56.6%) (Ogden et al., 2013).

Obesity has been linked with various negative consequences, including poorer psychosocial, medical, and economic outcomes. Obesity is associated several psychosocial consequences, including increased risk of depression (Luppino et al., 2010), higher rates of stigma and discrimination (Puhl & Heuer, 2009), and greater body image dissatisfaction (Gavin, Simon, & Ludman, 2010). In addition, obesity is associated with increased risk of disability and premature death (Berrington de Gonzalez et al., 2010; Flegal, Graubard, Williamson, & Gail, 2007). Further, the management of obesity is costly. Based on estimates from 2008, obesity is responsible for $147 billion dollars annually in healthcare costs in the U.S., which is a $40 billion dollar increase since 1998 (Finkelstein, Trogdon, Cohen, & Dietz, 2009). Obesity is also associated with an increased risk of various medical conditions, such as type 2 diabetes, cardiovascular disease, and some cancers (Barness, Opitz, & Gilbert-Barness, 2007; Flegal, Carroll, Ogden, & Curtin, 2010; Franken & Muris, 2005; Straub, 2014; Tirosh et al., 2011). In sum, obesity is a highly prevalent condition that has substantial psychosocial, medical, and economic consequences, making it an important public health concern.

Pathophysiology of and Traditional Risk Factors for Obesity

Obesity is thought to result from a combination of genetic, physiological, lifestyle, and environmental risk factors. Genetic factors explain 25-40% of the variance in BMI (Racette, Deusinger, & Deusinger, 2003; Wadden, Brownell, & Foster, 2002). In one study of twins, concordance rates for overweight and obesity were two times higher in monozygotic twins than in dizygotic twins (Stunkard, Foch, & Hrubec, 1986a). Furthermore, a study of adults who were adopted in childhood observed a strong correlation of the adopted adults' BMI with their biological parents' BMIs but not their adoptive parents' BMIs (Stunkard et al., 1986b). However, the increases in the prevalence of obesity since the 1980s occurred too rapidly to be primarily attributable to genetics (World Health Organization, 2000). It has been proposed that genes may interact with the environment, whereby those with a genetic predisposition to develop obesity may do so only when exposed to certain precipitating environmental factors, such as energy-dense diets or sedentary behaviors (Pi-Sunyer, 2002; Ravussin & Bogardus, 2000).

Physiological factors that contribute to obesity include energy balance and neuroendocrine processes. Traditional views of weight regulation postulate that obesity results from a chronic imbalance between energy intake and energy expenditure (Hill, Wyatt, & Peters, 2012; Racette et al., 2003). Energy intake is the fuel we consume in the form of foods and beverages and is measured in calories. Energy expenditure is the energy consumed by bodily functions (e.g., thermogenesis and basal metabolism), informal lifestyle activities (e.g., sitting upright), and formal exercise (e.g., going for a run). When energy intake is greater than energy expenditure, the excess energy intake is converted into triglycerides through a process called lipogenesis and is stored in the adipose tissue (Racette et al., 2003). When energy intake is lower than energy expenditure (e.g., during starvation or dieting), triglycerides stored in the adipose

tissue may be converted back into consumable energy through a process called lipolysis (Racette et al., 2003). When energy intake is greater than energy expenditure over an extended period of time, excess fat storage may occur, contributing to increased body mass and eventual obesity.

Although human and animal models have consistently demonstrated the importance of energy balance, the relationship between food intake and fat storage appears to be more complex. More recent perspectives emphasize the role of diet composition – the proportion of each type of macronutrient consumed (i.e., fat, carbohydrate, and protein) – in the development of obesity. Specifically, high consumption of certain macronutrients, primarily carbohydrates, promotes greater fat storage, increased hunger signaling, and slowed metabolism (Ludwig & Friedman, 2014). These metabolic and endocrine changes may promote changes in energy balance. For instance, increased hunger signaling may lead to increased energy intake, and slowed metabolism may lead to decreased energy expenditure (Ludwig & Friedman, 2014).

Neuroendocrine functioning, particularly related to leptin and insulin dysregulation, has also been implicated in the development of obesity. Leptin is a hormone that is synthesized in the adipose tissue. It is responsible for relaying information regarding satiety (i.e., fullness) to the hypothalamus (Hofbauer, 2002). Individuals with obesity have higher levels of circulating leptin (Considine et al., 1996), and chronically elevated circulating leptin levels cause leptin resistance, whereby the hypothalamus becomes less responsive to the satiety signal (Hofbauer, 2002). Therefore, dysregulation of leptin could lead to some individuals being unable to properly sense fullness, which may result in overeating and excess energy intake. Insulin is a hormone that is secreted by the pancreas after food is consumed. Insulin serves two roles in the regulation of energy balance: (1) it promotes the conversion of energy into triglycerides and (2) it prevents the breakdown of triglycerides for energy consumption (Barness et al., 2007). Similar to leptin,

individuals with obesity produce greater quantities of circulating insulin, which promotes greater fat storage and limits the breakdown of stored fat (Barness et al., 2007), both of which could contribute to greater adiposity.

Finally, environmental and lifestyle factors contribute to the development of obesity by affecting the quality and quantity of foods people consume and the amount and type of physical activity they engage in. In other words, they contribute to an imbalance of energy intake and energy expenditure as well as poorer overall diet quality. Over the last several decades, the overall pattern of dietary intake has changed. Based on data from NHANES between 1971 and 2004, energy intake increased by 434 kilocalories per day in men and 411 kilocalories per day in women (Yancy, Wang, & Maciejewski, 2014). Furthermore, there has been a significant increase in the consumption of energy-dense foods that are high in sugar and fat and low in fiber and other beneficial nutrients (Faulconbridge & Wadden, 2010; Yancy et al., 2014). This profile of diet composition may contribute to increases in energy intake and subsequent development of excess adiposity. In addition to changes in diet composition, environmental factors may contribute to changes in patterns of dietary intake. People are eating more meals away from home, both at fast food and sit-down restaurants (Harnack, Jeffery, & Boutelle, 2000; Smith, Ng, & Popkin, 2013). When food is prepared at home, less time is being spent preparing meals. In the U.S., the amount of time spent cooking declined between 1965 and 1992, with the greatest decreases occurring among low-income respondents (decreased by 41 minutes/day) (Smith et al., 2013). There is also an increased availability of convenience foods (e.g., frozen dinners) (Harnack et al., 2000), which are commonly high in sugar and fat. Evidence also indicates that portion sizes have increased for foods prepared at home and at restaurants (Nielsen & Popkin, 2003). To illustrate, in the U.S., the portion size of a hamburger increased by 97 kilocalories

between 1977 and 1996 (Nielsen & Popkin, 2003). Importantly, these environmental factors contribute to changes in overall diet composition, whereby Americans are eating larger portions of food that are high in fat and sugar, likely contributing to greater energy intake.

Insufficient physical activity and a sedentary lifestyle have also been proposed as lifestyle factors contributing to obesity. Environmental factors of urbanization, changes in transportation, and increased leisure time have been identified as contributors to decreased activity levels (Ahima, 2014). However, physical activity has been shown to account for only 10% of energy expenditure (Barness et al., 2007), and rates of physical activity have remained relatively stable since the 1980s (Westerterp & Speakman, 2008), raising the possibility that that increases in obesity may be predominantly due to changes in food consumption.

Depression as a Novel Risk Factor for Obesity

In addition to the aforementioned traditional risk factors for obesity, psychological factors have received increased attention. One such psychological factor is depression. Findings from a meta-analysis of nine prospective studies indicate that baseline depression significantly predicts future obesity (*OR*= 1.58) (Luppino et al., 2010). In this literature, several biological, psychological, and social mechanisms have been proposed as mechanisms underlying the link between depression and future obesity. Candidate biological mechanisms include hypothalamic–pituitary–adrenal (HPA) axis dysregulation, increased systemic inflammation, and neurotransmitter and neuropeptide dysregulation. Candidate psychosocial mechanisms include dietary behavior, decreased physical activity, greater alcohol use, and greater psychotropic medication use (Hawkins et al., 2015; Luppino et al., 2010; Markowitz, Friedman, & Arent, 2008). In the present study, I plan to focus on one of these factors – dietary behavior – as a candidate mechanism underlying the relationship between depression and future obesity risk.

Dietary Behavior as a Candidate Mechanism Underlying the Depression-to-Obesity Association

The majority of prospective studies in the depression-diet literature examine baseline diet as a predictor of future changes in depression. In these investigations, diet is viewed as a potentially modifiable risk factor for the development of depression. In contrast, strikingly few investigations have examined depression as a predictor of future changes in dietary behavior. This direction is important to examine because diet has been identified as a potential mechanism linking depression to future disease risk, particularly for obesity, type 2 diabetes, and cardiovascular disease (e.g., Elderon & Whooley, 2013; Everson, Maty, Lynch, & Kaplan, 2002; Hawkins et al., 2015). Despite this dearth of prospective evidence, there is an abundance of cross-sectional evidence linking depression to dietary behavior.

In the depression-diet literature, dietary behavior has been operationalized in many ways. In writing a comprehensive examination on depression as a potential predictor of dietary behavior implicated in obesity development, two overarching conceptualizations of dietary behavior emerged: (1) diet composition, comprised of dietary behaviors of total energy intake, macronutrient intake, dietary patterns, and type of food consumed and (2) the cyclic pattern of restriction and overconsumption, composed of the dietary behaviors of binge eating, night eating, dietary restraint, and meal skipping. The present study focuses on one of these overarching conceptualizations: diet composition. In the next sections, I will first define diet composition and then summarize and discuss the empirical evidence on the association of depression with each diet composition factor.

What Is Diet Composition, and How Does It Relate to Obesity?

Diet composition is defined as the relative contribution of macronutrients – fat, carbohydrate, and protein – to energy intake. Energy intake is the total amount of fuel or energy obtained from foods that are consumed and is measured in kilocalories (Whitney & Rolfes, 2013). Macronutrients are nutrients that are converted into energy and consumed by the body as fuel. There are three types of macronutrients – fats, carbohydrates, and proteins (Whitney & Rolfes, 2013). Macronutrients also have subordinating nutrient types. For instance, there are several types of fat, such as saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids (U.S. Department of Agriculture, 2015). Similarly, there are various types of carbohydrates, such as fiber, starches, and sugars (U.S. Department of Agriculture, 2015). Not all macronutrients provide the same amount of energy. For instance, fat is considered to be the most energy-dense macronutrient, as it provides the most energy per gram (Whitney & Rolfes, 2013).

Several aspects of diet composition have been linked with obesity risk. According to the energy balance perspective of weight regulation, energy intake contributes to the development of excess body fat when intake exceeds expenditure (e.g., Hill et al., 2012; Racette et al., 2003). Energy intake is comprised of the total amount of energy provided by each of the macronutrients. In the past, fat was thought to be the most obesogenic of the macronutrients because it has the highest energy density (Bray & Popkin, 1998). However, recent evidence demonstrates that carbohydrates also play a critical role in the development of obesity. Ludwig and Friedman (2014) have proposed that high consumption of carbohydrates promotes increased fat storage, which results in a cascade of metabolic adaptations that increase hunger (and thus energy intake) and decrease energy expenditure, resulting in greater adiposity. Although there is less evidence

linking protein intake to obesity risk, evidence from weight loss trials indicates that a high protein, low energy diet promotes weight loss (Johnston, Tjonn, & Swan, 2004; Noakes, Keogh, Foster, & Clifton, 2005) and helps maintain body weight after weight loss (Lejeune, Kovacs, & Westerterp-Plantenga, 2005; Westerterp-Plantenga, Lejeune, Nijs, van Ooijen, & Kovacs, 2004).

Empirical Evidence on Associations between Depression and Diet Composition Factors

To date, only one prospective study has examined depression as a predictor of change in diet composition over time. In a sample of adults with human immunodeficiency virus (HIV), Isaac et al. (2008) examined the association between new depression onset and diet composition. At each of four visits at an HIV clinic, participants' depression was measured using an abbreviated version of the Center for Epidemiologic Studies-Depression scale (CES-D), and diet composition was measured using three 24-hour dietary recalls. Those with clinically elevated depressive symptoms at Visit 1 were excluded, and new depression cases were identified as individuals who scored in the clinically elevated depressive symptoms range at two consecutive clinic visits. Those who did not meet these criteria were coded as nondepressed. Compared with nondepressed participants (n = 152), newly depressed participants (n = 90) had significantly greater decreases in total energy (-2,341 kcal), fat (-218.5 g), carbohydrate (-236.8 g), and protein (-212.3 g) intake between Visits 1 and 4 (approximately 18 to 24 months later). It is worth noting that this study was conducted in a sample of adults with HIV, who are at increased risk of both depression (prevalence estimates ranging from 22-45%) and decreased appetite (Penzak, Reddy, & Grimsley, 2000). Therefore, the findings may have limited generalizability. In addition, the measure of depressive symptoms was not a baseline measure and did not predict the changes in diet composition (Visits 1 to 4). Therefore, reverse causality is possible – diet changes may have proceeded the incidence of depression.

Numerous cross-sectional studies have investigated the association of depression with indices of diet composition, and the evidence is generally mixed. Briefly, three studies investigated energy intake among adolescents, with each reporting conflicting results. In a sample of 4,734 adolescents in the U.S., depressive symptoms were unrelated to energy intake measured by a self-reported food frequency questionnaire (Fulkerson, Sherwood, Perry, Neumark-Sztainer, & Story, 2004). Furthermore, there was a positive relationship between depressive symptoms and fat intake among boys but not girls (Fulkerson et al., 2004). In another study of 228 adolescents in the U.S., depressive symptoms were positively related to energy intake when energy intake was assessed as calories consumed during a buffet meal (Mooreville et al., 2014). Conversely, among adolescents in Japan (N = 477), those with clinically elevated depressive symptoms had significantly lower energy intake than their nondepressed counterparts (Hyakutake et al., 2016). Three additional cross-sectional studies investigated the association of depression and diet composition among older adults. In a sample of 23 older adults in the U.S. participating in a residential health program, greater depressive symptom severity was associated with greater saturated fat consumption (Anton & Miller, 2005), but data from a sample of 3,999 older adults in China demonstrated an inverse association between depression and total fat intake (Woo et al., 2006). Furthermore, in a sample of 279 older adults in Japan – although depressive symptoms were unrelated to total energy, fat, and protein intake – they were inversely associated with carbohydrate intake in men but not in women (Oishi, Doi, & Kawakami, 2009). In cross-sectional studies involving women only, elevated depressive symptoms have been associated with higher energy intake (Dressler & Smith, 2015), although this association may be stronger among women with obesity (Simon et al., 2008). Another investigation of 196 women with

overweight or obesity in the U.S. reported that depression was not related to calories from fat but was related to calories from saturated fats (Whitaker, Sharpe, Wilcox, & Hutto, 2014).

To summarize, findings from cross-sectional studies of depression and diet composition are notably mixed. There appears to be some evidence of no association between depression and protein intake, as four out of the five studies that investigated protein intake report no relationship (Christensen & Somers, 1996; Davison & Kaplan, 2012; Nanri et al., 2014; Oishi et al., 2009; Woo et al., 2006). For the remaining diet composition factors – total energy, fat, and carbohydrate intake – the evidence is inconsistent. A few studies highlight group differences in the magnitude of depression-diet composition relationships, such as differences by sex (Fulkerson et al., 2004; Oishi et al., 2009) and obesity status (Simon et al., 2008; Whitaker et al., 2014). However, only one of these studies (Simon et al., 2008) formally tested moderation of the depression-diet composition associations. Other studies highlight that depression may be differentially related to sub-categories of macronutrients (e.g., saturated fat) compared to total macronutrient levels (e.g., total fat) (Anton & Miller, 2005; Whitaker et al., 2014).

A key limitation of the depression-diet composition literature is that there is an absence of properly constructed and analyzed prospective studies examining depression as a predictor of changes in diet composition factors over time. Therefore, the directionality of the association has yet to be elucidated, and reverse causality remains a possibility. A second limitation of this literature is the variability in methodology across the studies, which could have contributed to the observed inconsistent findings. Specifically, the studies are notably heterogeneous with respect to the samples (e.g., participants varied by age, nationality, and obesity status) and the measurement of depression (e.g., depressive symptoms severity versus clinically elevated

depressive symptoms) and diet composition (e.g., food frequency questionnaires, 24-hour dietary recalls, and food consumed at a buffet meal).

Potential Moderators of Depressive Symptoms-Diet Composition Associations: Sex and Race

The relationship between depression and diet composition may be moderated by demographic factors, such as sex and race. Several investigations report differences by sex. For instance, among studies examining depression and fat intake, one study reported associations in males but not in females for fat intake (Fulkerson et al., 2004) and carbohydrate intake (Oishi et al., 2009). One possible mechanism contributing to sex differences in depression-diet composition associations is emotional eating, which is eating in response to negative affect. Although depression is positively associated with emotional eating in both men and women (Konttinen, Silventoinen, Sarlio-Lahteenkorva, Mannisto, & Haukkala, 2010b; van Strien, Konttinen, Homberg, Engels, & Winkens, 2016), the prevalence of and behavioral response to emotional eating varies by sex. Specifically, women report higher levels of emotional eating (Konttinen et al., 2010b; van Strien et al., 2016) and have higher rates of depression (Kessler et al., 2005) than men. In addition, when engaging in comfort eating, women prefer sweets and snacks that are energy dense and high in sugar (e.g., chocolate), whereas men prefer meal-type foods (e.g., steak and soup) (Wansink, Cheney, & Chan, 2003). Therefore, in the presence of depression, women may be more likely than men to consume sweets or high-energy foods.

Although no investigation has examined race differences in the depression-diet composition association, indirect evidence raises the possibility of moderation by race. For instance, environmental factors may contribute to race differences in the depression-diet composition association. Depression may be more strongly associated with greater intake of fast

food and convenience foods among non-Hispanic Black individuals than among non-Hispanic White individuals because those foods are more readily available. In studies of the geographical distribution of food availability in the U.S., data indicates that predominantly Black neighborhoods have 63% more fast-food restaurants (Block, Scribner, & DeSalvo, 2004) and have 52% fewer chain grocery stores (Powell, Slater, Mirtcheva, Bao, & Chaloupka, 2007) compared to predominantly white neighborhoods. Having limited access to grocery stores results in shopping for food at convenience stores that tend to sell prepared, high-energy foods and limited fresh produce, while concurrently charging high prices (Larson, Story, & Nelson, 2009). Therefore, in the presence of depression, non-Hispanic Black individuals may be more likely than non-Hispanic White individuals to consume fast food and convenience foods that are higher in total energy, fat, and carbohydrates due to increased accessibility.

The Present Study

The present study will address key gaps in the current depression-diet composition literature. First, there is an absence of properly constructed and analyzed prospective studies examining depression as a predictor of changes in dietary behavior. Among the prospective studies in this literature, all but one examine the reverse direction – dietary behavior as a predictor of future changes in depression. Furthermore, the one prospective study of depression-to-dietary behavior (Isaac et al., 2008) is of limited generalizability and does not rule out possibility of reverse causality. The dearth of depression-to-dietary behavior studies is striking, given that diet is commonly identified as a potential mechanism linking depression to risk of obesity, type 2 diabetes, and cardiovascular disease. Second, only a small number of studies have formally tested whether dietary factors are mediators of the depression-to-future obesity association. The only dietary factors that have been examined in this regard are eating behaviors

(i.e., external eating, emotional eating, and dietary restraint). Specifically, four studies identified emotional eating as a partial mediator of the depression-obesity association (Clum, Rice, Broussard, Johnson, & Webber, 2014; Goldschmidt et al., 2014; Konttinen et al., 2010b; van Strien et al., 2016). Third, few studies have examined sex and no studies have examined race as moderators of depression-dietary behavior associations. Thus, it is unknown whether these associations are stronger or only present in some demographic groups.

The present study will address these important knowledge gaps by achieving the following aims and testing the following hypotheses (see Figure 1):

Aim 1: To examine depressive symptom severity as a predictor of change in seven indices of diet composition – total energy intake, saturated fatty acid intake, monounsaturated fatty acid intake, polyunsaturated fatty acid intake, sugar intake, fiber intake, and protein intake – over time. I hypothesize that greater depressive symptom severity will predict (1) increases in the total energy intake, saturated fatty acid intake, and sugar intake and (2) decreases in fiber intake. I do not expect depressive symptom severity to predict changes in protein intake. I do not have guiding hypotheses for the associations between depressive symptom severity and changes in intake of monounsaturated and polyunsaturated fatty acids, given the lack of studies examining depression and these nutrient types.

Aim 2: To test changes in diet composition factors over time as mediators of the association between depressive symptom severity and change in adiposity over time. I hypothesize that change in diet composition will partially mediate the association between depressive symptom severity and change in adiposity.

Exploratory Aim 3: To explore whether the Aim 2 mediation models are moderated by sex and race. Given that this aim is exploratory, I do not have any guiding hypotheses.

To achieve these aims and test these hypotheses, I will examine data collected as part of the Coronary Artery Risk Development in Young Adults (CARDIA) study. The CARDIA study is well suited for this purpose for two reasons. First, it is a large prospective epidemiologic study of non-Hispanic Black and non-Hispanic White adults in the U.S. Second, it contains measures of diet composition and adiposity over 13 years and a measure of depressive symptom severity that proceeds this follow-up period.

METHODS

Study Design and Participants

The CARDIA study is a multicenter prospective cohort study of lifestyle and psychosocial factors that may influence the development and progression of cardiovascular disease in non-Hispanic Black and non-Hispanic White young adults. At baseline (Year 0; 1985-1986), 5,115 non-Hispanic Black and non-Hispanic White men and women aged 18-30 years were recruited from one of four urban areas: Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California (Friedman et al., 1988). Recruitment was balanced according to race (non-Hispanic Black versus non-Hispanic White), sex (male versus female), age (<25 years versus ≥25 years), and education (high school graduation or less versus more than high school graduation) (Friedman et al., 1988). After baseline, follow-up examinations were conducted 2, 5, 7, 10, 15, 20, and 25 years later, with retention rates of 90%, 85%, 80%, 77%, 72%, 69%, and 68%, respectively (https://www.cardia.dopm.uab.edu/exam-materials2/schedule-of-exams).

Data from Years 5 (1990-1991), 7 (1992-1993), and 20 (2005-2006) were used in the present study, as these are the years that allowed for an examination of baseline depressive symptoms (Year 5) and subsequent 13-year changes in diet composition (Year 7 to Year 20) and waist circumference (Year 7 to Year 20). Of note, depressive symptoms were first assessed in Year 5 but were not assessed in Year 7 when the diet composition data was collected, so concurrent assessment of baseline depressive symptoms and baseline diet composition is not possible.

From the full sample of 5,115 participants, 3,115 (60.9%) participated in all three assessment years included in the present study (Years 5, 7, and 20). To minimize the influence of potential confounders, I applied exclusion criteria. First, I excluded participants who were pregnant (n = 92) or recently pregnant within the past 8 weeks (n = 24) at any of the included assessment years. Currently and recently pregnant women were excluded because (1) pregnancy and the postpartum period are associated with increased depressive symptoms and body weight (Dave, Petersen, Sherr, & Nazareth, 2010; Vesga-Lopez et al., 2008), which could potentially contribute to an overestimation of the true association between depression and weight change in the general population, and (2) waist circumference was not assessed for pregnant women. Second, I excluded participants who had a BMI potentially indicative of anorexia nervosa (<18.5 kg/m^2; n = 94) because depressive disorders, under eating, and weight loss are common in adults with anorexia nervosa (Hudson, Hiripi, Pope, & Kessler, 2007). Including those with anorexia nervosa has the potential to lead to an underestimation of the true association between depression and change in diet composition in the general population. Finally, I excluded respondents who were missing data on key variables, including depressive symptom severity at Year 5 (n = 28), diet composition at Year 7 (n = 64) or Year 20 (n = 309), waist circumference at Year 7 (n = 10) or Year 20 (n = 12), education (n = 2), and physical activity at Year 7 (n = 16) or Year 20 (n = 8). After applying exclusions, I established a cohort of 2,449 adults, which was used in all of the primary analyses.

For sensitivity analyses using BMI as the dependent variable, I additionally excluded participants with missing data for BMI at Year 7 (n = 2) or Year 20 (n = 8). For sensitivity analyses reconducting all analyses after excluding those with prevalent chronic medical conditions of type 2 diabetes, cardiovascular disease, and cancer at baseline, I additionally

excluded participants who endorsed the presence of one or more of those medical conditions at Years 0, 2, 5, or 7 (n = 246). For analyses examining the stability of depressive symptoms over time (Years 5 to 20), I additionally excluded participants missing data on depressive symptoms at Year 20 (n = 51).

Measures

Depressive Symptoms

At Year 5, the Center for Epidemiologic Studies-Depression Scale (CES-D) was administered to measure depressive symptom severity (Radloff, 1977). The CES-D is a 20-item, self-report measure that asks participants how often they experienced symptoms of depression over the past week. Response options are: "rarely or none of the time;" "some of the time;" "much of the time;" or "most of the time" (see Figure 2). Scores for each item range from zero to three, and four items are reverse-scored (items 4, 8, 12, and 16). A continuous CES-D Total score was computed by summing the values for each of the 20 items, with possible scores ranging from 0 to 60. Higher total scores represent higher depressive symptom severity. Similarly, CES-D Total was computed for Year 20 for use in analyses examining stability of depressive symptoms over time (see Stability Analyses section).

The CES-D is a reliable and valid measure of depressive symptoms. The CES-D has good test-retest reliability (r = .51-.70 over an interval of 2 weeks to 8 weeks; r = .32-.49 over an interval of 12 months), and its internal consistency is good to excellent, with Cronbach's alpha values of 0.85 in a general population sample and 0.90 in a psychiatric patient sample (Radloff, 1977; Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977). CES-D Total scores have

been found to have moderate correlations with symptom ratings by clinicians and other self-reported measures of depressive symptoms, indicating good concurrent validity (Radloff, 1977).

Adiposity

During all examination years, measurement of waist circumference was obtained by CARDIA personnel during the anthropometry portion of the examination. Data from Years 7 and 20 were used in the present study. Waist circumference was measured using a Gulick II 150 cm anthropometric tape in Year 7 and a Gulick II Plus 300 anthropometric tape in Year 20, both of which allow for standardization of the tension of the measuring tape to ensure accurate measurement. Waist circumference was recorded in centimeters.

Although both waist circumference and BMI data are available in the CARDIA study, waist circumference was the dependent variable in the Aim 2 analyses. Waist circumference is likely a more relevant measure of health-related adiposity compared to BMI because it is (a) strongly and independently linked to cardiometabolic diseases and associated risk factors and (b) may be a more direct measure of health-related adiposity (i.e., central adiposity; see The Obesity Problem section for details). However, given that BMI is the widely-used index of overweight and obesity, sensitivity analyses were conducted with BMI as the dependent variable (see Sensitivity Analyses section). At Years 7 and 20, BMI was derived from measurements of height and weight obtained from the anthropometry examination. BMI was computed as weight in kilograms divided by height in meters squared.

Diet Composition

Diet composition was measured using the Diet History Questionnaire, which was administered in Years 0, 7, and 20. Because this study seeks to examine baseline depressive

symptoms (Year 5) as a predictor of subsequent changes in diet composition factors, dietary data was derived from dietary assessments for Years 7 and 20 only. The Diet History Questionnaire is a comprehensive food frequency questionnaire that asks about typical dietary intake over the past month. It is designed to provide accurate and reliable data on typical nutrient intake (e.g., total energy intake) (McDonald et al., 1991). Participants were asked whether they consumed any of 100 food types. For positive responses, they were asked follow-up questions related to the portion size and frequency of consumption of each food type. Cue cards were used to indicate the type of responses required and to facilitate recall of certain food types. Food models, measuring cups, and spoons were used to aid in the estimation of portion sizes.

The Diet History Questionnaire was used to determine the following diet composition variables: total energy intake, saturated fatty acid intake, polyunsaturated fatty acid intake, monounsaturated fatty acid intake, fiber intake, sugar intake, and protein intake. Nutrition values are derived using a database from the Nutrition Coordinating Center at the University of Minnesota (McDonald et al., 1991). This database is based on the U.S. Department of Agriculture's Nutrient Database and other data obtained from food manufacturers. For Years 7 and 20, values for six of the seven diet composition factors – total energy intake, saturated fatty acid intake, monounsaturated fatty acid intake, polyunsaturated fatty acid intake, fiber intake, and protein intake – were derived using this database. The seventh diet composition factor – sugar intake – was computed as the sum of intake of the following: glucose, fructose, galactose, lactose, and sucrose. For each diet composition factor, I created a residualized 13-year change variable by regressing the Year 20 diet composition variable (winsorized) on the Year 7 diet composition variable (winsorized) and saving the standardized residuals in SPSS.

The Diet History Questionnaire (DHQ) has been found to be a reliable and valid measure of diet composition. There is evidence of good test-retest reliability across two administrations of the Diet History Questionnaire one month apart in a subsample of 128 CARDIA participants at Year 0 (Liu et al., 1994). There is also evidence of adequate concurrent validity between the DHQ and the average of seven 24-hour dietary recalls, although variability in nutrient intakes appears to be larger among non-Hispanic Black participants than among non-Hispanic White participants (Liu et al., 1994).

Covariates

The following demographic factors were included as covariates: age (years), sex (0 = male, 1 = female), race (0 = non-Hispanic White, 1 = non-Hispanic Black), and education (grade). Demographic factors of age, sex, and race were self-reported at Year 0 during the recruitment telephone call. Although participants could endorse numerous racial/ethnic backgrounds – Hispanic, non-Hispanic Black, non-Hispanic White, American Indian or Alaskan Native, or Asian Pacific Islander – only respondents who endorsed non-Hispanic Black or non-Hispanic White were enrolled in CARDIA. Education was assessed at Year 5 via the Sociodemographic Questionnaire with the item, "What is the highest grade of regular school you have completed?", and response options ranged from 1 to 20+, whereby grades 1-6 represent elementary school, 7-8 represent junior high school, 9-12 represent high school, 13-16 represent college, and 17-20+ represent graduate school. The education assessment at Year 5 was selected to reflect the most recent level of education at baseline in the present study.

In addition to demographic factors, additional covariates included prevalent and incident select medical conditions (i.e., cardiovascular disease, type 2 diabetes, and cancer), incident pregnancy, and physical activity. Prevalent and incident medical conditions were included as

covariates because these chronic conditions are potential confounders of depression-diet composition-adiposity relationships. The diagnosis of each of these conditions is associated with increased rates of depression, changes in dietary intake, and increased rates of obesity (Barness et al., 2007; Doyle et al., 2006; Flegal et al., 2010; Forman-Hoffman et al., 2008; Franken & Muris, 2005; Ley, Hamdy, Mohan, & Hu, 2014; Mente, de Koning, Shannon, & Anand, 2009; Straub, 2014; Tirosh et al., 2011). In the CARDIA study, medical conditions were assessed at each examination year using the interviewer-administered Medical History Questionnaire. Cardiovascular disease was assessed with the item, "Has a doctor or nurse ever said you have heart problems?" Diabetes was assessed with the item, "Has a doctor or nurse ever said you have diabetes (high sugar in blood or urine)?" Cancer was assessed with the item, "Has a doctor or nurse ever said you have cancer or a malignant tumor?" To identify prevalent cases for each medical condition, participants who responded "yes" in one or more of the baseline examination years (Years 0, 2, 5, and 7) were coded as having the selected chronic medical condition and those who responded "no" at all four time-points were coded as not having the condition (0 = no; 1 = yes). To identify incident cases for each medical condition, participants who were free of the condition at baseline and who respond "yes" at any time-point during the follow-up period (Years 10, 15, or 20) were coded as an incident case of that condition; those with the condition present at baseline and those free of the condition at baseline and who responded "no" at all three follow-ups were coded as not being an incident case of that condition (0 = no; 1 = yes).

Regarding adjustment for incident pregnancy, data from CARDIA indicates that, compared to women who have not had a pregnancy, women with one or more pregnancies had significantly higher waist circumference 5 years later (Gunderson et al., 2004). Given the influence of pregnancy on waist circumference, incident pregnancy could lead to greater

increases in waist circumference in women than in men. In CARDIA, the number of pregnancies was assessed in the Follow-Up Questions for Pregnancy Questionnaire. Participants were asked "Altogether, how many times have you been pregnant?" Participants who reported a greater number of pregnancies at Year 20 than at Year 7 were coded as "yes" for incident pregnancy; all others were coded as "no" for incident pregnancy (0 = no; 1 = yes).

Physical activity was assessed using the Physical Activity Questionnaire. In this interviewer-administered questionnaire, participants were asked about the frequency of participation in 13 types of physical activities (e.g., jogging, swimming, or taking a walk) during the past 12 months. For Years 7 and 20, total activity scores were computed into exercise units by multiplying the frequency of participation by the intensity of the activity and then summing across all activities. I created a residualized 13-year change variable for physical activity by regressing the year 20 physical activity variable on the Year 7 physical activity variable and saving the standardized residuals in SPSS.

Potential Moderators

I conducted exploratory analyses examining sex (0 = male, 1 = female) and race (0 = non-Hispanic White, 1 = non-Hispanic Black) as moderators of the Aim 2 mediation models. The CARDIA study is well-suited to evaluate moderation by sex and race, as recruitment was intentionally balanced to obtain equal numbers of men versus women and non-Hispanic White versus non-Hispanic Black participants.

Analyses

Data Cleaning and Reduction

Frequencies were examined to assess for out-of-range values. Across all variables, except for height at Year 20, no out-of-range values were identified. For height at Year 20, two values were extremely low (71.5 and 107.5 cm) and inconsistent with values for height at Years 5 and 7 (both participants had a height of 170.5 cm at Years 5 and 7). Values were determined to be data entry errors and were corrected to reflect height obtained during Years 5 and 7. All relevant variables were calculated, and checks for computation errors were performed. All outliers (*z*-scores ≥ 3.0) in the dataset were identified. At Year 5, CES-D Total had outliers ($n = 32$). At Year 7, the following variables had outliers: waist circumference ($n = 28$), total energy intake ($n = 44$), saturated fatty acid intake ($n = 38$), monounsaturated fatty acid intake ($n = 42$), polyunsaturated fatty acid intake ($n = 49$), fiber intake ($n = 23$), sugar intake ($n = 56$), protein intake ($n = 39$), and physical activity ($n = 35$). At Year 20, the following variables had outliers: waist circumference ($n = 22$), total energy intake ($n = 44$), saturated fatty acid intake ($n = 45$), monounsaturated fatty acid intake ($n = 40$), polyunsaturated fatty acid intake ($n = 42$), fiber intake ($n = 29$), sugar intake ($n = 32$), protein intake ($n = 38$), and physical activity ($n = 31$). For variables of CES-D Total, waist circumference, and physical activity, outliers were not deleted or modified for the following three reasons: 1) these cases did not result in non-normal distributions, 2) some z scores ≥ 3.0 are expected in large samples, and 3) these cases are likely accurate values (Tabachnick & Fidell, 2001). For all continuous variables, normality of the distributions was assessed, with non-normality defined as skewness > 3.0 or kurtosis > 10.0 (Kline, 2004). All variables other than the diet composition variables were normally distributed. Given that the seven indices of diet composition at both Years 7 and 20 had non-normal

distributions and contained extreme outliers, values were winsorized to 3 standard deviations of the mean. Re-assessment of normality indicated that the winsorized diet composition variables had normal distributions (skewness < 3.0 or kurtosis < 10.0).

Software Used for Statistical Analyses

All primary analyses were conducted using a macro called PROCESS (Hayes, 2013) in SPSS statistical software (Version 24). PROCESS is a computational tool for path analysis based mediation and moderation that utilizes a bootstrapping approach to effect size estimation (Hayes, 2013; Preacher & Hayes, 2004). Bootstrapping involves resampling with replacement by repeatedly taking subsamples from the original sample and computing the effect size within each subsample. This process is repeated thousands of times to estimate the shape of the sampling distribution for the effect size. This distribution is used to determine upper and lower estimates of the effect size, from which a confidence interval is computed. There are three key strengths to using the PROCESS bootstrapping approach. First, it uses one statistical test to determine the interdict effect, which is advantageous compared to causal steps approaches, which require multiple tests to determine mediation (Hayes, 2013). Second, it does not require a normal sampling distribution, which allows for testing of effects in the presence of non-normality (Hayes & Preacher, 2014; Hayes & Scharkow, 2013; Preacher & Hayes, 2004). Third, it can be used in smaller samples because bootstrapping confers greater statistical power while simultaneously minimizing the type I error rate (Hayes & Preacher, 2014; Hayes & Scharkow, 2013).

To simultaneously address Aims 1 and 2, I ran seven mediation models. Specifically, I used PROCESS Model 4 to separately examine 13-year change in the seven diet composition variables as mediators of the association between baseline CES-D Total and 13-year change in

waist circumference. To address Aim 3, I ran 14 moderated mediation models using PROCESS Model 7 to separately examine sex and race as moderators of the seven mediation models described above.

Mediation Analyses (Aims 1 and 2)

To examine CES-D Total as a predictor of 13-year change in diet composition (Aim 1) and to examine the 13-year change in diet composition as a mediator of the association between CES-D Total and 13-year change in waist circumference (Aim 2), PROCESS Model 4 was used (see Panel a of Figure 3). CES-D Total score (z-scored) was entered as the predictor variable (X), Year 20 waist circumference (z-scored) was entered as the criterion variable (Y), and Year 7 waist circumference (z-scored) was included as a covariate to produce a residualized change criterion variable. The 13-year standardized residualized change variable for each diet composition factor was entered separately as the mediator variable (M) in seven separate models. Each model included adjustment for covariates (age; sex; race; education; Year 7 waist circumference; prevalent and incident cardiovascular disease, type 2 diabetes, and cancer; incident pregnancy; and 13-year change in physical activity). A 95% confidence interval using 10,000 bootstrap resamples was computed. I examined the effect of baseline CES-D Total on 13-year change in the diet composition variable, with significance indicated as $p < .05$ (Aim 1). I was also able to conclude that 13-year change in the diet composition variable significantly mediated the relationship between CES-D Total and 13-year change in waist circumference if the upper and lower bounds of the 95% confidence interval for the indirect effect did not include the value of zero (Aim 2).

Moderated Mediation Analyses (Aim 3)

To explore whether sex and race moderate the association between baseline CES-D Total and 13-year change in diet composition in the aforementioned mediation models, Hayes' PROCESS macro for Model 7 was used (see Panel b of Figure 3) (Hayes, 2013). Each moderator (W) was modeled separately as a modifier of the association between CES-D Total (X) and the 13-year change in the diet composition factor (M) in a mediation model in which 13-year change in the diet composition variable (M) serves as a mediator between CES-D Total (X) and Year 20 waist circumference (Y), adjusting for the covariates (age; sex; race; education; Year 7 waist circumference; prevalent and incident cardiovascular disease, type 2 diabetes, and cancer; incident pregnancy; and 13-year change in physical activity). Similar to the Aims 1 and 2 models, 95% confidence intervals using 10,000 bootstrap resamples were computed. I was able to conclude that a variable is a significant moderator if the upper and lower bounds of the index of moderated mediation did not include the value of zero. Given that moderated mediation was detected for the model in which sex was entered as the moderator and 13-year change in protein intake was entered as the mediator, I re-conducted the mediation model for 13-year change in protein intake stratified by sex.

Sensitivity Analyses

I ran two sets of sensitivity analyses. First, because BMI is the most widely-used index of overweight and obesity, I conducted sensitivity analyses with 13-year change in BMI as the dependent variable. Second, I conducted sensitivity analyses after excluding participants with prevalent cardiovascular disease, type 2 diabetes, and cancer. These models seek to address concerns that these conditions may be operating as confounders of the relationships of interest.

Stability Analyses

An underlying assumption of the models tested in this study is that depressive symptom severity and diet composition remain relatively stable over time. To test this assumption, I analyzed the stability of depressive symptoms and diet composition over time and explored moderation of this stability by age, sex, and race. To test for temporal stability of depressive symptoms, I conducted a linear regression analysis with Year 5 CES-D Total predicting Year 20 CES-D Total. To test for moderation, I created three interaction terms: (1) Year 5 CES-D Total (*z*-scored) *x* age (*z*-scored); (2) Year 5 CES-D Total (*z*-scored) x sex; and (3) Year 5 CES-D Total (*z*-scored) x race. These interaction terms were simultaneously entered into a linear regression model with Year 5 CES-D Total (*z*-scored), age (*z*-scored), sex, and race predicting the Year 20 CES-D Total (*z*-scored) variable. I conducted parallel stability analyses and moderation analyses for each of the seven diet composition variables, with Year 7 of the diet composition variable predicting Year 20 of the diet composition variable. In the presence of significant interaction terms, models were re-run stratified by the appropriate moderator.

RESULTS

Characteristics of Participants

Participant characteristics for the final sample of 2,449 non-Hispanic Black and White adults are presented in Table 1. Ages at baseline (Year 5) ranged from 26 to 45 years with a mean of 35.3 years. There were approximately equal numbers of men and women as well as non-Hispanic Black and non-Hispanic White participants, as would be expected given the CARDIA study's balanced recruitment by sex and race. At Year 5, the mean level of education was 14.7 years and 4.6% of the sample obtained less than a high school education.

Descriptive statistics for depressive symptom severity, adiposity, diet composition, and physical activity are shown in Table 2. Participants mean depressive symptoms score at Year 5 fell in the subclinical range (CES-D Total <16) (Radloff, 1977). At Year 7, waist circumference was below the high-risk range for men (>102 cm represents high risk) and women (>88 cm represents high risk). At Year 20, waist circumference was below the high-risk range for men but was slightly above the high-risk cut point for women. At Years 7 and 20, BMI fell into the overweight range (25-29.9 kg/m^2). Participants consumed more total energy at Years 7 and 20 than is recommended in USDA Dietary Guidelines (2,000 calories/day) (U.S. Department of Agriculture, 2015). Total energy intake in this sample was also higher than national averages of intake among U.S. adults based on data from the NHANES from 1999-2000 (Wright, Wang, Kennedy-Stephenson, & Ervin, 2003). This difference may be attributable to sample characteristics. For instance, the sample is comprised of young- and middle-aged adults, who tend to have higher energy intake than older adults (Morley, 2001). Similar to total energy, intake of all other diet composition factors is higher than national averages for intake (Ervin &

Ogden, 2013; National Center for Health Statistics, 2017; U.S. Department of Agriculture, 2008). Compared to prior studies of the CARDIA Physical Activity History questionnaire, participants in the current study are obtaining adequate physical activity (≥ 300 exercise units) (Parker, Schmitz, Jacobs, Dengel, & Schreiner, 2007).

The prevalence and incidence of potentially confounding medical conditions are reported in Table 3. At baseline, <1% of participants had cardiovascular disease, <4% had diabetes, and <6% had a history of cancer. Over the 13-year follow-up, 4.5% of participants developed cardiovascular disease, 6.9% developed diabetes, and 4.5% developed cancer. Over the 13-year follow-up, 14.3% of women had at least one pregnancy.

Mediation Analyses (Aims 1 and 2): Examining Change in Diet Composition Factors as Mediators between Baseline Depressive Symptoms and Change in Waist Circumference

To simultaneously examine (1) depressive symptom severity as a predictor of change in seven diet composition factors over time (Aim 1) and (2) changes in diet composition factors over time as mediators of the association between depressive symptom severity and change in adiposity over time (Aim 2), a series of mediation models were tested in using PROCESS model 4 (Hayes, 2013). In seven separate models, each residualized 13-year change in diet composition variable was examined as a mediator (M) between baseline CES-D Total (X) and 13-year change in waist circumference (Y). All models were adjusted for age; sex; race; education; Year 7 waist circumference; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; and 13-year change in physical activity.

Figure 4 depicts the results of the seven mediation models. In all models, greater baseline CES-D Total predicted greater 13-year increases in waist circumference (path *c*: $\beta = 0.032$, $p = .006$). Regarding Aim 1, greater baseline CES-D Total also predicted greater 13-year increases in

fiber intake (path *a*: β = 0.040, p = .0496) and protein intake (path *a*: β = 0.059, p = .004), and the association between greater baseline CES-D Total and 13-year change in total energy intake fell just short of significance (path *a*: β = 0.040, p = .054). CES-D Total did not predict changes in intake of the remaining diet composition factors of saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, and sugar (all ps $\geq$ .129). In sum, greater baseline depressive symptoms predicted increases in protein and fiber intake, and there is a trend for greater baseline depressive symptoms predicting increases in total energy intake.

With respect to 13-year change diet composition factors predicting 13-year change in waist circumference (path *b*), increases in total energy intake (path *b*: β = 0.034, p = .003), saturated fatty acid intake (path *b*: β = 0.032, p = .005), monounsaturated fatty acid intake (path *b*: β = 0.026, p = .025), sugar intake (path *b*: β = 0.029, p = .012), and protein intake (path *b*: β = 0.033, p = .005) predicted greater 13-year increases in waist circumference. Changes in polyunsaturated fatty acid intake and fiber intake were not related to changes in waist circumference (both ps $\geq$ .155). In all models, the direct effect of baseline CES-D Total on change in waist circumference remained significant after accounting for diet composition factors as mediators (path *c*s*:* βs = 0.030-0.032, *p*s = .005-.009).

Concerning Aim 2, tests of mediation (*ab*) revealed that 13-year change in total energy intake (indirect effect = 0.001, *95% CI* = 0.0001-0.004) and protein intake (indirect effect = 0.002, *95% CI* = 0.0004-0.005) partially mediated the association between baseline CES-D Total and 13-year change in waist circumference. Mediation was not observed for the five other diet composition factors (all other indirect effect *95% CI*s included zero).

Moderated Mediation Analyses (Aim 3): Exploring Sex and Race as Moderators of the Mediation Model

To explore whether the Aim 2 mediation models are moderated by sex and race, a series of exploratory moderated mediation models were tested using PROCESS model 7 (Hayes, 2013). In these 14 moderated mediation models, sex and race were entered separately as moderators (W) of the association between baseline CES-D Total (X) and the diet composition factor (M) in the Aim 2 mediation models. There was evidence of moderated mediation of CES-D Total by sex for protein intake (index of moderated mediation = 0.004, *95% C I* = 0.001-0.010) but not for the remaining six diet composition factors (index of moderated mediation *95% CI*s included zero; see Table 4). There was also no evidence of moderated mediation of CES-D Total by race for any of the seven diet composition factors (index of moderated mediation *95% CI*s included zero). Importantly, the one model in which significant moderated mediation was detected should be interpreted with caution due to elevated risk of type 1 error, as 14 exploratory models were tested to address Aim 3.

To further probe the significant moderated mediation model, models stratified by sex were conducted. As depicted in Figure 5, in men, greater baseline CES-D Total predicted 13-year increases in waist circumference (path *c*: β = 0.054, p = .003) and protein intake (path *a*: β = 0.110, p = .004), and the direct effect of CES-D Total on 13-year change in waist circumference remained significant after accounting for 13-year change in protein intake (path *c'*: β = 0.052, p = .004). However, 13-year change in protein intake was unrelated to 13-year change in waist circumference (path *b*: β = 0.014, p = .319). Conversely, in women, baseline CES-D Total was unrelated to 13-year change in waist circumference (path *c*: β = 0.021, p = .161) and 13-year change in protein intake (path *a*: β = 0.027, p = .246), whereas 13-year increases in protein intake

were associated with 13-year increases in waist circumference (path *b*: β = 0.061, p = .001). In both men and women, there was no evidence of mediation by 13-year change in protein intake (index of moderation *95% CI*s included zero), although this may be due, in part, to lower power in these stratified analyses. Taken together, although 13-year change protein intake did not partially mediate the relationship between baseline depressive symptoms and 13-year change in waist circumference in either sex, the relationship between baseline depressive symptoms and 13-year change in protein intake was stronger in men than in women.

Sensitivity Analyses

Two sets of sensitivity analyses were conducted. First, because BMI is the widely-used index of overweight and obesity, I conducted sensitivity analyses with 13-year change in BMI as the dependent variable (n = 2,439). In general, the pattern of results related to Aims 1, 2, and 3 remained the same with two notable exceptions (see Figures 6 and 7): (1) baseline CES-D Total did not predict 13-year change in BMI (path *c*: β = 0.019, p = .102) and (2) greater baseline CES-D Total predicted 13-year increases in total energy intake (path *a*: β = 0.042, p = .043), a finding that was a nonsignificant trend in the main analyses. Second, I re-conducted analyses after excluding those with prevalent cardiovascular disease, diabetes, and cancer (n = 2,203). In general, the pattern of results related to Aims 1, 2, and 3 remained the same with two notable exceptions (see Figures 8 and 9): (1) 13-year change in total energy intake no longer partially mediated the association between baseline CES-D Total and 13-year change in waist circumference (indirect effect = 0.001, *95% CI* = -0.0001-0.003), and (2) only a trend was observed for baseline CES-D total predicting 13-year change in fiber intake (β = 0.038, p = .081).

Stability Analyses

Linear regression analyses were conducted to examine the stability of depressive symptoms from Years 5 to 20 and the stability of diet composition factors from Years 7 to 20, exploring whether age, sex, and race moderate these associations. Regarding the stability of depressive symptoms over time, analyses demonstrate a medium correlation between Year 5 and Year 20 CES-D Total (r = 0.45) (Cohen, 1992), and the model explains 20% of the variance in depression at Year 20 (see Table 5). This finding is consistent with prior studies of the long-term temporal stability of depression, which report medium to large correlations between depressive symptom severity levels over 3- to 8-year follow-up periods (Lovibond, 1998; Wetherell, Gatz, & Pedersen, 2001). Specifically, one study examining temporal stability of depression and anxiety over time in a sample of Swedish adults indicates that depression, measured using the CES-D, remained stable over both 3- and 6-year follow-ups (rs = 0.52-0.55) (Wetherell et al., 2001). Similarly, a second study examining the temporal stability of depression over time in a sample of university students indicated that depression, measured using the Depression Anxiety Stress Scales, remained stable over 3- to 8-year follow-ups (rs = 0.19-0.47) (Lovibond, 1998). Moreover, the stability of CES-D Total in the present study is approaching the magnitude of test-retest correlations of measures of stable personality traits. To illustrate, a prior study of the stability of personality traits using the NEO Personality Inventory indicate large correlations (r = .51-.84) over a 7-year follow-up period (Costa & McCrae, 1992). In sum, there is evidence for adequate stability of depressive symptom severity over the 13-year follow-up period in the present study.

Moderation was detected for Year 5 CES-D Total by race (interaction term β = -0.11, p = .004; see Table 5) and demonstrated that the association between Year 5 and Year 20 CES-D

Total was stronger among non-Hispanic Blacks (β = 0.49, p < .001, r = 0.49, R^2 = 0.24) than non-Hispanic Whites (β = 0.38, p < .001, r = 0.38, R^2 = 0.14; see Table 8). There was no evidence of moderation by age or sex (ps ≥ 0.148). To my knowledge, no other study has examined differences in temporal stability of depression by race, and the underlying mechanisms to explain this difference are uncertain at this time.

Regarding the stability of diet composition factors over time, analyses revealed medium to large correlations between the Year 7 and Year 20 diet composition factors (rs = 0.40-0.58), and the models accounted for 16-34% of the variance in Year 20 of the respective diet composition factors, suggesting good stability over time in intake of each diet composition factor. Moderation by age was not detected for any of the models (all ps ≥ .115). Moderation by sex was detected for saturated fatty acid intake only (interaction term β = 0.08, p = .038; all other ps ≥ .059; see Table 6). Analyses stratified by sex reveal that the association between Year 7 and Year 20 saturated fatty acid intake is stronger among men (β = 0.53, p < .001, r = 0.53, R^2 = 0.28) than women (β = 0.43, p < .001, r = 0.43, R^2 = 0.18; see Table 7). Moderation by race was detected for total energy intake (interaction term β = -0.10, p = .006), saturated fatty acid intake (interaction term β = -0.13, p < .001), monounsaturated fatty acid intake (interaction term β = -0.14, p < .001), polyunsaturated fatty acid intake (interaction term β = -0.12, p = .002), and protein intake (interaction term β = -0.08, p = .015) but not for fiber intake (p = .052) and sugar intake (p = .530). As depicted in Table 8, analyses stratified by race reveal that the association between Year 7 and Year 20 for diet composition factors of total energy, saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, and protein intake were stronger in non-Hispanic Blacks than non-Hispanic Whites. In sum, there is evidence of stability in the intake of all diet composition factors over time. There is also evidence of moderation by sex for saturated

fatty acid intake, suggesting that the stability of this association is stronger among men than women. Most notably, there is evidence of moderation by race for the majority of diet composition factors (i.e., total energy, saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, and protein intake), with stronger stability in consumption over time among non-Hispanic Blacks than non-Hispanic Whites.

DISCUSSION

Summary of Results

The aims of the present study were: (1) to examine depressive symptom severity as a predictor of 13-year change in seven diet composition factors over time, (2) to test 13-year change in diet composition factors as mediators of the association between depressive symptom severity and 13-year change in adiposity, and (3) to explore whether the Aim 2 mediation models are moderated by sex and race. In mediation models, greater depressive symptom severity predicted 13-year change in waist circumference. Related to Aim 1, my hypotheses that greater baseline depressive symptom severity would predict increases in the total energy intake, saturated fatty acid intake, and sugar intake; predict decreases in fiber intake; and be unrelated to protein intake were generally not supported. In mediation models, a trend was observed for greater depressive symptom severity predicting 13-year increases in total energy intake; however, depressive symptom severity was unrelated to change in saturated fatty acid intake and sugar intake. Moreover, greater depressive symptom severity predicted 13-year increases in both protein intake and fiber intake, which were hypothesized to have null and inverse associations, respectively.

Related to Aim 2, my hypothesis that 13-year change in diet composition factors would partially mediate the association between baseline depressive symptom severity and 13-year change in adiposity was partially supported, as 13-year increases in total energy intake and protein intake were found to be partial mediators. Change in intake of the remaining diet composition factors of saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty

acids, fiber, and sugar did not mediate the depressive symptom-waist circumference change association.

Given the exploratory nature of Aim 3, I did not propose any moderated mediation hypotheses. Across the 14 models tested, only one instance of moderated mediation was detected, in which sex moderated the association between baseline depressive symptom severity and 13-year change in protein intake in the mediation model. Mediation models stratified by sex revealed that the relationship between baseline depressive symptoms and 13-year change in protein intake was stronger in men than in women. Other paths in this mediation model also varied by sex such that (1) depressive symptom severity predicted 13-year increases in waist circumference in men but not in women and (2) increases in protein intake were associated with 13- year increases in waist circumference in women but not in men. In both men and women, 13-year change in protein intake did not mediate the depressive symptom-waist circumference change association. Mediation may not have been detected due to decreased statistical power in these stratified analyses (*n* for men = 1,127; *n* for women = 1,322). Importantly, results from these moderated mediation analyses should be interpreted with caution due to elevated risk of type 1 error, as 14 exploratory models were tested to address Aim 3. In total, the Aim 3 analyses suggest that the associations observed in Aims 1 and 2 generally remain consistent across sex and race groups.

Fit with Existing Literature

To my knowledge, this is the first study to examine changes in dietary factors over time as mediators of the association between depressive symptom severity and change in adiposity over time and to explore sex and race as moderators of this mediation model. However, other researchers have examined specific pathways in my mediation models.

Regarding path a (baseline depression predicting changes in diet composition over time), only one study has examined this prospective association (Isaac et al., 2008), and my results contradict the findings of that study. In a sample of adults with HIV, Isaac et al. (2008) report that, compared to nondepressed participants, newly depressed participants had greater decreases in total energy, fat, carbohydrate, and protein intake over the 18- to 24-month follow-up period. In contrast, I found that greater depressive symptom severity predicted increases in intake of protein and fiber, and a similar trend was observed for total energy intake. Inconsistencies in study findings may be attributable to differences in the study samples. Isaac et al. (2008) used a sample of adults with HIV, who are at increased risk of both depression and decreased appetite (Penzak et al., 2000). Therefore, among adults with HIV, decreased appetite may be associated with decreased dietary intake leading to decreased intake of a variety of diet composition factors. This pathway may explain the link between new-onset depression and decreased intake observed in Isaac et al. (2008). However, this finding may be unique to adults with HIV, may be of limited generalizability, and may not replicate in samples more representative of the U.S. population, as was observed in the present study.

Given the paucity of research examining depression as a predictor of prospective changes in diet composition factors over time, it is also important to consider my findings in relation to the existing cross-sectional evidence. My findings that depressive symptom severity predicted 13-year increases in protein intake and that 13-year changes in protein intake partially mediated the depressive symptoms-waist circumference change association is inconsistent with prior research on depression and protein intake. Specifically, four out of the five prior studies of depression and protein intake report no relationship (Christensen & Somers, 1996; Davison & Kaplan, 2012; Nanri et al., 2014; Oishi et al., 2009; Woo et al., 2006). Existing cross-sectional

evidence linking depression to the other diet composition variables – total energy, fat, and carbohydrate intake – is mixed. The abundance of mixed evidence highlights the need for rigorous studies examining prospective associations between depression and diet composition factors in larger, representative samples. The present study adds to this literature by helping to address this need.

Regarding path b (associations between 13-year change in diet composition factors and 13-year change in waist circumference), the observed relationships are consistent with the prior literature (Bray & Popkin, 1998; Hill et al., 2012; Ludwig & Friedman, 2014; Racette et al., 2003), with increases in total energy intake, saturated fatty acid intake, monounsaturated fatty acid intake, and sugar intake being associated with increases in waist circumference. However, changes in protein intake were positively associated with changes in waist circumference, which is inconsistent with the limited evidence from weight loss trials indicating that a high protein, low energy diet promotes weight loss (Johnston et al., 2004; Noakes et al., 2005) and helps maintain body weight after weight loss (Lejeune et al., 2005; Westerterp-Plantenga et al., 2004). It is possible that this inconsistent finding is driven by greater overall intake rather than intake of specific nutrients, as greater overall intake has the potential to contribute to greater protein intake and increased waist circumference over time.

Regarding path c (baseline depression predicting 13-year change in waist circumference), the results of the present study are consistent with meta-analytic findings indicating that baseline depression significantly predicts the subsequent development of obesity, defined as BMI $\geq$ 30 mg/m^2 (*OR*= 1.58) (Luppino et al., 2010). Notably, in the present study, mediation models stratified by sex demonstrated that depressive symptom severity predicted 13-year change in waist circumference and BMI in men but not in women. This finding is inconsistent with prior

meta-analytic findings that sex does not moderate the depression-to-obesity pathway (Luppino et al., 2010). Furthermore, among the few studies that have reported moderation by sex, depression was more strongly predictive of obesity among women than men (Hasler et al., 2005; Rhew et al., 2008; Richardson et al., 2003). At this time, it is unclear why the present study's findings with regard to sex differences in the depression-to-obesity pathway are inconsistent with prior literature.

Although no study has examined diet composition factors as mediators between baseline depressive symptoms and adiposity change over time, inferences can be taken from literature examining mediation of this association by emotional eating. Emotional eating is defined as eating in response to emotional arousal such as negative affect (van Strien, Frijters, Bergers, & Defares, 1986). Among people high in emotional eating, eating may reduce negative affect, thus making it a candidate factor to examine in relation to depression. Numerous cross-sectional studies report that greater depressive symptoms are associated with greater emotional eating (Clum et al., 2014; Goldschmidt et al., 2014; Konttinen et al., 2010b; van Strien et al., 2016) and that emotional eating partially mediates the depression-adiposity relationship (Clum et al., 2014; Goldschmidt et al., 2014; Konttinen et al., 2010b). Therefore, emotional eating may partially account for the association between depression and obesity. Importantly, emotional eating is associated with higher consumption of certain types of foods, particularly energy-dense sweets and high-fat snacks (Konttinen, Mannisto, Sarlio-Lahteenkorva, Silventoinen, & Haukkala, 2010a), which may contribute to specific profiles of diet composition intake (i.e., higher intake of sugar and saturated fat). Given this prior evidence, I was surprised that depressive symptom severity did not predict increases in intake of sugar and saturated fats in the present study. However, it is plausible that the finding that 13-year change in total energy intake partially

mediated the association between depressive symptom severity and 13-year change in adiposity may be explained, in part, by the mechanism of emotional eating.

Regarding moderation by sex and race, no prior study of depression and diet composition has reported tests of moderation by these demographic factors. Only three cross-sectional studies have conducted analyses stratified by sex (without accompanying tests of moderation) and report that (1) depressive symptoms are positively associated with total fat intake among American adolescent boys but not girls (Fulkerson et al., 2004), (2) depressive symptoms are inversely associated with carbohydrate intake among older Japanese men but not women (Oishi et al., 2009), and (3) depressive symptoms are inversely associated with higher carbohydrate intake among older Japanese women but not men (Umegaki et al., 2009). The present study is inconsistent with these cross-sectional studies, as only the association between baseline depressive symptom severity and change in protein intake in the mediation models was found to be moderated by sex such the relationship between baseline depressive symptoms and 13-year change in protein intake was stronger in men than in women. To my knowledge, no study has examined associations between depressive symptoms and diet composition factors stratified by race.

Explanation for Study Findings

Most of my findings did not support my hypotheses, although there was one notable exception: 13-year change in total energy intake significantly mediated the association between depressive symptom severity and 13-year change in waist circumference. Although not significant, there was also a trend for greater depressive symptoms predicting greater 13-year increases in total energy intake. These findings are plausible for several reasons. First, there is strong, consistent evidence linking greater energy intake to increased adiposity (Hill et al., 2012;

Racette et al., 2003). Second, there are mechanisms that have the potential to link depression to greater energy intake, including emotional eating and deficits in planning/executive functioning. Emotional eating may serve as a mechanism linking depression to greater energy intake because (1) depression is associated with increased emotional eating (Clum et al., 2014; Goldschmidt et al., 2014; Konttinen et al., 2010b; van Strien et al., 2016) and (2) greater emotional eating is associated with intake of energy-dense foods, particularly foods that are high in sugar and fat (Konttinen et al., 2010a). Depression has also been linked to deficits in executive functioning (Snyder, 2013), a critical neurocognitive skill involved in planning. Although no prior research has examined this specific pathway, it is plausible that elevated depressive symptoms may be associated with intake of convenience foods that require less planning and have high energy density (e.g., prepackaged meals) rather than intake of more nutritious foods that take more planning and are lower in energy density (e.g., home-cooked meals that include vegetables and lean protein). Third, the presence of atypical depression and the associated symptom of increased appetite may be contributing to increased total energy intake over time. According to the DSM 5, depression can include symptoms of increased *or* decreased appetite (American Psychiatric Association, 2013). Atypical depression is characterized by hyperphagia (increased appetite/weight gain) and hypersomnia (excessive sleep) (American Psychiatric Association, 2013; Quitkin, 2002). Prior research has shown that atypical depression, compared to other depression subtypes (i.e., melancholic depression) is a stronger predictor of obesity (Lasserre et al., 2014; Polanka, Vrany, Patel, & Stewart, 2017), is related to poorer diet quality (Rahe et al., 2015), and is associated with greater craving of "comfort foods" (e.g., chocolate or cake) (Parker & Crawford, 2007). Therefore, the presence of atypical depression and the associated symptom

of increased appetite may be contributing, in part, to my finding that total energy intake partially mediates the depression-to-obesity association.

Although other significant findings were detected in the present study, they were inconsistent with my hypotheses. Specifically, depressive symptom severity predicted 13-year increases in protein and fiber intake and 13-year change in protein intake partially mediated the association between depressive symptoms and 13-year change in waist circumference. As previously discussed, these findings are inconsistent with prior literature. One possible explanation for the inconsistent findings is that this study examined depressive symptom severity as a predictor of 13-year changes in diet composition over time, whereas other studies have used predominantly cross-sectional data to examine associations between baseline depression and concurrent dietary intake. Otherwise, the underlying mechanisms to explain these findings are uncertain and replication is needed to father clarify these prospective associations.

The majority of hypotheses in this study were not supported due to null findings. When one observes null findings, two explanations are plausible: (1) the findings reflect the true state of nature or (2) the findings do not reflect the state of nature and, instead, are due to methodological issues (Kazdin, 2003). Assuming the first explanation is true, my null findings indicate that depressive symptom severity does not predict change over time in intake of saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, and sugar. My null findings also suggest that these diet composition factors do not mediate the association between depressive symptom severity and change in waist circumference over time. However, given that the cross-sectional evidence for associations of depression with carbohydrate and fat intake are inconsistent and the present study is the first to prospectively examine these associations and test for mediation, the true nature of these relationships remains unclear.

Assuming the second explanation is true, methodological issues may be responsible for my null findings (Kazdin, 2003). The primary methodological issue relevant to the present study is inadequate measurement of key variables. Overall, CARDIA utilized high quality, well-validated measures of depressive symptom severity, waist circumference, and diet composition. However, specific limitations related to the assessment of depressive symptom severity and diet composition factors are worthy of mention.

Related to measurement of depressive symptoms, an examination of items in the CES-D revealed that the symptom of appetite disturbance is assessed with only with the item: "I did not feel like eating; my appetite was poor." (see Figure 2, item 2) (Radloff, 1977). As previously discussed, depression can include symptoms of increased *or* decreased appetite (American Psychiatric Association, 2013). In light of prior research demonstrating that atypical depression's association with obesity and poorer diet quality compared to other depression subtypes (Lasserre et al., 2014; Parker & Crawford, 2007; Polanka et al., 2017; Rahe et al., 2015), it is plausible that the association between depressive symptom severity and change in diet composition may be stronger or solely present among those with atypical depression. In the present study, the CES-D may not capture the presence of increased appetite and atypical depression, thus limiting my ability to detect the association between depressive symptom severity and change in diet composition over time.

Inadequate measurement of diet composition may also limit my ability to detect the hypothesized associations. Diet composition was assessed in 1992 and 2005 by the DHQ, which included a food frequency questionnaire assessing typical intake of certain types of foods over the past month. Although food frequency questionnaires are the commonly accepted method for assessing dietary intake in epidemiologic studies (Thompson & Subar, 2008), they have several

weaknesses that could lead to inaccurate estimates of dietary intake (Shim, Oh, & Kim, 2014). First, they contain a finite list of types of foods consumed that may not adequately capture the foods consumed by some people, such as unique or atypical foods. Second, they often lack detailed information about the manner in which foods are prepared (e.g., baked versus oil-cooked meats). Third, as with any self-report dietary assessment, food frequency questionnaires are subject to recall bias and social desirability, potentially leading to under- or over-reporting of intake.

In addition to these general concerns regarding the use of food frequency questionnaires, several concerns specific to the CARDIA assessment of diet composition are worth noting. First, in the validation study conducted by CARDIA, the DHQ was found to be reliable and valid; however, reporting of nutrients was notably low and intake did not correlate with 24-hour recall as strongly for non-Hispanic Black as for non-Hispanic White participants (Liu et al., 1994). It was suspected that non-Hispanic Black respondents may have been over-reporting consumption on the food frequency assessment and/or under-reporting intake on 24-hour recall assessment (Liu et al., 1994). This may contribute to larger measurement error in non-Hispanic Black than in non-Hispanic White participants. Second, the CARDIA DHQ was initially validated in 1993.

Second, to date, no article has been published regarding the validity of this measure over the follow-up period. Given that the second assessment of dietary intake was conducted in 2005 and that the DHQ relies on a list of certain types of food items that were identified in 1992 or earlier, it may not accurately reflect shifts in eating patterns over time (e.g., transitions to consuming more processed and fast foods). To illustrate, the average change in energy intake from Year 7 (1992) to Year 20 (2005) was -451.9 kilocalories. Similarly, intake of each macronutrient decreased over the 13-year follow-up. In a study of trends in energy intake over

time based on data from the NHANES, energy intake has remained relatively consistent from 1988-2006, with a mean energy intake of 2,234 kilocalories in 1988-1994 and 2,243 kilocalories in 2005-2006 (Ford & Dietz, 2013). This study also examined trends in intake according to age and generally revealed that energy intake was lower for older compared to younger respondents (Ford & Dietz, 2013), suggesting that intake decreases as people age. The observed decrease in intake over time in the present study may be attributable to either (1) truly decreased intake over time as people age or (2) inadequate measurement of diet composition over the follow-up period. If the latter were true, it would limit my ability to detect associations between depressive symptom severity and 13-year changes in diet composition factors.

Although inadequate measurement of key variables is a potential explanation of my null findings, Kazdin's (2003) other sources of null findings are not as plausible. First, insufficient power is unlikely to have affected the present study, as the sample was larger in size (n = 2,449). Second, it is not likely that inconsistent implementation of the study protocol introduced error, as CARDIA is a rigorously conducted study with a standardized protocol and extensive training of personnel. Third, it is unlikely that confounders may be contributing to the observed associations, as the present study adjusted for numerous potential confounders. Although it is not feasible to rule out all possible sources of confounding, the observed relationships in this study occur independently of age; sex; race; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; 13-year change in physical activity.

Strengths and Limitations

The present study has several strengths. First, the CARDIA study allowed for a prospective analysis of depressive symptom severity predicting 13-year change in multiple diet composition factors and adiposity indicators, which helps to further elucidate the depression-to-

diet and depression-to-obesity pathways. Second, the CARDIA study utilizes a large sample of non-Hispanic Black and non-Hispanic White adults from four large urban centers in the U.S. (Friedman et al., 1988). Although this sample is not fully representative of the U.S. population, it improves upon prior studies in this literature and, thus, has greater external validity. In addition, because the CARDIA study balanced recruitment by sex and race, it provided a good opportunity to test for moderation by these demographic factors. Third, the present study is the first in this literature to formally test for statistical mediation and moderated mediation.

Several limitations should be also noted. First, the CARDIA study does not provide concurrent assessment of depressive symptoms and diet composition at baseline. Depressive symptoms were first assessed at Year 5 and were not assessed at Year 7 when diet composition data was first collected. Therefore, this study does not account for potential changes in depressive symptoms or diet composition that occurred between Year 5 and 7. Importantly, analyses of the temporal stability of depressive symptom severity in the present study yielded adequate stability over the follow-up years. Second, as previously discussed, the measure of depressive symptom severity assesses only decreased appetite (and not increased appetite). Therefore, it may not adequately capture the presence of increased appetite and atypical depression, potentially limiting my ability to detect associations between depressive symptom severity and change in diet composition over time. Third, diet composition was assessed by self-report, which is limited by recall bias and social desirability (Thompson & Subar, 2008). Additionally, the diet composition measure contains a finite list of types of foods consumed that may not adequately capture intake of unique or atypical foods or the manner in which foods are prepared, which may contribute to an under-representation of intake. Nonetheless, it is common for epidemiologic studies to use food frequency questionnaires due to their ease of

administration (Thompson & Subar, 2008), and the DHQ is a valid and reliable assessment of typical nutrient intake (Liu et al., 1994). Fifth, because the CARDIA study only includes non-Hispanic Black and non-Hispanic White participants from urban centers, I am unable to examine the depression-diet composition-adiposity associations in other sociodemographic groups, such as Hispanic/Latinos, non-Hispanic Asians, and rural populations. Thus, the findings of the present study may not generalize to these groups. Despite this limitation, the present study is the first to examine the prospective association between depression and diet in a larger sample of adults in the U.S.

Recommendations for Future Research

My recommendations for future research in this area are two-fold. First, future investigations should further clarify the prospective associations between depression, diet composition, and adiposity by (1) examining these associations in more representative samples of the U.S. population; (2) examining depressive symptom clusters and/or depressive disorder subtypes separately as predictors of change in diet composition and adiposity to elucidate differences in atypical versus nonatypical depression, (3) examining other dietary behaviors as mechanisms linking depression to future obesity risk, such as emotional eating, mealtime frequency, overall diet quality, and intake of certain foods types (e.g., sweets, fried foods, and fast foods), and (4) formally testing for statistical mediation and moderation using state-of-the-art statistical approaches, such as PROCESS. Continued investigation of moderation by sex and race will be of benefit to elucidate in whom the depression-diet-obesity pathway may be of greatest concern.

Second, future research should test interventions that simultaneously target depression and dietary intake to reduce risk of depression-related obesity. Recent clinical trials demonstrate

that, although combined approaches to treating depression and weight loss result in reductions in both depression and body weight (Faulconbridge, Wadden, Berkowitz, Pulcini, & Treadwell, 2011; Linde et al., 2011; Pagoto et al., 2013), comparative effectiveness trials (comparing combined depression and weight loss intervention approaches to weight loss interventions alone) yield inconsistent evidence. Specifically, one study demonstrated that, compared to weight loss intervention alone, the combined approach results in greater reductions in depressive symptoms but similar reductions in weight (Pagoto et al., 2013), and another demonstrated that both treatment approaches result in similar reductions in depression and weight (Linde et al., 2011). Although findings in the present study need to be replicated, they suggest that energy intake may be a modifiable target for interventions that simultaneously target depression and diet to prevent or manage depression-related obesity.

Conclusions

My results from the CARDIA study data demonstrate that greater depressive symptom severity predicted 13-year increases in intake of protein and fiber, and a similar trend was observed for total energy intake. Depression did not predict changes in the other diet composition factors. Mediation analyses revealed that 13-year increases in total energy intake and protein intake partially mediated the association between depressive symptom severity and 13-year increases in waist circumference. Changes in the other diet composition factors did not mediate this association. Exploratory analyses examining moderation of path a (depression-to-diet composition change) by sex and race yielded only one significant moderated moderation model (7.1% of 14 models tested). Due to risk of type I error, this finding should be interpreted with caution.

Although most of my hypotheses were not supported, the findings of this study are compelling given their novelty in the larger depression-diet literature. This is the first study to examine baseline depression as a predictor of change in multiple diet composition factors over time using a larger epidemiologic dataset. Moreover, no other study has formally tested changes in diet composition factors as mediators of the association between depression and change in adiposity over time. This study provides initial evidence that greater total energy intake and protein intake may be among the mechanisms linking depression to future obesity risk.

This study has implications for research and clinical practice. Concerning research, more research is needed to further clarify the prospective associations among depression, diet composition, and adiposity. If replicated, the findings of the present study have the potential to inform the development of novel interventions to be tested clinical trials. Psychological interventions have been adapted to target obesity (i.e., cognitive, behavioral, and mindfulness-based interventions) and have begun to address some obesity-promoting dietary behaviors (Cooper et al., 2010; Cooper, Fairburn, & Hawker, 2004; O'Reilly, Cook, Spruijt-Metz, & Black, 2014). Findings from the present study suggest that total energy intake may be one potential target for interventions designed to prevent or manage depression-related obesity. With regard to clinical implications, providers should be aware that depression may confer excess obesity risk, in part, through increased total energy intake and protein intake. Providers should consider assessing depressive symptoms and associated changes in diet. For depressed individuals who endorse increased dietary intake, interventions could be tailored to provide treatment for both depression and eating-related concerns. These efforts may be beneficial for reducing of depression-related obesity in susceptible individuals.

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TABLES

Table 1. Demographic Characteristics of Participants

Age, years	35.3 ±3.6
Women, %	54.0
Race/Ethnicity	
Non-Hispanic White, %	43.8
Non-Hispanic Black, %	56.2
Education, years	14.7 ±2.4
Education, less than high school, %	4.6

Note. n = 2,449; Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as percentage.

Table 2. Characteristics of Respondents for Depressive Symptoms, Adiposity, Diet Composition, and Physical Activity at Years 5, 7, and 20

	Year 5	Year 7	Year 20	Change Score
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
CES-D Total[a]	10.6 ± 8.0	--	9.0 ±7.7	-1.5 ±8.3
Adiposity				
Waist circumference, full sample, cm	--	84.0 ±13.5	92.3 ±14.9	8.3 ±8.5
Waist circumference, men, cm	--	88.3 ±11.3	96.5 ±13.3	8.2 ±7.7
Waist circumference, women, cm	--	80.4 ±14.2	88.6 ±15.2	8.4 ±9.3
Body mass index, kg/m^{2} [b]	--	26.7 ±5.7	29.5 ±6.6	2.8 ±3.7
Diet Composition Variables				
Total energy, kilocalories	--	2,819 ±1,360	2,364 ±1,110	-451 ±1359
Saturated fatty acids, grams	--	38.7 ±22.9	35.7 ±17.7	-8.0 ±23.6
Monounsaturated fatty acids, grams	--	41.4 ±24.0	37.0 ±21.4	-4.1 ±27.0
Polyunsaturated fatty acids, grams	--	22.6 ±13.5	21.7 ±15.8	-0.0 ±21.8
Fiber, grams	--	21.2 ±12.1	21.6 ±11.0	-1.7 ±16.5
Sugar, grams	--	153.9 ±88.2	125.2 ±75.9	-26.5 ±96.4
Protein, grams		104.2 ±57.8	90.6 ±46.2	-13.5 ±50.2
Physical Activity Exercise Units	--	344.6 ±272.9	342.3 ±272.1	-2.3 ±266.4

Note. *n* = 2,449. *SD* = standard deviation.
[a]CES-D is reported on a reduced sample of *n* = 2,398 at Year 20 due to missing data.
[b]Body mass index is reported on a reduced sample of *n* = 2,447 at Year 7 and *n* = 2,441 at Year 20 due to missing data.

Table 3. Prevalence and Incidence of Potentially Confounding Medical Conditions

Prevalent cardiovascular disease, %	0.8
Incident cardiovascular disease, %	4.4
Prevalent diabetes, %	3.7
Incident diabetes, %	6.9
Prevalent cancer, %	6.0
Incident cancer, %	4.5
Incident pregnancy, % of women	14.3

Note. n = 2,449.

Table 4. Results from Exploratory Moderated Mediation Analyses

Model	Mediator	Moderator of Path A	Index of Moderated Mediation				Evidence of moderated mediation
			Index	*Standard Error*	*95% CI Lower*	*95% CI Upper*	
Model 1	Total energy intake	Sex	0.002	0.002	-0.001	0.007	No
Model 2	Saturated fatty acid intake	Sex	0.002	0.002	-0.001	0.007	No
Model 3	Monounsaturated fatty acid intake	Sex	0.001	0.002	-0.001	0.005	No
Model 4	Polyunsaturated fatty acid intake	Sex	0.000	0.001	-0.002	0.003	No
Model 5	Fiber intake	Sex	0.000	0.001	-0.002	0.002	No
Model 6	Sugar intake	Sex	0.002	0.002	-0.001	0.007	No
Model 7	Protein intake	Sex	0.004	0.002	0.001	0.010	Yes
Model 8	Total energy intake	Race	0.000	0.002	-0.003	0.003	No
Model 9	Saturated fatty acid intake	Race	0.001	0.002	-0.001	0.005	No
Model 10	Monounsaturated fatty acid intake	Race	0.001	0.001	-0.001	0.004	No
Model 11	Polyunsaturated fatty acid intake	Race	0.000	0.001	-0.002	0.001	No
Model 12	Fiber intake	Race	0.000	0.001	-0.001	0.002	No
Model 13	Sugar intake	Race	-0.001	0.001	-0.004	0.002	No
Model 14	Protein intake	Race	0.001	0.002	-0.001	0.005	No

Note: All models include baseline CES-D Total as the independent variable and 13-year change in waist circumference as the dependent variable. All models are adjusted for age; sex; race; education; Year 7 waist circumference; prevalent and incident cardiovascular disease, type 2 diabetes, and cancer; incident pregnancy; and 13-year change in physical activity. Please see Figure 1 for a visual representation of these models. n = 2,449; CES-D = Center for Epidemiologic Studies-Depression Scale.

Table 5. Stability Analyses Examining CES-D Total at Year 5 as a Predictor of CES-D Total at Year 20 and Testing for Moderation by Age, Sex, and Race

	β	*p*-value	*r*	R^2
CES-D Total				
Stability Model[a]	0.45	<.001**	0.45	0.20
Interaction Model[b]	--	--	0.46	0.21
Interaction Term: Year 5 CES-D Total x age	-0.002	.915	--	--
Interaction Term: Year 5 CES-D Total x sex	0.06	.148	--	--
Interaction Term: Year 5 CES-D Total x race	-0.11	.004**	--	--

Note. n = 2,398; CES-D = Center for Epidemiologic Studies-Depression Scale; *p < .05; **p < .01.

[a] Regression model in which the Year 5 CES-D is entered as the independent variable and Year 20 CES-D is entered as the dependent variable.

[b] Stability model with further adjustment for age, sex, and race, and the three interaction terms.

Table 6. Stability Analyses Examining Each Diet Composition Factor at Year 7 as a Predictor of that Diet Composition Factor at Year 20 and Testing for Moderation by Age, Sex, and Race

	β	p-value	r	R^2
Total Energy Intake				
Stability Model[a]	0.58	<.001**	0.58	0.34
Interaction Model[b]	--	--	0.60	0.36
Interaction Term: Year 7 Total Energy Intake x age	0.02	.327	--	--
Interaction Term: Year 7 Total Energy Intake x sex	0.06	.079	--	--
Interaction Term: Year 7 Total Energy Intake x race	-0.10	.006**	--	--
Saturated Fatty Acid Intake				
Stability Model[a]	0.54	<.001**	0.54	0.29
Interaction Model[b]	--	--	0.56	0.31
Interaction Term: Year 7 Saturated Fatty Acid Intake x age	0.03	.115	--	--
Interaction Term: Year 7 Saturated Fatty Acid Intake x sex	0.08	.038*	--	--
Interaction Term: Year 7 Saturated Fatty Acid Intake x race	-0.13	<.001**	--	--
Monounsaturated Fatty Acid Intake				
Stability Model[a]	0.47	<.001**	0.47	0.22
Interaction Model[b]	--	--	0.49	0.24
Interaction Term: Year 7 Monounsaturated Fatty Acid Intake x age	0.02	.276	--	--
Interaction Term: Year 7 Monounsaturated Fatty Acid Intake x sex	0.04	.326	--	--
Interaction Term: Year 7 Monounsaturated Fatty Acid Intake x race	-0.14	<.001**	--	--
Polyunsaturated Fatty Acid Intake				
Stability Model[a]	0.40	<.001**	0.40	0.16
Interaction Model[b]	--	--	0.42	0.18
Interaction Term: Year 7 Polyunsaturated Fatty Acid Intake x age	-0.01	.482	--	--
Interaction Term: Year 7 Polyunsaturated Fatty Acid Intake x sex	0.03	.435	--	--
Interaction Term: Year 7 Polyunsaturated Fatty Acid Intake x race	-0.12	.002**	--	--

Table 6. Stability Analyses Examining Each Diet Composition Factor at Year 7 as a Predictor of that Diet Composition Factor at Year 20 and Testing for Moderation by Age, Sex, and Race (Continued)

	β	p-value	r	R^2
Fiber Intake				
Stability Model[a]	0.51	<.001**	0.51	0.25
Interaction Model[b]	--	--	0.51	0.26
Interaction Term: Year 7 Fiber Intake x age	0.01	.484	--	--
Interaction Term: Year 7 Fiber Intake x sex	0.04	.308	--	--
Interaction Term: Year 7 Fiber Intake x race	-0.07	.052	--	--
Sugar Intake				
Stability Model[a]	0.45	<.001**	0.45	0.20
Interaction Model[b]	--	--	0.47	0.22
Interaction Term: Year 7 Sugar Intake x age	0.01	.412	--	--
Interaction Term: Year 7 Sugar Intake x sex	0.06	.130	--	--
Interaction Term: Year 7 Sugar Intake x race	-0.02	.530	--	--
Protein Intake				
Stability Model[a]	0.55	<.001**	0.55	0.30
Interaction Model[b]	--	--	0.57	0.32
Interaction Term: Year 7 Protein Intake x age	0.01	.389	--	--
Interaction Term: Year 7 Protein Intake x sex	0.07	.059	--	--
Interaction Term: Year 7 Protein Intake x race	-0.08	.015*	--	--

Note. n = 2,449; CES-D = Center for Epidemiologic Studies-Depression Scale; *p < .05; **p < .01.

[a] Regression model in which the Year 7 diet composition variable is entered as the independent variable and the Year 20 diet composition variable is entered as the dependent variable.

[b] Stability model with further adjustment for age, sex, and race, and the three interaction terms.

Table 7. Stability Analyses Stratified by Sex

	Men					Women				
	n	*β*	*p*-value	*r*	R^2	*n*	*β*	*p*-value	*r*	R^2
Depressive Symptoms (Year 5 predicting Year 20)										
CES-D Total	--	--	--	--	--	--	--	--	--	--
Diet Composition Variables (Year 7 predicting Year 20)										
Total Energy Intake	--	--	--	--	--	--	--	--	--	--
Saturated Fatty Acid Intake	1,127	0.53	<.001**	0.53	0.28	1,322	0.43	<.001**	0.43	0.18
Monounsaturated Fatty Acid Intake	--	--	--	--	--	--	--	--	--	--
Polyunsaturated Fatty Acid Intake	--	--	--	--	--	--	--	--	--	--
Fiber Intake	--	--	--	--	--	--	--	--	--	--
Sugar Intake	--	--	--	--	--	--	--	--	--	--
Protein Intake	--	--	--	--	--	--	--	--	--	--

Note. CES-D = Center for Epidemiologic Studies-Depression Scale; **$p < .01$.

Table 8. Stability Analyses Stratified by Race

	non-Hispanic Black					non-Hispanic White				
	n	*β*	*p*-value	*r*	R^2	*n*	*β*	*p*-value	*r*	R^2
Depressive Symptoms (Year 5 predicting Year 20)										
CES-D Total	1,043	0.49	<.001**	0.49	0.24	1,355	0.38	<.001**	0.38	0.14
Diet Composition Variables (Year 7 predicting Year 20)										
Total Energy Intake	1,073	0.63	<.001**	0.63	0.40	1,376	0.51	<.001**	0.51	0.26
Saturated Fatty Acid Intake	1,073	0.62	<.001**	0.62	0.38	1,376	0.44	<.001**	0.44	0.20
Monounsaturated Fatty Acid Intake	1,073	0.57	<.001**	0.57	0.33	1,376	0.36	<.001**	0.36	0.13
Polyunsaturated Fatty Acid Intake	1,073	0.43	<.001**	0.43	0.19	1,376	0.32	<.001**	0.32	0.10
Fiber Intake	--	--	--	--	--	--	--	--	--	--
Sugar Intake	--	--	--	--	--	--	--	--	--	--
Protein Intake	1,073	0.60	<.001**	0.60	0.36	1,376	0.49	<.001**	0.49	0.24

Note. CES-D = Center for Epidemiologic Studies-Depression Scale; **$p < .01$.

FIGURES

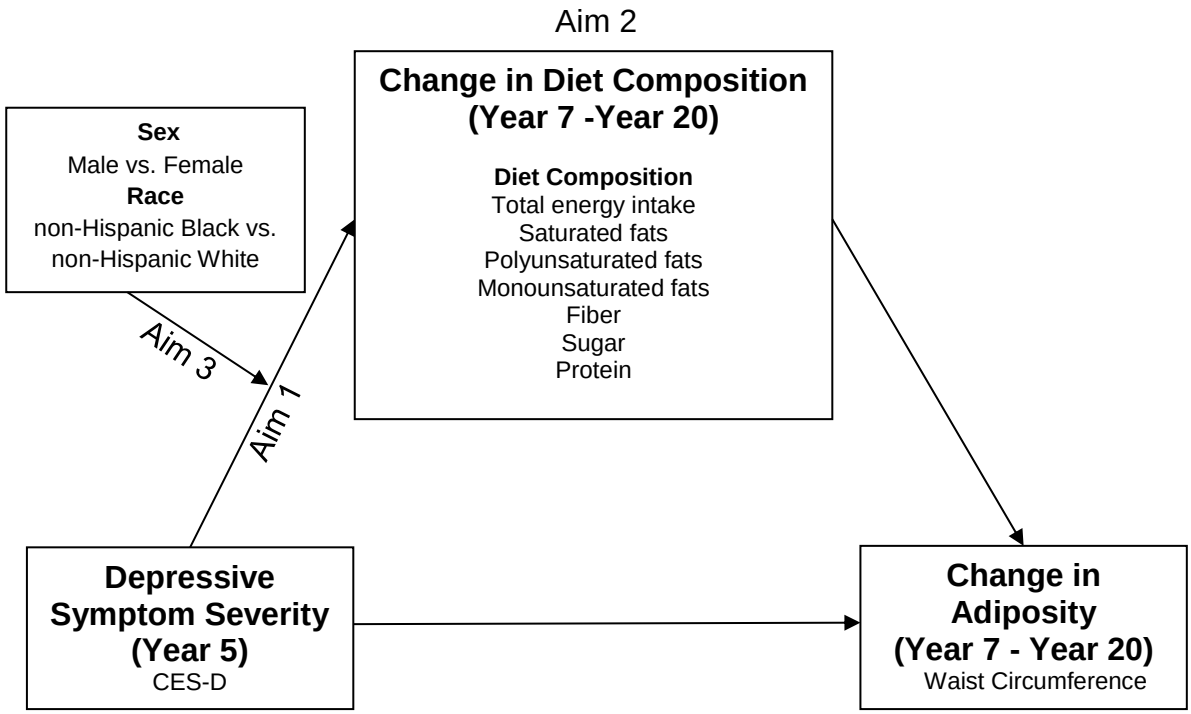

Figure 1. Conceptual Model Depicting Associations between Depressive Symptom Severity, Change in Diet Composition Factors, and Change in Adiposity

This model identifies the three aims of the present study: (1) to examine depressive symptom severity as a predictor of 13-year change in seven diet composition factors over time, (2) to test 13-year change in diet composition factors as mediators of the association between depressive symptom severity and 13-year change in adiposity, and (3) to explore whether the Aim 2 mediation models are moderated by sex and race.

Center for Epidemiologic Studies-Depression Scale (CES-D), NIMH

Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the past week.

	During the Past Week			
	Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	Most or all of the time (5-7 days)
1. I was bothered by things that usually don't bother me.	☐	☐	☐	☐
2. I did not feel like eating; my appetite was poor.	☐	☐	☐	☐
3. I felt that I could not shake off the blues even with help from my family or friends.	☐	☐	☐	☐
4. I felt I was just as good as other people.	☐	☐	☐	☐
5. I had trouble keeping my mind on what I was doing.	☐	☐	☐	☐
6. I felt depressed.	☐	☐	☐	☐
7. I felt that everything I did was an effort.	☐	☐	☐	☐
8. I felt hopeful about the future.	☐	☐	☐	☐
9. I thought my life had been a failure.	☐	☐	☐	☐
10. I felt fearful.	☐	☐	☐	☐
11. My sleep was restless.	☐	☐	☐	☐
12. I was happy.	☐	☐	☐	☐
13. I talked less than usual.	☐	☐	☐	☐
14. I felt lonely.	☐	☐	☐	☐
15. People were unfriendly.	☐	☐	☐	☐
16. I enjoyed life.	☐	☐	☐	☐
17. I had crying spells.	☐	☐	☐	☐
18. I felt sad.	☐	☐	☐	☐
19. I felt that people dislike me.	☐	☐	☐	☐
20. I could not get "going."	☐	☐	☐	☐

SCORING: zero for answers in the first column, 1 for answers in the second column, 2 for answers in the third column, 3 for answers in the fourth column. The scoring of positive items is reversed. Possible range of scores is zero to 60, with the higher scores indicating the presence of more symptomatology.

Figure 2. Center for Epidemiologic Studies-Depression Scale (CES-D).

Figure 2. Center for Epidemiologic Studies-Depression Scale (CES-D).

The CES-D is a 20-item self-report measure of depressive symptom severity. Scores for each item range from zero to three, and four items are reverse-scored (items 4, 8, 12, and 16). A continuous CES-D Total score was computed by summing the values for each of the 20 items, with possible scores ranging from 0 to 60 (Radloff, 1977).

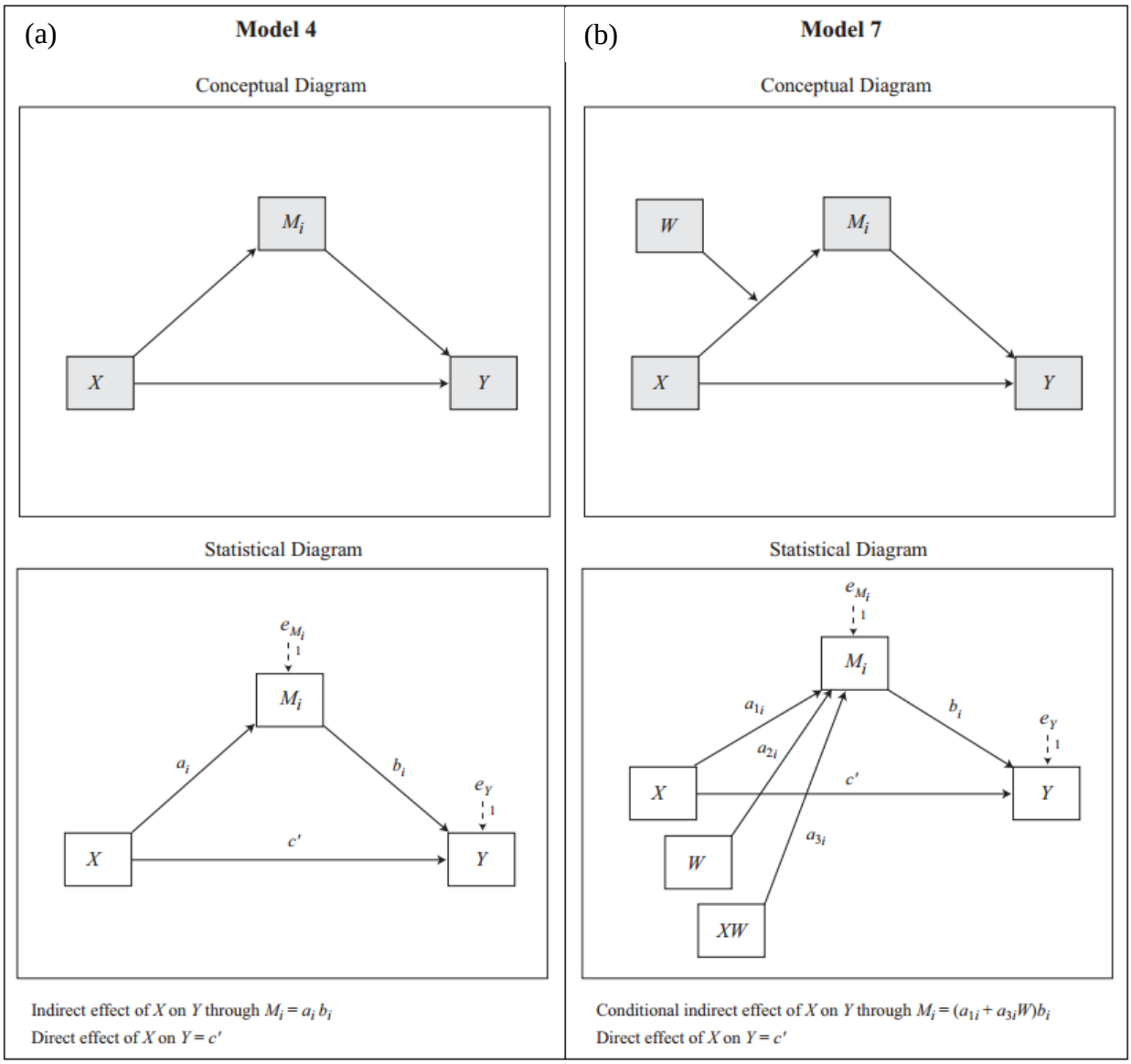

Figure 3. Hayes PROCESS Models for Mediation and Moderated Mediation

Panel (a) depicts PROCESS Model 4 used for the Aim 1 and 2 analyses. This mediation model depicts a mediator (M) of the association between predictor (X) and criterion (Y). Panel (b) depicts PROCESS Model 7 used for the Aim 3 analyses. In this moderated mediation model, a moderator (W) is identified of the association between predictor (X) and mediator (M) in a model with a mediator (M) of the association between predictor (X) and criterion (Y) (Hayes, 2013).

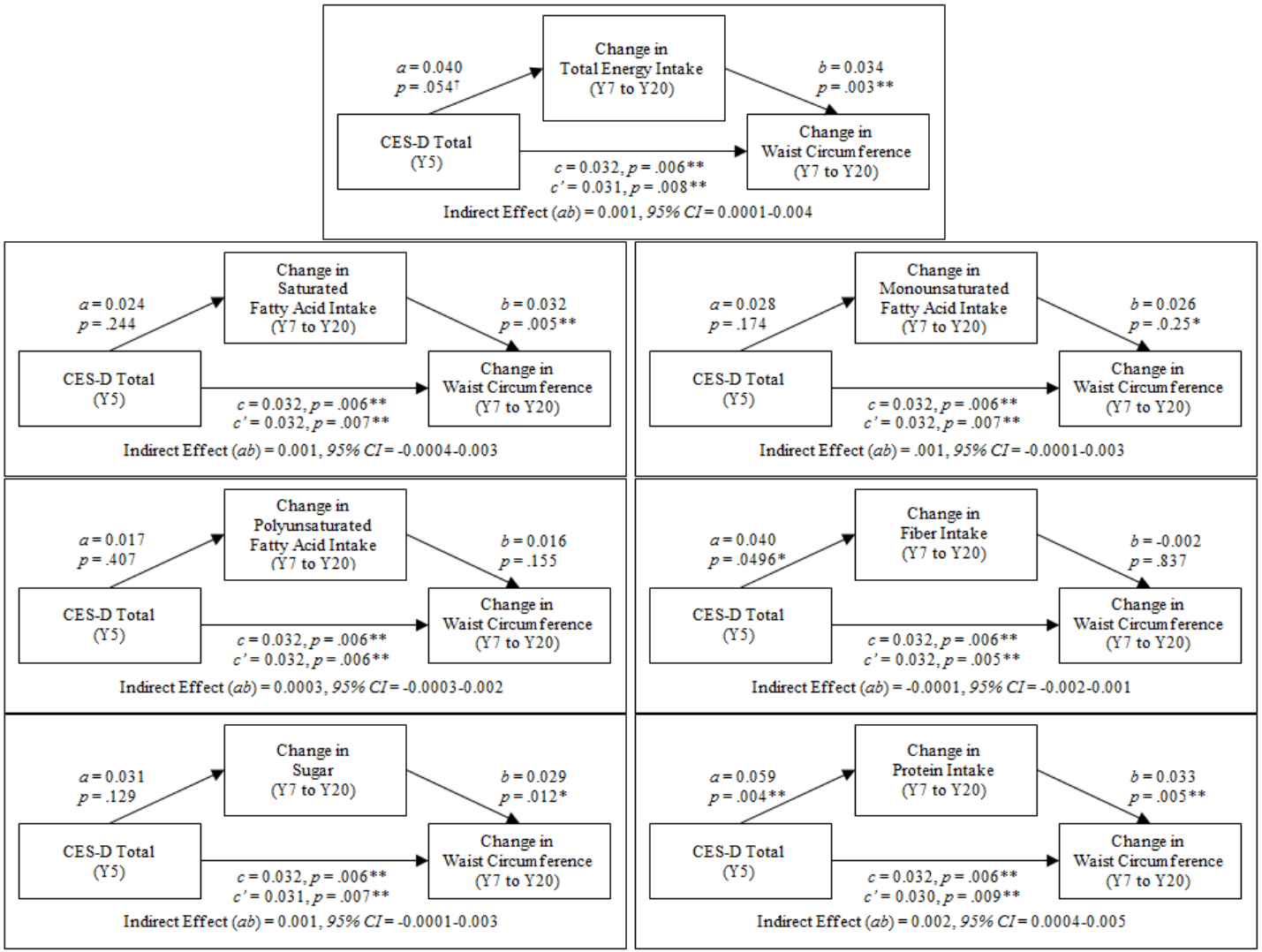

Figure 4. Results of Mediation Models Separately Examining 13-Year Change in Diet Composition Factors as Mediators of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Waist Circumference.

Figure 4. Results of Mediation Models Separately Examining 13-Year Change in Diet Composition Factors as Mediators of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Waist Circumference.

All models were adjusted for age; sex; race; education; Year 7 waist circumference; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; and 13-year change in physical activity. Standardized regression coefficients (betas) are presented. CES-D = Center for Epidemiologic Studies-Depression Scale. n = 2,449. † $p < .10$; *$p < .05$; **$p < .01$.

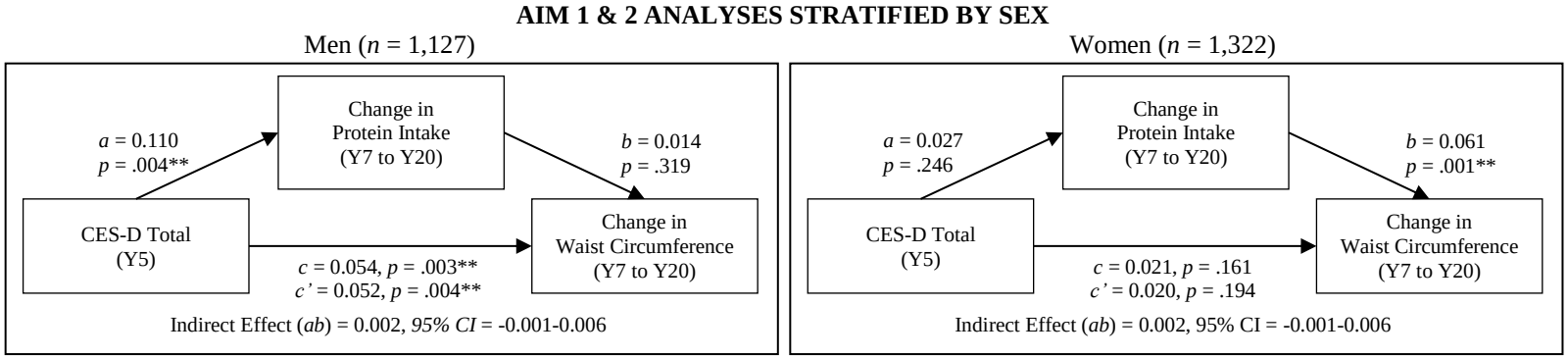

Figure 5. Results of Mediation Models Examining 13-Year Change in Protein Intake as a Mediator of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Waist Circumference Stratified by Sex.

Models were adjusted for age; race; education; Year 7 waist circumference; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; and 13-year change in physical activity. Standardized regression coefficients (betas) are presented. CES-D = Center for Epidemiologic Studies-Depression Scale. n = 2,449. † $p < .10$; *$p < .05$; **$p < .01$.

SENSITIVITY ANALYSES: AIM 1 & 2 ANALYSES WITH BMI AS DEPENDENT VARIABLE

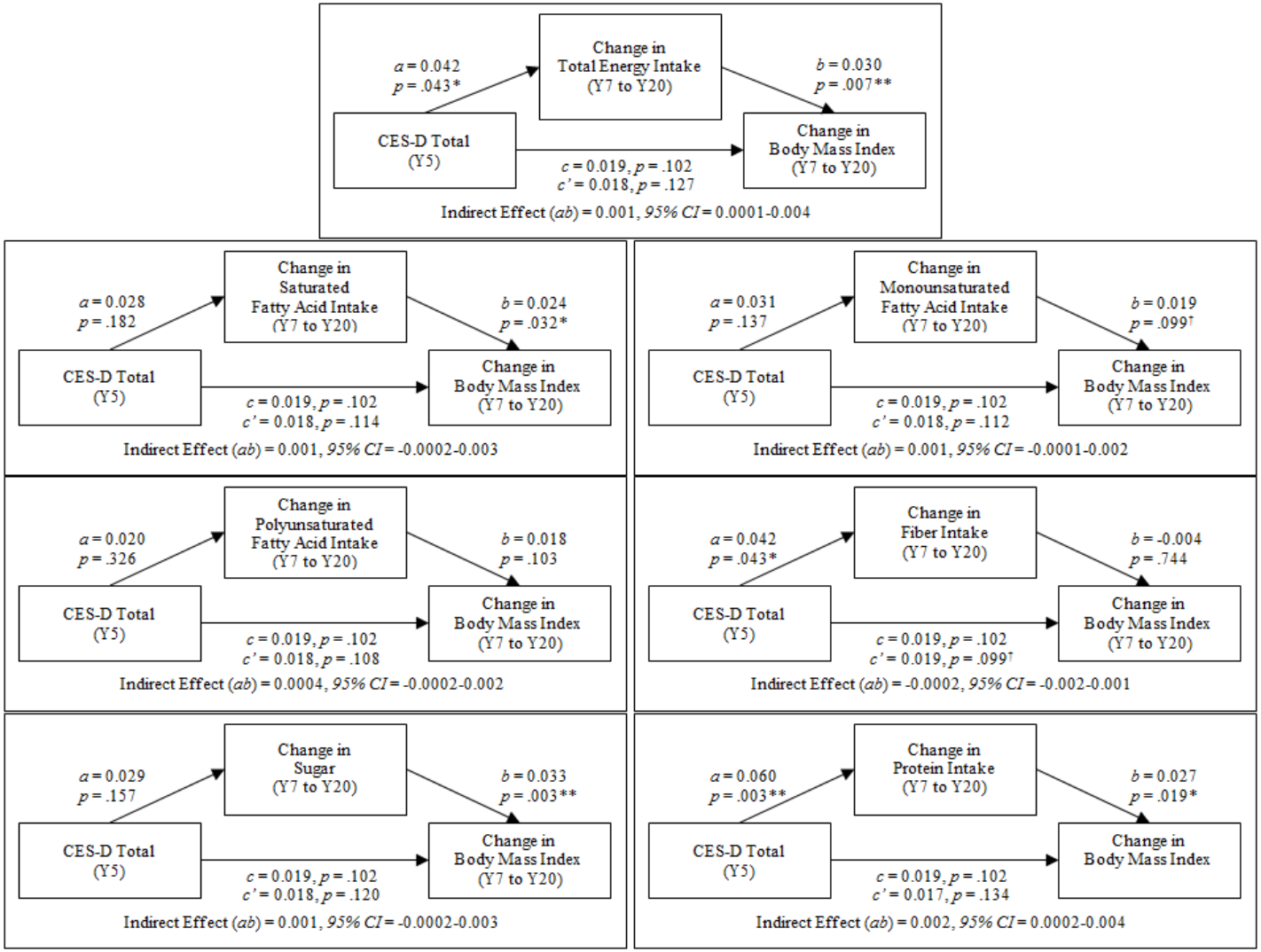

Figure 6. Results of Mediation Models Separately Examining 13-Year Change in Diet Composition Factors as Mediators of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Body Mass Index.

Figure 6. Results of Mediation Models Separately Examining 13-Year Change in Diet Composition Factors as Mediators of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Body Mass Index.

All models were adjusted for age; sex; race; education; Year 7 body mass index; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; and 13-year change in physical activity. Standardized regression coefficients (betas) are presented. CES-D = Center for Epidemiologic Studies-Depression Scale. n = 2,439. † $p < .10$; *$p < .05$; **$p < .01$.

SENSITIVITY ANALYSES: AIM 1 & 2 ANALYSES STRATIFIED BY SEX WITH BMI AS DEPENDENT VARIABLE

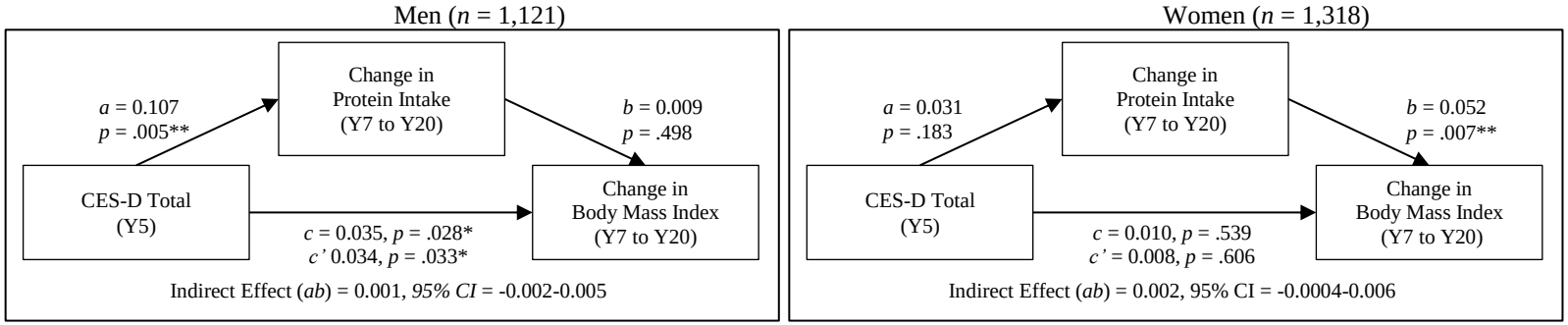

Figure 7. Results of Mediation Models Examining 13-Year Change in Protein Intake as a Mediator of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Body Mass Index Stratified by Sex.

Models were adjusted for age; race; education; Year 7 body mass index; prevalent and incident cardiovascular disease, diabetes, and cancer; incident pregnancy; and 13-year change in physical activity. Standardized regression coefficients (betas) are presented. CES-D = Center for Epidemiologic Studies-Depression Scale. n = 2,439. $^{\dagger}p < .10$; $*p < .05$; $**p < .01$.

SENSITIVITY ANALYSES: AIM 1 & 2 ANALYSES AFTER EXCLUDING PREVALENT COMORBID MEDICAL CONDITIONS

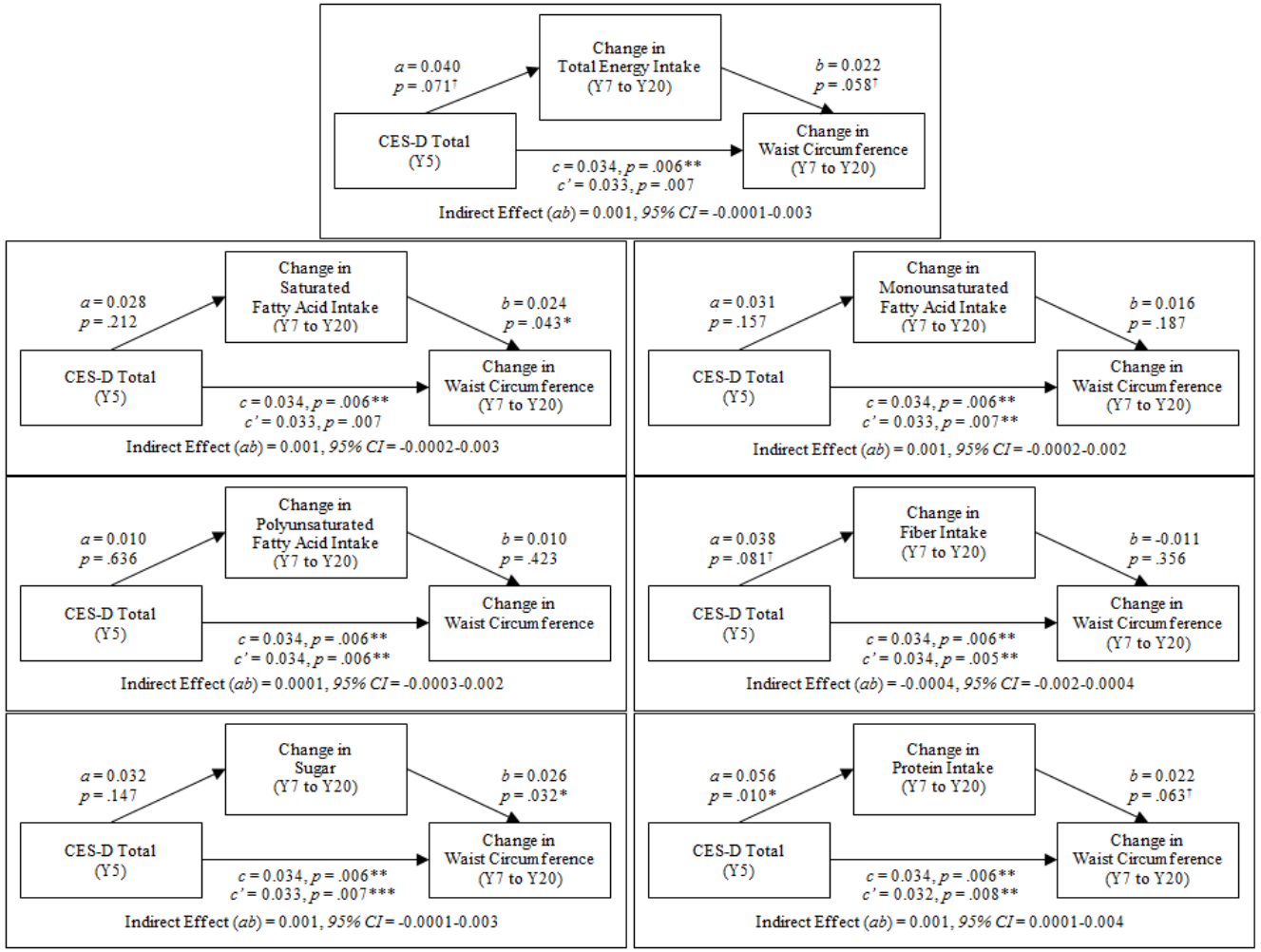

Figure 8. Results of Mediation Models Separately Examining 13-Year Change in Diet Composition Factors as Mediators of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Waist Circumference After Additionally Excluding those with Prevalent Comorbid Medical Conditions.

Figure 8. Results of Mediation Models Separately Examining 13-Year Change in Diet Composition Factors as Mediators of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Waist Circumference After Additionally Excluding those with Prevalent Comorbid Medical Conditions.

All models were adjusted for age; sex; race; education; Year 7 waist circumference; incident cardiovascular disease, diabetes, cancer, and pregnancy; and 13-year change in physical activity. Standardized regression coefficients (betas) are presented. CES-D = Center for Epidemiologic Studies-Depression Scale. n = 2,203. † $p < .10$; *$p < .05$; **$p < .01$.

SENSITIVITY ANALYSES: AIM 1 & 2 ANALYSES STRATIFIED BY SEX AFTER EXCLUDING PREVALENT COMORBID MEDICAL CONDITIONS

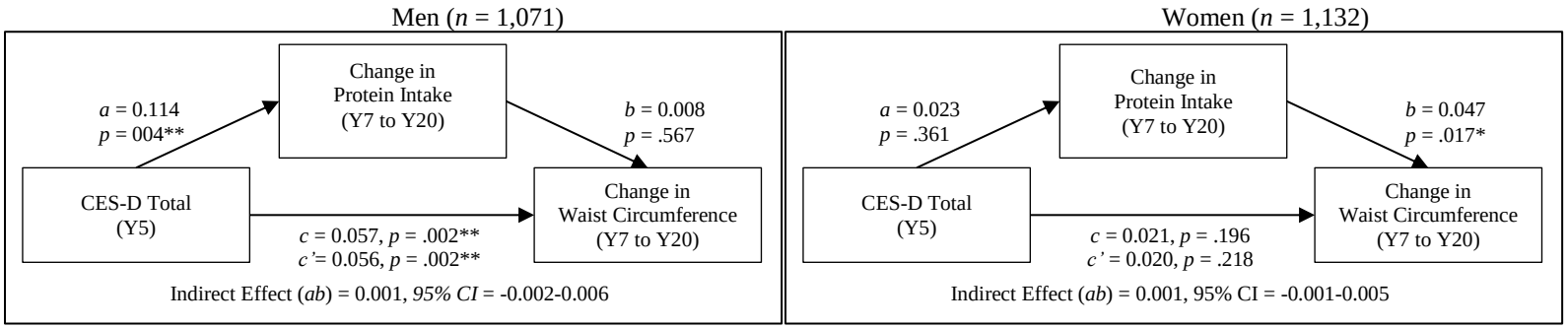

Figure 9. Results of Mediation Models Examining 13-Year Change in Protein Intake as a Mediator of the Association between Baseline Depressive Symptom Severity (CES-D Total) and 13-Year Change in Waist Circumference Stratified by Sex After Additionally Excluding those with Prevalent Comorbid Medical Conditions.

Models were adjusted for age; race; education; Year 7 waist circumference; incident cardiovascular disease, type 2 diabetes, cancer, and pregnancy; and 13-year change in physical activity. Standardized regression coefficients (betas) are presented. CES-D = Center for Epidemiologic Studies-Depression Scale. n = 2,203. † $p < .10$; *$p < .05$; **$p < .01$.