

THE EFFECT OF CHANGES IN BMI AND FAT INTAKE
ON BLOOD LIPIDS IN OBESE, MIDDLE-AGED WOMEN

By

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To my parents who have encouraged me to pursue all my dreams and to my sisters who have kept me laughing all the while

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Obese individuals who lose weight commonly show improvements in their LDL-cholesterol (LDL-C) and total cholesterol (TC), risk factors for heart disease. It remains unclear whether improvements are due to weight loss, dietary change, or both. In the current study, we hypothesized that change in BMI would predict change in LDL-C and TC, and that change in reported saturated and total fat intake would add to the explained variance. We examined this with separate hierarchical regressions, with change in BMI (block one) and self-reported fat intake (block two) as the predictor variables and change in LDL-C or TC as the dependent variables. Additional regressions were conducted for changes during a period of weight loss (i.e., Month 0 to Month 6), and a period of extended care (i.e., Month 6 to Month 18). The sample included 232 obese women from rural communities (mean±SD, age=59.8±6.3 years, BMI=36.8±4.8 kg/m²). At baseline, Month 6 and 18, height and weight were measured, blood lipids were analyzed, and dietary intake was assessed. From Month 0 to Month 6, a reduction in BMI predicted improvements in LDL-C and TC, while reductions in fat intake were not associated with these changes. During Month 6 to Month 18, neither change in BMI nor change in fat intake predicted changes in LDL-C and TC. These results suggest that the beneficial

impact of a lifestyle intervention on serum cholesterol is more closely related to weight loss and that these improvements may be limited to periods in which an individual is losing weight.

CHAPTER 1 INTRODUCTION

Overview

Obese adults commonly report elevated serum cholesterol levels and demonstrate an atherogenic blood lipid profile. Unfortunately, high total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides in combination with low high-density lipoprotein cholesterol (HDL-C) have been found to contribute to cardiovascular disease, a leading cause of mortality in the US (American Heart Association, 2011). Considering the large impact that both obesity and subsequent elevations in serum cholesterol may have, it is necessary to further explore approaches to improve the blood lipid profile among obese adults. This current study is based on findings from the Treatment of Obesity in Underserved Rural Settings (TOURS) program, a lifestyle intervention for obese adults trying to lose weight and improve their health (Perri et al., 2008). Notably, many participants in the program experienced significant improvements in their LDL-C and TC during the first 6 months of the weight loss intervention, yet these benefits were almost entirely lost during the 12-month extended-care program. Therefore, the current study aimed to better understand these fluctuations in serum cholesterol levels. The first objective was to observe if change in self-reported saturated fat intake predicted change in LDL-C, after controlling for change in BMI. Similarly, the second objective was to predict change in TC by accounting for change in self-reported total fat intake, while controlling for change in BMI. Both of these aims were designed to address and possibly explain the loss in these desired LDL-C and TC levels.

Obesity

Prevalence and Associated Health Risks

According to data from the latest Nutrition Examination survey (NHANES), the prevalence of obesity within the United States remains high, although it has begun to level off. Currently, more than 35% of adults over the age of 20 are classified as obese (Body Mass Index, BMI (calculated in kg/m^2) ≥ 30) with an additional 34% considered overweight (BMI = 25-29.9 kg/m^2) (Flegal, Carroll, Kit, & Ogden, 2012). These prevalence rates vary according to several factors, including gender, race, age, and an individual's place of residence. Age-adjusted rates of obesity are higher for women than men and are highest for non-Hispanic Blacks across both genders (Flegal et al., 2012). Additionally, self-reported obesity is 28% higher among adults in rural counties, contributing to their higher prevalence of chronic health conditions (Eberhardt & Pamuck, 2004). National survey estimates indicate that adults in rural areas demonstrate poorer health outcomes than their urban-living counterparts.

Obesity is a risk factor for increased morbidity and mortality (Must et al., 1999). Being overweight or obese increases the likelihood of developing diabetes mellitus, hypertension, hypercholesterolemia, asthma, and arthritis (Mokdad et al., 2003; NHLBI Obesity Education Initiative, 1998). As a result of these health conditions, obese individuals are also at an increased risk for cardiovascular disease and adverse cardiac events (e.g., congestive heart failure, stroke, cardiac arrhythmias, etc.) (Klein et al., 2004). In fact, research suggests that cardiovascular disease death rates are directly related to BMI, with the risk of cardiovascular disease mortality among obese adults (BMI > 35) being 2 to 3 times that of lean adults (BMI 18.5-24.9) (Calle, Thun, Petrelli, Rodriguez, & Heath, 1999).

Cardiovascular disease is a prominent health concern in the United States that affects an alarmingly high number of adults over the age of 20 (i.e., 82.6 million) (American Heart

Association, 2011). Currently, cardiovascular disease stands as the leading cause of mortality in the US and in 2007 its direct and indirect costs were estimated to be 286.6 billion dollars (American Heart Association, 2011). Risk factors for cardiovascular disease increase among individuals who have less than optimal lipid and lipoprotein concentrations, a problem that afflicts an estimated 98.8 million US adults (American Heart Association, 2011). Multiple factors influence serum cholesterol levels and contribute to the prominence in high TC (> 200 mg/dL) seen among US adults. Examples of cholesterol-raising factors include diet composition (e.g., intake of foods high in saturated fat), genetics, and excess weight (National Cholesterol Education Program (NCEP), 2002). Taken together, this indicates that hypercholesterolemia, as well as cardiovascular disease, are common problems and individuals diagnosed with them would benefit from successful interventions.

Lifestyle Interventions for Obesity

Reducing the prevalence of overweight and obesity has become an important public health initiative and research continuously shows the benefits of diminished weight and body fat on health. Therefore, attention has been given to developing lifestyle, or behavioral intervention programs, that promote weight loss through dietary changes and increased physical activity in order to produce an energy deficit and achieve weight loss (Wadden, Crerand, & Borck, 2005). Cognitive-behavioral strategies such as self-monitoring, goal setting, and problem solving are employed to assist participants in a lifestyle intervention to modify their eating and exercise habits (Dorsten & Lindley, 2011). For most participants, goals focus on adopting a low-calorie eating pattern while increasing moderate intensity physical activity, such as walking.

The National Heart, Lung and Blood Institute (NHLBI) Obesity Education Initiative recommends that overweight and obese adults achieve a 10% reduction in body weight in order to obtain health benefits such as improved blood pressure, blood sugar, and serum cholesterol

levels (1998). However, a weight loss as moderate as 3-5% of total body weight has also been found to significantly reduce health risks associated with obesity (Douketis, Macie, Thabane, & Williamson, 2005; Vidal, 2002). In fact, a weight loss of 3-5% can improve cardiovascular disease risk factors by decreasing LDL-C, triglycerides, and blood pressure, as well as increasing HDL-C and improving glucose tolerance (Datillo & Kris-Etherton, 1992; Flechtner-Mors, Ditschuneit, Johnson, Suchard, & Adler, 2000; Lalonde et al., 2002).

Lifestyle interventions, conducted over a 6 month period (i.e., involving 24 weekly group sessions), typically produce weight losses of 5 to 10 kg and achieve many of the above-mentioned improvements in health (Jeffrey et al., 2000; McTigue et al., 2003). However, weight loss is difficult to sustain and shorter-term studies are unable to capture the effect of weight regain on health. In fact, it is typical for adults to regain about 30-35% percent of their lost weight within the year following their weight loss, and many adults will have regained all their lost weight within 5 years (Anderson, Konz, Frederich, & Wood, 2001; Wadden, Butryn, & Byrne, 2004). Therefore, focus is shifting towards programs that incorporate follow-up and maintenance strategies.

Results from lifestyle interventions that incorporate extended-care sessions, such as the Look AHEAD trial (Kuller, Simkin-Silverman, Wing, Meilahn, & Ives, 2000) and the Diabetes Prevention Program (Ratner, 2006) indicate that participants in longer-term treatments demonstrate slower weight regain. These studies also document the benefits of extended care sessions on reducing the incidence of health conditions such as diabetes, dyslipidemia, and hypertension (Kuller et al., 2000; Perri et al., 2008; Ratner, 2006).

Blood Lipids

Basic Description of Lipids and Lipoproteins

As mentioned above, overweight and obesity is associated with the development of abnormal serum cholesterol levels (NHLBI Obesity Education Initiative, 1998). In turn, high TC increases the risk of an adult experiencing a cardiac event (American Heart Association, 2011). To better understand this connection between excess weight and cholesterol, as well as the ability of cholesterol to influence physical health, it is helpful to learn about serum cholesterol.

Cholesterol is a fat-like substance (lipid), manufactured in the liver (NCEP, 2002). It is a component of cell membranes and is necessary to synthesize bile acid in the liver, steroid hormones in endocrine cells (e.g., ovaries), and vitamin D in the skin (Krieger, 1998). Cholesterol itself does not travel through the body; instead, carriers consisting of protein (lipoproteins) transport it through the blood and to various tissues (NCEP, 2002). Within a fasting individual, three main types of lipoproteins are found, including low-density lipoproteins (LDL), high-density lipoproteins (HDL), and very low-density lipoproteins (VLDL) (NCEP, 2002). An additional lipoprotein type, intermediate-density lipoprotein (IDL), is present but it receives less attention and is usually included with LDL measurements (NCEP, 2002).

Of the abovementioned carriers, the National Cholesterol Education Program has identified LDL as the most influential because it contributes to about 60-70% of total serum cholesterol levels. Each LDL consists of one apolipoprotein (ApoB-100), a protein that binds the lipids together. An additional 20-30% of total serum cholesterol is composed of HDL, known for their protective properties against coronary heart disease (CHD), and the final 10-15% is composed of VLDL, precursors to LDL (2002).

Currently, LDL is the primary target for clinical management of serum cholesterol, in part because it is the most prominent cholesterol carrier, but mainly because it is the major

atherogenic lipoprotein (i.e., it accelerates atherosclerosis) (NCEP, 2002). The notion that LDL contributes to atherogenesis is supported by research on genetic disorders (e.g., familial hypercholesterolemia) as well as controlled clinical trials and longitudinal cohort studies. For example, individuals diagnosed with familial hypercholesterolemia have elevated serum cholesterol concentrations, independent of lifestyle, medications, or diet, and experience premature atherosclerosis that frequently results in CHD (Scientific Steering Committee, 1991). Similarly, evidence from controlled clinical trials, such as the INTERHEART study (Yusuf et al., 2004) and longitudinal cohort studies, such as the Framingham Heart study (Wilson et al., 1998) suggest a direct relationship between TC and LDL-C levels and the development of CHD, so that lowering serum cholesterol can reduce the incidence of cardiac events (Gould, Davies, Alemao, Yin, & Cook, 2007; Heart Protection Study Collaborative Group, 2002; Scandinavian Simvastatin Survival Study Group, 1994). Additional support comes from a meta-analysis conducted by Gould et al. (2007) assessing the relationship between cholesterol reductions and changes in cardiac events from studies where more than half the patients had no history of CHD. Their analysis indicated that a 38.7 mg/dL decrease in TC among participants resulted in a reduction of 40.8% for CHD mortality and a reduction of 28.8% for any CHD event (e.g., fatal or non-fatal myocardial infarction). Collectively, these findings illustrate the contribution of cholesterol, specifically LDL-C, in the accumulation of fatty streaks and plaques, which can culminate in a cardiac event. Considering the substantial burden associated with cardiovascular disease, there could be a strong impact if one of its well-known risk-factors (i.e., cholesterol) could be successfully modified without pharmacological interventions.

Weight Loss to Lower Serum Cholesterol Levels

While the high incidence of cardiovascular disease and its direct relationship with hypercholesterolemia has been established, the most effective approach to achieve desirable

serum lipid levels among individuals identified as being at-risk has yet to be established. An approach that lowers TC, LDL-C, and triglycerides, while successfully raising HDL-C, would be optimal to protect against heart disease. The National Cholesterol Education Program has also identified obesity (i.e., BMI \geq 30) as a risk factor for CHD, and considering that obesity and high cholesterol often occur concurrently, their panel recommends lifestyle interventions that promote weight loss through diet modifications and increased physical activity to reduce cholesterol levels (2002).

The effect of weight loss on blood lipids and lipoproteins has been well established in the literature. Generally speaking, weight loss is associated with improvements in cholesterol levels. Results from randomized clinical trials have consistently indicated that during an initial period of active weight loss (i.e., 6 months to 1 year), participants experience a decrease in serum cholesterol levels (Gögebakan et al., 2011; Kuller et al., 2001; Look AHEAD Research Group, 2007; Perri et al., 2008). Furthermore, a meta-analysis conducted by Datillo (1992) concluded that for every kilogram decrease in body weight during a period of active weight loss, there is a 0.9 mg/dL decrease in TC and a 0.36 mg/dL decrease in LDL-C. Therefore, weight loss can effectively reduce serum cholesterol, although these reductions may be modest.

Notably, weight loss results in metabolic changes that effect serum cholesterol. When an individual loses weight, they reduce their abdominal obesity, which differentially disturbs metabolic processes and contributes to the risk of cardiovascular disease (Fox et al., 2007; NCEP, 2002; Reaven, Abbasi, & McLaughlin, 2004). Abdominal obesity is comprised of intra-abdominal visceral fat and abdominal subcutaneous fat and the distribution of these fats varies within obese and non-obese individuals; specifically, some adults have a larger amount of visceral fat and others have more subcutaneous fat (Reaven et al., 2004). However, these two

types of adipose tissues are not the same. Studies utilizing imaging techniques have revealed that intra-abdominal fat is more harmful than subcutaneous fat (Duncan, Ahmadian, Jaworski, Sarkadi-Nagy, & Sul, 2007; Fujioka, Matsuzawa, Tokunaga, & Tarui, 1987; Pascot et al., 1999; Reaven et al., 2004). In fact, adults with a larger proportion of visceral fat have higher base rates of LDL-C, TC, and triglycerides, and lower levels of HDL-C, compared to counterparts with more subcutaneous fat (Nieves et al., 2003). For that reason, intra-abdominal fat is a stronger predictor of cardiometabolic risk factors and can provide information beyond anthropometrics, such as BMI or waist circumference (Fox et al., 2007; Liu et al., 2010).

The strong association of visceral adipose tissue with cardiometabolic risk factors, such as the blood lipid profile, is a function of its impact on hepatic metabolism (Després & Lemieux, 2006; Nieves et al., 2003; Pascot et al., 1999). Specifically, an increase in visceral adipose tissue leads to an increase in free fatty acids that travel to the liver and alter hepatic lipase activity (Carr et al., 2001; Nieves et al., 2003; Pascot et al., 1999). Hepatic lipase is an enzyme that plays a role in determining the size and density of LDL-C and HDL-C, as well as the concentration of serum cholesterol. When hepatic metabolism is deregulated by the accumulation of free fatty acids, the liver produces smaller and denser LDL and HDL particles, which have been identified as a contributor to atherosclerosis (Carr et al., 2001; Carr et al., 1999; NCEP, 2002). Another result of this deregulation is a decline in the liver's ability to remove remaining lipoproteins from the blood, consequently increasing the amount of cholesterol circulating in the body (Carr et al., 2001; Nieves et al., 2003). Taken together, this implies that an increase in intra-abdominal fat stimulates the production of harmful lipoproteins (i.e., small and dense) while simultaneously hindering the liver's ability to remove excess cholesterol from the bloodstream.

This highlights the importance of weight loss in order to reduce abdominal obesity and improve regulation of hepatic metabolism. A reduction in visceral adiposity has been shown to improve the size of lipoproteins produced in the liver, as well as reduce serum cholesterol levels (Purnell et al., 2000). In addition, weight loss can improve cholesterol production through mechanisms not fully understood. For example, the impact of weight loss may differ depending on how it was achieved. When an individual engages in caloric restriction in order to reduce their body weight by 5%, they may see an increase in the size of their LDL particles (Varady, Bhutani, Klempel, & Kroger, 2011). On the other hand, when this 5% reduction in body weight is reached through physical activity, an individual may experience an increase in the size of their HDL particles, while also experiencing an improvement in the proportion of their small HDL to large HDL particles (Varady et al., 2011).

As mentioned above, weight loss modifies cholesterol synthesis, and simultaneously influences cholesterol absorption among various populations such as healthy and non-healthy adults (e.g., having type 2 diabetes) as well as those classified as having a normal weight or excess weight (i.e., obese) (Leichtle et al., 2011; Simonen, Gylling, & Miettinen, 2002). However, this characteristic response of cholesterol may not be long lasting. Leichtle et al. monitored serum cholesterol among participants throughout a 2-year dietary intervention, and during the first 6 months observed a decrease in serum cholesterol levels. This common improvement was noted to be a function of increased cholesterol absorption and decreased cholesterol synthesis. However, over the subsequent 18-month period, a rebound of these effects was observed so that cholesterol production greatly increased (2011). As a result, despite participants maintaining an overall weight loss, serum cholesterol levels returned to their baseline values, with some even surpassing it. This novel finding may help provide clarity to

results from lifestyle interventions measuring changes in cholesterol as a function of weight loss over the long term. As mentioned above, shorter-term lifestyle interventions report a decrease in blood lipids as a function of weight loss. However, among studies that include some type of follow-up or extended-care program, a trend has emerged where participant TC or LDL-C levels return to baseline values (Gögebakan et al., 2011; Kuller et al., 2001; Layman et al., 2009; Perri et al., 2008). Therefore, while cholesterol has been observed to increase after a prolonged period of time, the catalyst for this change has yet to be identified.

Dietary Changes to Lower Serum Cholesterol Levels

In addition to weight loss, the National Cholesterol Education Program encourages adults to modify their dietary intake in order to improve serum cholesterol levels, and specifically LDL-C (2002). In particular, the National Cholesterol Education Program has promoted a reduction in dietary fat intake, emphasizing the cholesterol-raising properties of dietary saturated fat (2002). It should be noted that despite this recommendation, dietary fat is an essential component of bodily functioning; however, in excess it can contribute to the energy imbalance that leads to obesity and an increase in the blood lipid profile (Lichtenstein et al., 1998).

Regarding dietary fat, it is mostly made of triglycerides (98%), and upon entering the body undergoes hydrolysis to be broken down into several components (Lichtenstein et al., 1998). After hydrolysis, the remaining components of dietary fat are mainly free fatty acids. The differences in dietary fat become apparent at this point, and the free fatty acids are classified by the presence or absence of double bonds. First, a fatty acid with no double bond is deemed a saturated fatty acid. Next, a fatty acid with a double bond is recognized as an unsaturated fatty acid, which is further classified as either a monounsaturated (the presence of one double bond) or a polyunsaturated (the presence of two or more double bonds) fatty acid (Food and Nutrition

Board, 2005; Lichtenstein et al., 1998). Last, a fatty acid that has at least one double bond in a trans configuration is appropriately titled a trans fatty acid (Food and Nutrition Board, 2005).

In general, excess dietary fat is harmful to the body because it travels back to the liver where it may be further metabolized into a component of LDL (Food and Nutrition Board, 2005). Similar to excess dietary fat, saturated fat is taken back to the liver and is metabolized into a component of LDL, but it differentially affects the concentration of serum cholesterol because at the same time, it suppresses the expression of LDL receptors, which results in higher amounts of LDL-C in circulation (Mustad et al., 1997). For this reason, dietary saturated fat is targeted as the most influential LDL-C raising nutrient (NCEP, 2002).

For the average American, saturated fat comprises 11% of their daily caloric intake and is most often consumed as high-fat dairy products (i.e., whole milk, cheese, butter, ice cream and cream); high-fat meats; tropical oils such as palm or coconut oil; and baked products/mixed dishes (NCEP, 2002). Among adults whose total caloric intake is mainly a function of their dietary fat intake, a “lipid triad” may be observed, indicating the presence of abnormally high LDL-C and triglycerides, and low HDL-C.

Experimental studies have explored the relationship of fat intake on the blood lipid profile, by comparing fat intake to other nutrients (e.g., carbohydrates), and also by manipulating the types of fat an individual consumes. In relation to other nutrients, saturated fat generally has a more harmful impact on blood lipids. Howard et al. (2010) reported that over a 6-year period, postmenopausal women on a low-fat, higher-carbohydrate diet experienced greater decreases in LDL-C and non-HDL-C than those on a high-fat, lower-carbohydrate diet. Additionally, they found that these decreases in LDL-C and HDL-C were larger among those with greater declines in their saturated or trans fat intake. Similar studies have been conducted to explore the effect of

saturated fatty acids compared to unsaturated fatty acids (Summers et al., 2002; Vessby et al., 2001). Vessby et al. (2001) prescribed healthy adults a diet with the same proportion of nutrients, including relatively similar amounts of total fat, but modified the amount of saturated fat or monounsaturated fat in their diet. As a result of the higher saturated fatty acid diet, the participant's serum cholesterol and LDL-C increased significantly by 2.5 and 4.1%, respectively. On the other hand, the monounsaturated fatty acid diet significantly reduced serum cholesterol and LDL-C concentrations by 2.7 and 5.2%. Finally, in short-term studies where adults have decreased their overall dietary fat intake, they have experienced a subsequent decrease in TC, LDL-C, and HDL-C (Cole et al., 1995; Ginsberg et al., 1998; Lefevre et al., 2005). Within these studies, differences in cholesterol reductions as a response to reduced fat intake have been reported depending on an individual's baseline weight. Interestingly, men with a BMI ≥ 25 kg/m² had 30% smaller reductions in LDL-C concentrations than men with a lower BMI, despite equal reductions in their dietary fat intake (Ginsberg et al., 1998). A similar phenomenon has been observed among women so that those with a BMI of 24-30 kg/m² had smaller LDL-C concentration reductions than those with a lower BMI when fat and cholesterol were equally reduced (Cole et al., 1995).

The NCEP has also identified total fat intake as a contributor to serum cholesterol levels. While dietary total fat includes monounsaturated and polyunsaturated fatty acids, which do not negatively impact serum cholesterol levels or lipoprotein production, it does incorporate trans fatty acids, which has a similar effect on the blood lipid profile as saturated fatty acids (Lichtenstein et al., 1998). Therefore, total fat intake includes an additional element that may increase our understanding of changes in serum cholesterol levels.

Specific Aims and Hypothesis

Obese individuals who lose weight commonly show reductions in LDL-C and TC, important risk factors for heart disease. However, it is unclear if improvements are due to weight loss, dietary change, or both. In the current study we address the following specific aims:

Specific Aim 1

To understand the contribution of changes in self-reported dietary saturated fat intake on changes in LDL-C, beyond what is accomplished by changes in BMI, during a lifestyle intervention for obesity. We sought to explore the impact of changes in self-reported saturated fat intake on LDL-C during a period of weight loss (i.e., Month 0 to Month 6), as well as during a period of extended care (i.e., Month 6 to Month 18). With regard to changes observed during Month 0 to Month 6, we hypothesized (a) that weight loss would predict lower LDL-C and (b) that decreased dietary saturated fat intake would significantly add to the explained variance in the lower LDL-C levels. For the changes observed during Month 6 to Month 18, we hypothesized (a) that weight regain would predict higher LDL-C and (b) that increased dietary saturated fat intake would significantly add to the explained variance in the higher levels of LDL-C as well.

Specific Aim 2

To determine the impact of changes in dietary total fat intake on changes in TC, after controlling for change in BMI during periods of weight loss and extended care. We hypothesized that accounting for change in dietary total fat intake would increase the explained variance for changes in TC, above what is accounted for by changes in BMI alone. Therefore, we predicted (a) that weight loss would predict the decrease in TC and (b) that modifications to dietary intake (i.e., decreased total fat intake) would make a unique contribution to predicting lower TC levels. On the other hand, we hypothesized (a) that increases in BMI during a 12-month period of

extended care would predict the increase in TC and (b) that higher fat intake would also make a unique contribution to predicting the rise in TC levels.

CHAPTER 2 MATERIALS AND METHODS

Participants

The current study included 232 women between the ages of 50 and 75 having a BMI ≥ 30 kg/m², yet weighing less than 159kg (350lbs). Participants were from underserved rural areas in North Central Florida recruited via direct solicitation, such as direct mailings and presentations at community events. Interested participants were encouraged to complete a brief phone screen, and those who met initial eligibility criteria were scheduled for a subsequent screening visit. At the first screening visit the study was described in detail to potential participants, informed consent was obtained, personal demographic information was collected, as was a comprehensive medical history and a current medication inventory. Based on a cursory review of this information, participants were scheduled for a second screening visit. The second screening visit included: questionnaires regarding dietary intake, physical activity, health related quality of life, depressive symptoms and problem solving; height, weight and girth measurements; resting heart rate and blood pressure; a fasting blood draw to assess metabolic and lipid profiles; a 6-minute walk test; and an electrocardiogram.

Following these assessment visits, the individuals screening results were reviewed to determine if the woman qualified for participation in the study. Exclusion criteria was limited to conditions that would affect an individuals ability to adhere to treatment, interfere with treatment outcomes, as well as those for which increased physical activity and dietary modifications could be harmful. Exclusions included diseases likely to limit lifespan, such as cancer requiring treatment in the past 5 years (exception: non-melanoma skin cancer), serious infectious diseases (e.g., self-reported HIV, self-reported tuberculosis or treatment), cardiovascular events within the

last 6 months (e.g., stroke, angina, myocardial infarction), chronic hepatitis, cirrhosis, chronic malabsorption syndrome, chronic pancreatitis, irritable bowel syndrome, previous bariatric surgery, history of solid organ transplantation, history of musculo-skeletal conditions that limit walking, chronic lung diseases limiting physical activity, serum creatinine > 1.5 mg/dL, anemia (hemoglobin < 10 g/dL). Additional exclusions were made based on metabolic and lipid profiles; participants could not have a fasting blood glucose > 125 mg/dL at screening if not known to be diabetic (diabetic patients under active treatment will be enrolled if approved by primary provider), a fasting serum triglycerides > 400 mg/dL or a resting blood pressure > 140/90 mmHg, despite appropriate drug treatment. Those who reported a psychiatric condition, current use of prescription weight-loss drugs, or weight loss greater than 4.5 kg (10 lbs) in the preceding 6 months were excluded as were those with any behavior that would adversely affect participation in TOURS (e.g., excessive alcohol intake; unable to read English at the 5th grade level; likely to move out the county in next 2 years).

Of the 298 women who were enrolled in the study and began Phase 1, 234 were randomized to one of the three extended-care conditions. Of these 234 women, 2 individuals were removed from the current analysis due to incomplete data. Therefore, the included 232 women were between the ages of 50 and 75 ($M = 59.8$, $SD = 6.3$), had a mean pretreatment BMI of 36.8 kg/m^2 ($SD = 4.8$), and weight of 96.7 kg ($SD = 15.0$). The majority of the women were Caucasian ($n = 181$, 78%) or African American ($n = 42$, 18%), with the rest identifying themselves as Hispanic ($n = 4$, 2%) or Other ($n = 5$, 2%). Regarding their education, almost the same number of women completed 12 or fewer years of education ($n = 95$, 41%) as those who completed trade or vocational school or had an associates degree ($n = 97$, 42%); similarly, the women were evenly split ($n = 20$, 9% and $n = 20$, 9%) between receiving a bachelor's degree and

having post baccalaureate education or training. Baseline characteristics are presented in Table 2-1.

Procedure: The Treatment of Obesity in Underserved Rural Settings (TOURS) Intervention

Contingent on their eligibility status, included participants were enrolled in the TOURS study, designed to explore the effectiveness of three extended-care programs on sustained weight loss (Perri et al., 2008). All included women completed an initial 6-month lifestyle modification program for weight loss, delivered at local Cooperative Extension Service offices. During this first phase, the women attended group meetings with 10-14 other participants, and a group leader, who was either a Family and Consumer Sciences (FCS) Agent or an individual with a bachelor's or master's degree, and experience providing nutrition education and dietary interventions. The lifestyle intervention consisted of a modified version of the Diabetes Prevention Program and focused on achieving weight loss through the following avenues; a moderate reduction in caloric intake (i.e., 500 – 100 kcal), an increase in physical activity, and cognitive-behavioral strategies which supported the development of the other two goals (The Diabetes Prevention Program, 1999). Therefore, the participants were encouraged to maintain a low-calorie diet (i.e., 1200 kcal/d), increase their physical activity (i.e., 30min/d of walking), and to participate in a range of cognitive-behavioral skills related to their self-management (e.g., goal setting) and self-monitoring. In addition, the materials in each session focused on providing relevant information to women living in rural areas, as well as those from different cultural backgrounds (i.e., African American and Hispanic women). This included demonstrations of healthy cooking and food tastings of healthier alternatives to commonly prepared foods in southern, rural households.

After completion of the 6-month intervention, participants were randomly assigned to one of three extended-care programs (i.e., one of two experimental programs or to the education control condition), each lasting 12 months. While women in each extended-care program were encouraged to maintain improvements in their diet and physical activity, the modality of each program differed. Regarding the experimental extended-care programs, one was conducted in a face-to-face group counseling session (as in Phase 1) and the other was delivered via an individual telephone counseling session. Still, both experimental extended-care programs utilized problem-solving approaches to help overcome barriers to weight loss or maintenance. On the other hand, women in the education control condition received biweekly newsletters in the mail focused on strategies to maintain a healthy lifestyle, but they did not directly interact with a group leader or other participants.

Measures

Several measures were administered to participants at baseline (Month 0), after 6 months of lifestyle treatment (Month 6), and following participation in a 12-month extended-care program (Month 18) to assess changes in BMI, changes in self-reported dietary composition (i.e., saturated and total fat intake), and changes in their blood lipid profile (i.e., LDL-C and TC).

Anthropometry

Throughout the lifestyle intervention, height and weight measurements were obtained. At Month 0, height was taken with a stadiometer, measuring to the nearest 0.1 centimeter. Weight was assessed with a balance beam scale, measuring in kilograms, at Month 0, as well as at Month 6 and Month 18. Taken together, these measurements were used to compute the body mass index (kg/m^2) for each participant at each time point (i.e., Month 0, 6, and 18).

Dietary Assessment

Self-reported saturated fat and total fat intake were derived from The Block 95 Food Frequency Questionnaire (FFQ) and measured at Month 0, 6, and 18 (Block et al., 1986). The Block 95 FFQ is a paper-and-pencil form with multiple-choice questions, assessing caloric intake, consumption of specific food groups (e.g., whole grains, fruits and vegetables), dietary fat, and macro- and micro-nutrient intakes. The Block FFQ assesses dietary patterns over the previous year, querying for types of foods, their frequency, and portion size (Block et al., 1986). Respondents reported how often they usually consumed each food, as number of times per day, week, month or year, and whether their usual portion size of that food was ¼ cup, ½ cup, 1 cup or 2 cups (example of these portion sizes were illustrated on the final page of the questionnaire). Participants answered supplementary questions regarding their overall frequency of fruit and vegetable consumption; the frequency of fat or oil in cooking and types used; dietary supplements and vitamins; and demographic information. Taken together, this data was utilized to produce daily estimates of saturated fat intake and total fat intake in grams.

The Block FFQ has been updated and validated, and its ability to estimate intake as compared to 4-day diet records is generally in the range of $r = 0.5-0.6$, suggesting moderate to good abilities to assess dietary intake (Block, Woods, Potosky, & Clifford, 1990). Similarly, the questionnaire has been shown to differentiate between population groups with different nutritional intakes as compared to reference data (i.e., 4-day diet records); however, its ability to accurately predict intake of several dietary components (e.g., percent calories from fat, saturated fat, carbohydrates) was significantly weaker among participants educated on reducing their fat intake, as compared to estimates from their 4-day diet records (Block et al., 1990).

Blood Lipids

Levels of LDL-C and TC were analyzed at Month 0, 6 and 18 to assess for changes in the blood lipid profile as a result of the lifestyle intervention. Under aseptic conditions, using standard venipuncture techniques, 15cc samples of blood were drawn and analyzed for lipid profile (e.g., TC and LDL-C). The blood samples were analyzed by Quest Diagnostics Clinical Laboratories, which is accredited by the College of American Pathologists. The most recent external proficiency ratings for Quest Diagnostics in northern Florida indicated a pass rate of 99.76% and an error rate of 2,417 ppm. The proficiency-testing data of Quest Diagnostics met the requirements of NHLBI's Lipid Standardization Program.

Statistical Analysis

The statistical software package SPSS 18.0 for Windows (SPSS Inc., IL) was used to conduct the statistical analysis for this research study.

Specific Aim 1

Paired samples t-test were conducted for each variable to determine how BMI, saturated fat intake, and LDL-C changed throughout the lifestyle intervention (i.e., from Month 0 to Month 6, and Month 6 to Month 18). Next, change scores were obtained for BMI, saturated fat intake, and LDL-C. These scores were calculated for the weight loss period by obtaining the difference of each variable (i.e., BMI, saturated fat intake, LDL-C) from Month 6 and Month 0; a separate change score was calculated for the extended-care period by obtaining the difference of each variable from Month 18 to Month 6. The predictor variables, change in BMI and change in saturated fat intake, were skewed and kurtic and normalized with the Blom transformation (Blom, 1958). Finally, we examined the independent contributions of change in BMI and change in saturated fat intake on change in LDL-C with hierarchal regressions, with change in BMI (block one) and change in self-reported saturated fat intake (block two) as the predictor variables

and change in LDL-C as the dependent variable. One regression was conducted (a) with change scores during the period of weight loss (i.e., Month 0 to Month 6), and a second (b) with change scores during the period of extended care (i.e., Month 6 to Month 18).

Specific Aim 2

We examined the hypothesis that change in BMI would predict change in TC, and that change in total fat would also significantly add to the explained variance in change in TC, through the same processes that were described above. However, for this aim, the hierarchical regressions had change in BMI (block one) and change in self-reported total fat intake (block two) as the predictor variables and change in TC as the dependent variable. Similar to above, one regression was conducted (a) with change scores during the period of weight loss (i.e., Month 0 to Month 6), and a second (b) with change scores during the period of extended care (i.e., Month 6 to Month 18).

Table 2-1. Baseline Characteristics (N = 232)

Variable	
Age in years, <i>M (SD)</i>	59.8 (6.3)
BMI in kg/m ² , <i>M (SD)</i>	36.8 (4.8)
Weight in kg, <i>M (SD)</i>	96.7 (15.0)
Ethnicity, <i>n (%)</i>	
Caucasian	181 (78%)
African American	42 (18%)
Hispanic	4 (2%)
Other	5 (2%)
Education, <i>n (%)</i>	
≤ 12 years	95 (41%)
12 < 16	97 (42%)
≥ 16 years	40 (18%)

CHAPTER 3 RESULTS

Specific Aim 1

At the study's onset, participants mean BMI was 36.8 kg/m² ($SD = 4.8$) and their daily saturated fat was calculated to average 24.4 g ($SD = 15.6$). In terms of their baseline blood lipids, mean LDL-C was 121.1 mg/dL ($SD = 29.2$), which is classified in the “near optimal” range (i.e., 120 – 129 mg/dL) by the National Education Cholesterol Program (2002) and is similar to baseline blood lipids among healthy, obese individuals participating in other lifestyle interventions (Kuller et al., 2001). After completing the 6-month lifestyle intervention, BMI decreased ($M = 33.3$ kg/m², $SD = 4.9$), as did self-reported saturated fat intake ($M = 13.9$ g, $SD = 7.2$). To explore these improvements, paired samples t-test were conducted and revealed that both BMI and self-reported saturated fat intake significantly decreased from Month 0 to Month 6 (BMI, $t(231) = -24.6$, $p < .001$; saturated fat intake, $t(231) = -11.6$, $p < .001$). Similarly, LDL-C was reduced at Month 6 ($M = 116.1$ mg/dL, $SD = 29.9$) and this was a significant improvement from baseline, as determined by a paired samples t-test ($t(231) = -3.0$, $p < .01$).

To explore the contribution of change in saturated fat intake to predict change in LDL-C, beyond what change in BMI predicted during Month 0 to Month 6, a hierarchical regression was employed, using transformed change scores for each predictor variable. The initial model was significant, $F(1,230) = 11.35$, $p < .01$, with change in BMI predicting change in LDL-C ($\beta = .22$, $p < .01$) and accounting for 4.7% of the explained variance. Entry of change in saturated fat intake accounted for an additional 1.2% of the explained variance, but this was not a significant increase in the explained variance of the change in LDL-C, $F(2,229) = 7.14$, $p < .01$. Change in

BMI, however, remained significant ($\beta = .19, p < .01$), suggesting that initial weight loss is associated with changes in LDL-C. Results are presented in Table 3-1.

At the completion of the extended-care period (i.e., Month 18), participants tended to regain weight (BMI, $M = 33.9 \text{ kg/m}^2, SD = 5.3$) and eat higher quantities of saturated fat ($M = 14.7 \text{ g}, SD = 7.9$). Additionally, their LDL-C rose and was equivalent to baseline levels ($M = 122.1 \text{ mg/dL}, SD = 33.4$).¹ Dependent samples t-test revealed a significant effect of time on BMI ($t(231) = 4.5, p < .001$), self-reported saturated fat intake ($t(231) = 2.0, p < .05$), and LDL-C ($t(231) = 3.4, p < .01$). Although both BMI and LDL-C increased during Month 6 to Month 18, change in BMI did not significantly predict change in LDL-C, $F(1,230) = .06, p = .81$. Similarly, change in self-reported saturated fat intake did not significantly add to the explained variance in change in LDL-C, $F(2,229) = .10, p = .90$. Results are presented in Table 3-2.

Specific Aim 2

Before beginning treatment, participants mean BMI was $36.8 \text{ kg/m}^2 (SD = 4.8)$, their mean self-reported total fat intake was $86.0 \text{ g} (SD = 56.1)$ and their mean TC was $206.4 \text{ mg/dL} (SD = 31.5)$. Unlike their LDL-C which was classified in the “near optimal range”, their average TC was classified as “borderline high” by the National Education Cholesterol Program (2002). From Month 0 to Month 6, women in the study lost weight ($M = 33.3 \text{ kg/m}^2, SD = 4.9$), decreased their total fat intake ($M = 50.4 \text{ g}, SD = 25.6$) and their TC improved ($M = 194.3 \text{ mg/dL}, SD = 33.7$). As reported above, paired samples t-tests revealed that the average weight loss between this time period was a significant improvement. Additional paired samples t-test demonstrated that participants significantly reduced the amount of total fat in their diet, $t(231) = -10.8, p < .001$,

¹ Of note, we examined differences between changes in weight, saturated fat intake, and LDL-C between participants in the 3 extended-care conditions and none were found.

and that their TC also decreased significantly, $t(231) = -6.6, p < .001$. These findings indicated that participants made improvements in their diet, were losing weight, and experienced improved serum cholesterol levels. In fact, their mean cholesterol at Month 6 was no longer classified as “borderline high” but was considered “desirable” (National Education Cholesterol Program, 2002).

We examined the ability of change in total fat intake to predict change in TC, after controlling for the contribution of change in BMI from Month 0 to Month 6. A hierarchical regression revealed that change in BMI significantly predicted the changes seen in TC ($\beta = .31, p < .001$), so that a decrease in weight predicted a decrease in TC, $F(1,230) = 24.81, p < .001$, accounting for 9.7% of the explained variance. Entry of change in total fat intake contributed an additional 1.4% explained variance and approached significance in terms of its ability to predict changes in TC ($\beta = .12, p = .06$). In this step, change in BMI continued to significantly predict changes in TC ($\beta = .29, p < .001$), but the overall model did not improve, $F(2,229) = 14.29, p < .001$. Results are presented in Table 3-3.

As reported above, during the extended-care period (i.e., Month 6 to Month 18) participants experienced weight regain (BMI, $M = 33.9 \text{ kg/m}^2, SD = 5.3$) they introduced a small amount of total fat back into their diet ($M = 53.1 \text{ g}, SD = 28.8$) and their TC rose so that it was slightly over the recommended level ($M = 203.0 \text{ mg/dL}, SD = 36.4$). Notably, the increase in total fat intake was not significant, $t(231) = 1.6, p = .10$, as revealed by the paired samples t-test.² As seen before, the paired samples t-test indicated that the change in weight was significant ($p < .001$), as was the increase in TC, $t(231) = 4.4, p < .001$. To examine the predictive ability of

² Of note, we examined differences between changes in weight, total fat intake, and TC between participants in the 3 extended-care conditions and none were found.

change in total fat on TC, independent of change in BMI from Month 6 to Month 18, a hierarchical regression was utilized. Results indicated that the increase in weight did not significantly predict the increase in TC, $F(1,230) = .10, p = .75$. In addition, change in total fat intake was not able to significantly predict change in TC levels, and the overall model remained not significant, $F(2,229) = .24, p = .79$. Results are presented in Table 3-4.

Table 3-1. Summary of Hierarchical Regression Analysis for Variables Predicting Changes in LDL-C from Month 0 to Month 6 ($N = 232$).

Variable	B	SE B	β	ΔR^2
Step 1				.047**
Δ in BMI	5.54	1.65	.22**	
Step 2				.012
Δ in BMI	4.92	1.68	.19*	
Δ in Sat. Fat Intake	2.84	1.68	.11	

Note. * $p < .05$ ** $p < .001$

Table 3-2. Summary of Hierarchical Regression Analysis for Variables Predicting Changes in LDL-C from Month 6 to Month 18 ($N = 232$).

Variable	B	SE B	β	ΔR^2
Step 1				0
Δ in BMI	-.43	1.76	-.02	
Step 2				0
Δ in BMI	-.34	1.78	-.01	
Δ in Sat. Fat Intake	-.68	1.78	-.03	

Table 3-3. Summary of Hierarchical Regression Analysis for Variables Predicting Changes in TC from Month 0 to Month 6 ($N = 232$).

Variable	B	SE B	β	ΔR^2
Step 1				.097**
Δ in BMI	8.90	1.79	.31**	
Step 2				.014
Δ in BMI	8.31	1.81	.29**	
Δ in Total Fat Intake	3.38	1.81	.12	

Note. * $p < .05$ ** $p < .001$

Table 3-4. Summary of Hierarchical Regression Analysis for Variables Predicting Changes in TC from Month 6 to Month 18 ($N = 232$).

Variable	B	SE B	β	ΔR^2
Step 1				0
Δ in BMI	.64	2.00	.02	
Step 2				0
Δ in BMI	.47	2.00	.02	
Δ in Total Fat Intake	1.25	2.00	.04	

CHAPTER 4 DISCUSSION

Summary and Interpretation of the Results

For the first aim, change in BMI, change in saturated fat intake, and change in LDL-C were examined at baseline, after the 6-month weight loss intervention (i.e., Month 6) and at the conclusion of the 12-month extended-care phase (i.e., Month 18). During the weight loss phase, changes in weight, dietary composition, and cholesterol decreased as expected; the participants lost a significant amount of weight, they reported a significant decrease in their saturated fat intake, and their LDL-C showed a significant improvement. During these 6 months, their almost 10% decrease in BMI was similar to improvements in weight reported among other lifestyle interventions, such as the Diabetes Prevention Program (Ratner, 2006) and the Women's Healthy Lifestyle Project (Kuller et al., 2001). Similarly, the improvements observed in LDL-C were comparable to changes in interventions reporting improvements in LDL-C levels as a function of weight loss among obese, yet healthy participants (Kuller et al., 2001; Vidal, 2002).

The current study found that a decrease in BMI predicted a decrease in LDL-C, which was observed among the participants from Month 0 to Month 6. However, during this time period, participants reported a significant decrease in their saturated fat intake, yet this improvement in their diet composition did not predict the improvements seen in LDL-C, after controlling for what was explained by weight loss. While this finding is inconsistent with previous research that has asserted that a decrease in saturated fat intake contributes to a decrease in LDL-C, these other studies measured the effect of reduced fat intake on serum cholesterol, as opposed to the effect of both change in weight and dietary composition (Howard et al., 2010; Lefevre et al., 2005; Lichtenstein et al., 1998; Siri-Tarino, Sun, Hu, & Krauss, 2010). Therefore, while

reductions in saturated fat intake have been shown to improve LDL-C, these improvements may be better accounted for by a reduction in weight, which may explain why change in saturated fat intake did not predict change in LDL-C in the current study.

The contribution of change in saturated fat intake to predict change in LDL-C, beyond change in BMI, was also explored during a 12-month period of extended care. During these 12-months, participants tended to regain weight, increase their consumption of foods containing saturated fat, and experience an increase in their average LDL-C, which approached baseline levels. Despite these changes, participants still maintained on average, an 8% decrease in their BMI since beginning the program 18 months prior. Therefore, considering that participants achieved and maintained a substantial amount of weight loss throughout the intervention, it was unexpected that the increase in reported saturated fat intake and BMI would not predict the increase observed in LDL-C. Of note, while it is unique to report that change in fat intake and BMI were not associated with change in LDL-C, the observed increase in LDL-C is consistent with the literature. In fact, other interventions utilizing dietary modifications, weight loss, or both, have observed an increase in TC and LDL-C over the long term, despite sustained dietary changes. (Gögebakan et al., 2011; Kuller et al., 2001; Layman et al., 2009; Perri et al., 2008). Taken together, this may indicate that improvements in serum cholesterol as a function of weight loss and dietary changes may not be long lasting (Leichtle et al., 2011).

For the second aim, the change in TC was explored, notably as it related to change in reported total fat intake. As mentioned above, the participants reduced their BMI by almost 10% during the first 6 months of the lifestyle intervention. Additionally, they demonstrated significant improvements in their reported total fat intake and their TC. Similar to what has been observed and reported by other researchers, results from the current study indicated that the decrease in

BMI predicted the decrease in TC (Datillo, 1992; Datillo & Kris-Etherton, 1992). However, the finding that change in total fat intake did not contribute to the explained variance in change in TC was contrary to research supporting a relationship between modifications to dietary composition and TC.

A separate analysis was conducted to observe if change in BMI and total fat intake could increase the explained variance of change in TC during a period of time when many participants were experiencing an increase in their weight and an increase in their consumption of calories. Interestingly, while participants regained weight and experienced an increase in TC that was comparable to its level at baseline, reported total fat intake only marginally increased. Still, results from the current study were novel in finding that an increase in BMI and reported total fat intake did not predict changes observed in TC.

Implications and Relevance to the Current Literature

The results of this current study evaluating the role of self-reported fat intake on change in serum cholesterol levels, beyond the impact of weight loss or weight gain, has implications and relevance to current literature. In general, both weight and fat intake have been shown to affect the blood lipid profile. Several lifestyle interventions have found that when overweight or obese adults with a high blood lipid profile lose weight, they commonly experience an improvement in their LDL-C and TC levels (Gögebakan et al., 2011; Kuller et al., 2001; Layman et al., 2009; Perri et al., 2008). This improvement in serum cholesterol, as a function of weight loss, has been attributed to a reduction in adipose tissue, which improves hepatic metabolism (Leichtle et al., 2011; Simonen et al., 2002). Regarding fat intake, interventions also show that when overweight adults modify their dietary intake so that they are consuming less fat, they experience subsequent improvements in LDL-C and TC (Cole et al., 1995; Ginsberg et al., 1998; Lefevre et al., 2005).

However, with an increase in lifestyle interventions that include longer-term treatment programs, there has been a heightened awareness that improvements obtained in LDL-C and TC are not always maintained. One study showed that adults in a 4-month period of active weight loss experienced initial improvements in TC and LDL-C that were not sustained during an 8-month weight maintenance period (Layman et al., 2009). Additional lifestyle interventions have observed the same trend in LDL-C and TC, despite their participants maintaining an overall weight loss (Gögebakan et al., 2011; Layman et al., 2009; Perri et al., 2008). One exception to this is the Women's Healthy Lifestyle Project, which did report increases in LDL-C after 6 months, yet LDL-C did not approach baseline levels for another 48 months; therefore, while LDL-C did worsen over time, it appeared to do so more slowly than in other studies (Kuller et al., 2001). Of note, over 30% of participants in the Women's Healthy Lifestyle Project were on hormone replacement therapy throughout the study and they were noted to have smaller increase in their LDL-C than non-hormone users, which may have influenced the overall smaller increase in LDL-C.

The current study attempted to further explore self-reported fat intake as a possible cause for the changes observed in both LDL-C and TC throughout a lifestyle intervention for weight loss. Results of this study indicate that obese individuals may benefit more from weight loss, rather than modifications to their dietary content, when they are trying to reduce LDL-C and TC levels; however, it is unlikely and ill-advised for an individual to maintain a negative energy balance over the long-term, necessary to produce weight loss and subsequent improvements in LDL-C and TC. Furthermore, while we acknowledge the National Cholesterol Education Program recommendations to reduce saturated fat intake to improve LDL-C, results from this study indicate that the effect of saturated and total fat intake on serum cholesterol levels may not

significantly differ. For that reason, treatment for high cholesterol may not need to be overly concerned with types of fat, and instead may benefit from focusing on a reduction in total fat. Considering that it may be simpler to teach individuals to reduce their overall fat content, rather than how to reduce specific types of fats (e.g., saturated fat vs. trans fat vs. unsaturated fat), this may be beneficial in terms of clinical treatment.

Findings from this study add to the body of literature demonstrating the ability of weight loss to produce short-term benefits on blood lipids. It remains unclear, however, why improvements in serum cholesterol were not lasting given that the majority of people lost weight and sustained beneficial changes to their diet. One possible explanation may be that changes in LDL-C and TC observed from Month 0 to Month 6 were a function of decreased calorie intake, rather than weight loss. This would mean that despite losing weight from Month 0 to Month 18, because participants were no longer in an active state of weight loss, they were unable to sustain improvements in their serum cholesterol. Additional support for this theory comes from a recent study by Gögebakan et al. (2011) which compared the effect of calorie restriction to diet modifications on blood lipids. Results from this analysis indicated that during a period weight loss, improved nutrient intake (i.e., low-fat, low glycemic index food pattern) led to improvements in TC and LDL-C, yet these changes were not sustained when participants increased their caloric intake while maintaining the same dietary composition. Therefore, it may be that a negative calorie balance is needed in order to produce improvements in TC and LDL-C and the inability to maintain this in the long-term may lead to the loss in previously improved serum cholesterol levels.

Limitations to the Present Study

When interpreting the results and implications of the current study, it is important to note several limitations. First, the current study targeted obesity among a specific population of

healthy women living in rural areas. Men were not included, nor were any adults younger than 50. For these reasons, results from the study may not be as easily translated to the general population. A second limitation to the study is also a function of the inclusion and exclusion criteria. Adults who were enrolled in TOURS could not have any uncontrolled medical condition, including uncontrolled blood lipids. Therefore, adults included in this analysis were considered to have “above optimal” cholesterol levels, which is still within an acceptable range. This requirement to have acceptable blood lipids limits the results in two ways. For one, it may have hindered our ability to see a true effect of fat intake on cholesterol because participants did not begin the study with “at-risk” serum cholesterol levels. Similarly, our analysis included a truncated range of serum cholesterol levels which also makes these results less easily translated to a population of adults with high blood lipids.

An additional limitation of the study is that in the current analysis, we did not control for adults who may have initiated or discontinued treatment for abnormal blood lipids. Therefore, some women may have been taken off cholesterol-lowering medications when they lost weight and saw improvements in their blood lipids. Consequently, this may have contributed to an increase in their cholesterol over the following 12 months, when they tended to regain weight.

Another limitation relates to the validity of the Block Food Frequency Questionnaire (FFQ). As mentioned above, the finding that change in self-reported fat intake did not predict change observed in both LDL-C and TC was not consistent with previous research. There is some indication that the inconsistency between these findings and other research may be partially attributed to the validity of the Block FFQ. The Block FFQ is a useful measure of diet composition and was utilized to assess saturated fat and total fat intake (Block et al., 1986). However, the ability of the Block FFQ to evaluate consumption of macronutrients, such as fat, is

somewhat weaker than its accuracy when evaluating the consumption of specific food groups (e.g., vegetables, grains, fruits, etc.) (Mares-Perlman et al., 1993). This translates to a limitation to accurately assess the participant's daily intake of total and saturated fat.

The last limitation to this study is the reliance on participants to accurately complete the Block FFQ. It is possible, and likely, that as education on dietary composition increased and a relationship between the participants and group leaders developed, the participants felt a need to give socially desirable responses (Fisher, 1993). Therefore, the participants may have somewhat underestimated consumption of foods that they had been encouraged to eat more sparingly, such as sweets with high-fat content. This would in turn make it more difficult to assess a relationship between dietary fat intake and serum cholesterol. Similarly, the Block FFQ prompted respondents to report their food consumption over the past year, forcing them to rely on their memory and potentially leading to inaccuracies in their estimates. Taken together, the discrepancy between this study and previous research that links fat intake to cholesterol levels may be influenced by the ability of the Block FFQ to provide precise and accurate estimations of fat intake.

Despite these limitations, this study has several notable strengths. One strength of the study is the length of the lifestyle intervention. For example, while many of the abovementioned studies observed fluctuations in cholesterol over multiple time points, their maintenance periods tended to be shorter in duration. A second strength of the current study is that participants were educated on methods to improve their nutrition to eat a healthy diet, yet at no time were they prescribed any specific meal requirements. In many interventions, participants are either given meals to eat or are assigned diets with varying nutrient content. Therefore, the changes observed

in nutrient intake and serum cholesterol levels among participants in the current study are more similar to what would be experienced by those in the general population.

Summary and Conclusion

In summary, this study has two main findings. The first finding, consistent with previous research, is that the beneficial impact of a lifestyle intervention on LDL-C and TC is more closely related to weight loss than to a decrease in fat intake among obese adults. The second finding is that improvements in serum cholesterol levels may be limited to those periods in which an individual is losing weight. Based on these findings, we have several suggestions for future research. First, since a trend is developing among longer-term interventions to observe a loss of previously acquired improvements in LDL-C and TC, future studies should explore potential reasons for this. One possible explanation that should be explored is the effect of reduced caloric intake on blood lipids. As mentioned above, it may be that a negative energy deficit, as opposed to overall weight loss, is required to initiate and maintain an increase in cholesterol absorption and a decrease in synthesis. Second, given that this study did not account for women discontinuing or starting lipid-lowering medications, future studies should monitor this more closely and examine its impact on changes observed in serum cholesterol. Third, present studies tend to focus on recruiting a population of adults classified as having either normal or abnormal blood lipids and do not normally include participants who significantly differ in their baseline cholesterol levels. Therefore, it would be interesting to observe how adults who have high or low baseline serum cholesterol respond to the same lipid-improving treatment (i.e., weight loss or dietary modifications).

LIST OF REFERENCES

- American Heart Association Heart Disease and Stroke Statistics Writing Group. (2011). Heart disease and stroke statistics—2011 update: a report from the American Heart Association. *Circulation, 123*, e18–e209.
- Anderson, J. W., Konz, E. C., Frederich, R. C., & Wood, C. L. (2001). Long-term weight-loss maintenance: a meta-analysis of U.S. studies. *American Journal of Clinical Nutrition, 74*, 579–584.
- Block, G., Hartman, A.M., Dresser, C.M., Carroll, M.D., Gannon, J., & Gardner, L. (1986). A databased approach to diet questionnaire design and testing. *American Journal of Epidemiology, 124*, 453 – 469.
- Block, G., Woods, M., Potosky, A., & Clifford, C. (1990). Validation of a self-administered diet history questionnaire using multiple diet records. *Journal of Clinical Epidemiology, 43*(12), 1327-1335.
- Blom, G. (1958). *Statistical elements and transformed beta variables*. Wiley, New York.
- Calle, E. E., Thun, M. J., Petrelli, J. M., Rodriguez, C., & Heath, C. W. Jr. (1999). Body-mass index and mortality in a prospective cohort of US adults. *New England Journal of Medicine, 341*, 1097–1105.
- Carr, M. C., Hokanson, J. E., Zambon, A., Deeb, S. S., Barrett, P. H., Purnell, J. Q., & Brunzell, J. D. (2001). The contribution of intraabdominal fat to gender differences in hepatic lipase activity and low/high density lipoprotein heterogeneity. *The Journal of Clinical Endocrinology and Metabolism, 86*, 2831-2837.
- Carr, M. C., Hokanson, J. E., Deeb, S. S., Purnell, J. Q., Mitchell, E. S., & Brunzell, J. D. (1999). A hepatic lipase gene promoter polymorphism attenuates the increase in hepatic lipase activity with increasing intra-abdominal fat in women. *Arteriosclerosis, Thrombosis, and Vascular Biology, 19*, 2701-2707.
- Cole, T. G., Bowen, P. E., Schmeisser, D., Prewitt, T. E., Aye, P., Langenberg, P., Dolecek, T. A., Brace, L. D., & Kamath, S. (1995). Differential reduction of plasma cholesterol by the American Heart Association Phase 3 Diet in moderately hypercholesterolemic, premenopausal women with different body mass indexes. *American Journal of Clinical Nutrition, 55*, 385-394.
- Dattilo, A. M., & Kris-Etherton, P. M. (1992). Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *American Journal of Clinical Nutrition, 56*, 320–832.
- Després, J. P., & Lemieux, I. (2006). Abdominal obesity and metabolic syndrome. *Nature, 444*, 881-887. doi:10.1038/nature05488.

- The Diabetes Prevention Program. (1999). Design and methods for a clinical trial in the prevention of type 2 diabetes. *Diabetes Care*, 22(4), 623-634.
- Dorste, B. V., & Lindley, E. M. (2011). Cognitive and behavioral approaches in the treatment of obesity. *Medical Clinics of North America*, 95(5), 971-988.
- Douketis, J. D., Macie, C., Thabane, L., & Williamson, D. F. (2005). Systematic review of long-term weight loss studies in obese adults: Clinical significance and applicability to clinical practice. *International Journal of Obesity*, 29, 1153-1167. doi:10.1038/sj.ijo.0802982.
- Duncan, R. E., Ahmadian, M., Jaworski, K., Sarkadi-Nagy, E., & Sul, H. S. (2007). Regulation of lipolysis in adipocytes. *Annual Review of Nutrition*, 27, 79-101. doi: 10.1146/annurev.nutr.27.061406.093734.
- Eberhardt, M. S., & Pamuck, E. R. (2004). The importance of place of residence: Examining health in rural and nonrural areas. *American Journal of Public Health*, 94(10), 1682-1686.
- Fisher, R. J. (1993). Social desirability bias and the validity of indirect questioning. *Journal of Consumer Research*, 21(2), p. 303-315. doi: 10.2307/2489277.
- Flechtner-Mors, M., Ditschuneit, H. H., Johnson, T. D., Suchard, M. A., Adler, G. (2000). Metabolic and weight loss effects of long-term dietary intervention in obese patients: Four-year results. *Obesity Research*, 8, 399-402.
- Flegal, L. M., Carroll, M. D., Kit, B. K., & Ogden, C. L. (2012). Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *The Journal of the American Medical Association*, 307(5), 491-497. doi: 10.1001/jama.2012.39.
- Food and Nutrition Board, National Academy of Sciences, Institute of Medicine. (2005). *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*. Washington, DC: National Academy Press.
- Fox, C. S., Massaro, J. M., Hoffmann, U., Pou, K. M., Maurovich-Horvat, P., Liu, C., Vasan, R. S., Murabito, J. M., Meigs, J. B., Cupples, L. A., D'Agostino, R. B., & O'Donnell, C. J. (2007). Abdominal visceral and subcutaneous adipose tissue compartments: Association with metabolic risk factors in the Framingham Heart Study. *Circulation*, 116, 39-48. doi: 10.1161/CIRCULATIONAHA.106.675355.
- Fujioka, S., Matsuzawa, Y., Tokunaga, K., & Tarui, S. (1987). Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. *Metabolism*, 36(1), 54-59.
- Ginsberg, H. N., Kris-Etherton, P., Dennis, B., Elmer, P. J., Ershow, A., Lefevre, M., Pearson, T., Roheim, P., Ramakrishnan, R., Reed, R., Stewart, K., Stewart, P., Phillips, K., & Anderson, N. (1998). Effects of reducing dietary saturated fatty acids on plasma lipids and lipoproteins in healthy subjects: The DELTA Study, protocol 1. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 18, 441-449.

- Gögebakan, O., Kohl, A., Osterhoff, M. A., van Baak, M. A., Jebb, S. A., Papadaki, A., Martinez, J. A., Handjieva-Darlenska, T., Hlavaty, P., Weickert, M. O., Holst, C., Saris, W. H. M., Astrup, A., & Pfeiffer, A. F. H. (2011). Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors: The Diet, Obesity, and Genes (DiOGenes) Study: A randomized, controlled trial. *Circulation*, *124*, 2829-2838.
- Martinez, J. A., Handjieva-Darlenska, T., Hlavaty, P., Weickert, M. O., Holst, C., Saris, W. H. M., Astrup, A., & Pfeiffer, A. F. H. (2011). Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors: The Diet, Obesity, and Genes (DiOGenes) Study: A randomized, controlled trial. *Circulation*, *124*, 2829-2838. doi: 10.1161/CIRCULATIONAHA.111.033274.
- Gould, A. L., Davies, G. M., Alemao, E., Yin, D. D., & Cook, J. R. (2007). Cholesterol reduction yields clinical benefits: Meta-analysis including recent trials. *Clinical Therapeutics*, *29*(5), 778-794. doi:10.1016/j.clinthera.2007.05.012.
- Heart Protection Study Collaborative Group. (2002). MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomized placebo-controlled trial. *Lancet*, *360*, 7-22.
- Howard, B. V., Curb, D., Eaton, C. B., Kooperberg, C., Ockene, J., Kostis, J. B., Pettinger, M., Rajkovic, A., Robinson, J. G., Rossouw, J., Sarto, G., Shikany, J. M., & Van Horn, L. (2010). Low-fat dietary pattern and lipoprotein risk factors: the Women's Health Initiative Dietary Modification Trial. *American Journal of Clinical Nutrition*, *91*, 860-874.
- Jeffcoate, W. (1998). Obesity is a disease: food for thought. *Lancet*, *351*, 903-904.
- Jeffery, R. W., Drewnowski, A., Epstein, L. H., Stunkard, A. J., Wilson, G. T., Wing, R. R., et al. (2000). Long-term maintenance of weight loss: Current status. *Health Psychology*, *19*(Suppl. 1), 5-16
- Klein, S., Burke, L. E., Bray, G. A., Blair, S., Allison, D. B., Pi-Sunyer, X., Hong, Y., & Eckel, R. H. (2004). Clinical implications of obesity with specific focus on cardiovascular disease: A statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: Endorsed by the American College of Cardiology Foundation. *Circulation*, *110*, 2952-2967. doi: 10.1161/01.CIR.0000145546.97738.1E.
- Knowler, W. C., Barrett-Connor, E., Folwer, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., Nathan, D. M. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine*, *346*, 393-403.
- Krieger, M. (1998). The "best" of cholesterol, the "worst" of cholesterol: A tale of two receptors. *Proceedings of the National Academic of Sciences of the United States of America*, *95*, 4077-4080.

- Kuller, L. H., Simkin-Silverman, L. R., Wing, R. R., Meilahn, E. N., & Ives, D. G. (2001). Women's healthy lifestyle project: A randomized clinical trial: Results at 54 months. *Circulation, 103*, 32-37. doi: 10.1161/01.CIR.103.1.32.
- Lalonde, L., Gray-Donald, K., Lowensteyn, I., Marchand, S., Dorais, M., Michaels, G., Llewellyn-Thomas, H. A., O'Connor, A., Grover, & S. A. (2002). Comparing the benefits of diet and exercise in the treatment of dyslipidemia. *Preventative Medicine, 35*, 16-24. doi:10.1006/pmed.2002.1052.
- Layman, D. K., Evans, E. M., Erickson, D., Seyler, J., Webet, J., Bagshaw, D., Griel, A., Posta, T., & Kris-Etheron, P. (2009). A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *The Journal of Nutrition, 139*, 514-521. doi:10.3945/jn.108.099440.
- Lefevre, M., Champagne, C. M., Tulley, R. T., Rood, J. C., & Most, M. M. (2005). Individual variability in cardiovascular disease risk factor responses to low-fat and low- saturated-fat diets in men: Body mass index, adiposity, and insulin resistance predict changes in cholesterol. *American Journal of Clinical Nutrition, 82*, 957-963.
- Leichtle, A. B., Helmschrodt, C., Ceglarek, U., Shai, I., Henkin, Y., Schwarzfuchs, D., Golan, R., Gepner, Y., Stampfer, M. J., Blüher, M., Stumvoll, M., Thiery, J., & Fielder, G. M. (2011). Effects of a 2-year dietary weight-loss intervention on cholesterol metabolism in moderately obese men. *American Society of Nutrition, 04(5)*, 1189-1195. doi: 10.3945/ajcn.111.018119.
- Lichtenstein, A. H., Kennedy, E., Barrier, P., Danford, D., Ernst, N. D., Grundy, S. M., Leveille, G. A., Van Horn, L., Williams, C. L., & Booth, S. L. (1998). Dietary fat consumption and health. *Nutrition Reviews, 56*, S3-S28.
- Liu, J., Fox, C. S., Hickson, D. A., May, W. A., Hairston, K. G., Carr, J. J., & Taylor, H. A. (2010). Impact of abdominal visceral and subcutaneous adipose tissue on cardiometabolic risk factors: The Jackson Heart Study. *The Journal of Clinical Endocrinology and Metabolism, 95(12)*, 5419-5426. doi: 10.1210/jc.2010-1378.
- Look AHEAD Research Group. (2007). Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes. *Diabetes Care, 30*, 1374-1383. doi: 10.2337/dc07-0048.
- Mares-Perlman, J. A., Klein, B. E. K., Klein, R., Ritter, L. L., Fisher, M. R., & Freudenheim, J. L. (1993). A diet history questionnaire ranks nutrient intakes in middle-aged and older men and women similarly to multiple food records. *Journal of Nutrition, 123*, 489-501.
- McTigue, K. M., Harris, R., Hemphill, B., Lux, L., Sutton, S., Bunton, A. J., & Lohr, K. N. (2003). Screening and interventions for obesity in adults: summary of the evidence for the U.S. Preventive Services Task Force. *Annals of Internal Medicine, 139(11)*, 933-949.

- Mokdad, A. H., Ford, E. S., Bowman, B. A., Dietz, W. H., Vinicor, F., Bales, V. S., & Marks, J. S. (2003). Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *The Journal of the American Medical Association*, 289, 76-79.
- Must, A., Spadano, J., Coakley, E. H., Field, A. E., Colditz, G., & Dietz, W. H. (1999). The disease burden associated with overweight and obesity. *The Journal of the American Medical Association*, 282,1523-1529.
- Mustad, V. A., Etherton, T. D., Cooper, A. D., Mastro, A. M., Pearson, T. A., Jonnalagadda, S. S., & Kris-Etherton, P. M. (1997). Reducing saturated fat intake is associated with increased levels of LDL receptors on mononuclear cells in healthy men and women. *The Journal of Lipid Research*, 38, 459-468.
- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2002). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*, 106, 3143-3421.
- National Heart, Lung, and Blood Institute (NHLBI) Obesity Education Initiative. (1998). *Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the Evidence Report* (NIH Publication No. 98-4083). Bethesda, MD: National Institutes of Health.
- Nieves, D. J., Cnop, M., Retzlaff, B., Walden, C. E., Brunzell, J. D., Knopp, R. H., & Kahn, S. E. (2003). The atherogenic lipoprotein profile associated with obesity and insulin resistance is largely attributable to intra-abdominal fat. *Diabetes*, 52, 172-179.
- Pascot, A., Lemieux, S., Lemieux, I., Prud'Homme, D., Tremblay, A., Bouchard, A., Nadeau, A., Couillard, C., Tchernof, A., Bergeron, J., & Després, J. P. (1999). Age-related increase in visceral adipose tissue and body fat and the metabolic risk profile of premenopausal women. *Diabetes Care*, 22(9). 1471-1478.
- Perri, M. G., Limacher, M. C., Durning, P. E., Janicke, D. M., Lutes, L. D., Bobroff, L. B., Dale, M. S., Daniels, M. J., Radcliff, T. A., & Martin, A. D. (2008). Extended-care programs for weight management in rural communities: The treatment of obesity in underserved rural settings (TOURS) randomized trial. *Archives of Internal Medicine*, 168, 2347 - 2354.
- Perry, M. J., Mackun, P. J., Baker, J. D., Joyce, C. D., Lollock, L. R., & Pearson, L. S. (2001). Population change and distribution: 1990 to 2000. *Census 2000 Brief*. Washington DC:US Census Bureau.
- Purnell, J. Q., Kahn, S. E., Albers, J. J., Nevin, D. N., Brunzell, J. D., & Schwartz, R. S. (2000). Effect of weight loss with reduction of intra-abdominal fat on lipid metabolism in older men. *The Journal of Clinical Endocrinology and Metabolism*, 85, 977-982.
- Ratner, R. E. for the Diabetes Prevention Program Research Group. (2006). An update on the diabetes prevention program. *Endocrine Practice*, 12(Suppl. 1), 20-24.

- Reaven, G., Abbasi, F., & McLaughlin, T. (2004). Obesity, insulin resistance, and cardiovascular disease. *Recent Progress in Hormone Research*, *59*, 207-223.
- Scandinavian Simvastatin Survival Study Group. (1994). Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S). *Lancet*, *344*, 1383-1389.
- Scientific Steering Committee (SCC) on behalf of the Simon Broome register group. (1991). Risk of fatal coronary heart disease in familial hypercholesterolemia. *British Medical Journal*, *303*, 893-896.
- Simonen, P. P., Gylling, H., & Miettinen, T. A. (2002). Body weight modulates cholesterol metabolism in non-insulin dependent type 2 diabetics. *Obesity Research*, *10*(5), 328-335.
- Siri-Tarino, P. W., Sun, Q., Hu, F. B., & Krauss, R. M. (2010). Saturated fat, carbohydrate, and cardiovascular disease. *American Journal of Clinical Nutrition*, *91*, 502-509.
- Subar, A.F., Thompson, F.E., Kipnis, V., Midthune, D., Hurwitz, P., McNutt, S., McIntosh, A., & Rosenfeld, S. (2001). Comparative validation of the Block, Willett, and National Cancer Institute Food Frequency Questionnaires. *American Journal of Epidemiology*, *154*, 1089-1099.
- Summers, L. K. M., Fielding, B. A., Bradshaw, H. A., Ilic, V., Beysen, C., Clark, M. L., Moore, N. R., & Frayn, K. N. (2002). Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. *Diabetologia*, *45*, 369-377.
- Tuomilehto, J., Lindstrom, J., Eriksson, J. G., Valle, T. T., Hamalainen, H., Ilanne-Parikka, P., Keinanen-Kiukaaniemi, S., Laakson, M., Louheranta, A., Rastas, M., Salminen, V., & Uusitupa, M. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, *344*, 1343-1350.
- Varady, K. A., Bhutani, S., Klempel, M. C., & Kroger, C. M. (2011). Comparison of effects of diet versus exercise weight loss regimens on LDL and HDL particle size in obese adults. *Lipids in Health and Disease*, *10*(119), 1-5. doi:10.1186/1476-511X-10-119.
- Vessby, B., Uusitupa, M., Hermansen, K., Riccardi, G., Rivellese A. A., Tapsell, L. C., Näslén, C., Berlund, L., Louheranta, A., Rasmussen, B. M., Calvert, G. D., Maffetone, A., Pederson, E., Gustafsson, I. B., & Storlien, L. H. (2001). Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU study. *Diabetologia*, *44*, 312-319.
- Vidal, J. (2002). *Updated Review on the Benefits of Weight Loss*. *International Journal of Obesity*, *26*, S25-S28. doi:10.1038/sj.ijo.802215.

- Wadden, T. A., Butryn, M. L., & Byrne, K. J. (2004). Efficacy of lifestyle modification for long-term weight control. *Obesity Research, 12*, 151s–162s.
- Wadden, T. A., Crerand, C. E., & Borck, J. (2005). Behavioral Treatment of Obesity. *Psychiatric Clinics of North American, 28*, 151-170.
- Wilson, P. W. F., D'Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H., & Kannel, W. B. (1998). Prediction of coronary heart disease using risk factor categories. *Circulation, 97*, 1837-1947.
- Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Z, Avezum, A., Lanas, F., McQueen, M., Budaj, A., Pais, P., Varigos, J., & Lisheng, L.; INTERHEART Study Investigators. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet, 364*(9438), 937-952.

BIOGRAPHICAL SKETCH

Samantha Minski was born in Miami, Fl. She graduated from Dr. Michael Krop Senior High School in 2006. Samantha then attended the University of Florida and graduated *summa cum laude* in 2010 with a Bachelor of Science in psychology and a minor in education. Following graduation, Samantha was accepted to the Clinical and Health Psychology doctoral program at the University of Florida. As a graduate student, Samantha continues to pursue her research interest of obesity treatment.