# Light-Intensity Physical Activity and the Association between BMI and Cardiometabolic Risk Factors in Adults with Obesity

by

**Ronald E. Jackson**

B.S., Ball State University, 2013

M.S., Texas State University, 2016

Submitted to the Graduate Faculty of the

School of Education in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

University of Pittsburgh

2021

UNIVERSITY OF PITTSBURGH

SCHOOL OF EDUCATION

This dissertation was presented

by

**Ronald E. Jackson**

It was defended on

September 9, 2021

and approved by

Nancy W. Glynn, Ph.D., Associate Professor, Department of Epidemiology

Christopher E. Kline, Ph.D., Associate Professor, Department of Health and Human Development

Charity G. Patterson, Ph.D., Professor, Department of Physical Therapy

Dissertation Director: John. M. Jakicic, Ph.D., Distinguished Professor, Department of Health and Human Development

**Light-Intensity Physical Activity and the Association between BMI and Cardiometabolic Risk Factors in Adults with Obesity**

Ronald E. Jackson, PhD

University of Pittsburgh, 2021

The increased prevalence of chronic health conditions associated with obesity is a significant public health concern. It is generally accepted that physical activity elicits significant health benefits, however, many health benefits have been examined within the context of moderate-to-vigorous physical activity. Routine physical activity can improve several metabolic risk factors associated with cardiovascular disease and is associated with a lower risk of mortality. Currently, there is little evidence that has examined the association of light-intensity physical activity (LPA) and weight loss. Additionally, the relationship between LPA and cardiovascular disease risk factors is unclear. **Purpose:** The purpose of this study was to examine the associations between light-intensity physical activity BMI and cardiometabolic risk factors in adults with obesity. **Methods:** Three hundred and eighty-three adults with overweight and obesity (age: 45.6± 8.0 years; BMI: 32.4± 3.8 kg/m2) were randomized to DIET, DIET+PA150, and DIET+PA250. 375 participants provided data for baseline analyses, 320 participants provided data for 6-month analyses and 301 participants provided data for 12-month analyses for this study. The intervention prescribed a calorie restricted diet (1200-1800 kcal/day) and physical activity (0, 150, 250 min/week). **Results**: In adjusted analyses, LPA was associated with significant reductions in body weight from baseline to 6 months (p=0.006) and baseline to 12 months (p=0.003), with similar patterns shown for body mass index and percent body fat. LPA was negatively associated with total cholesterol (p=0.007), LDL cholesterol(p=0.011), triglycerides(p=0.007), and insulin(p=0.038) from baseline to 6 months. HDL was positively

associated with LPA (p=0.038) from baseline to 12 months. A positive association between LPA and cardiorespiratory fitness expressed as minutes was shown from baseline to 6 months (p=0.032). **Conclusion:** This study provides evidence that within the context of a behavioral weight loss intervention, LPA is significantly associated with reductions in body weight and body fatness, and with some other cardiometabolic risk factors. These findings suggest that even in the absence of MVPA, LPA may have modest but clinically important influences on some health-related outcomes in adults with overweight or obesity.

## Table of Contents

## List of Tables

# 1.0 Introduction

## 1.1 Background

Obesity is a significant public health issue in the United States.[1,2] National surveillance data shows that there has been a significant increase in the prevalence of obesity in the United States over the last few decades. In the 1970s, the prevalence of obesity (i.e., body mass index [BMI] >30 kg/m$^2$) was approximately 15 percent and since then the rates have continued to increase.[3] Based on data from 2015-2016, more than 30 percent of American adults were classified with obesity and the prevalence of severe obesity (BMI >40 kg/m$^2$) was 7.7 percent.[4] According to the U.S. Department of Health and Human Services and the Centers for Disease Control and Prevention, through 2017-2018 the prevalence of obesity has increased to 42.4 percent, and the prevalence of severe obesity has increased to 9.2 percent.[2]

There are subgroups of the population that appear to be impacted by obesity to a greater extent than others. The National Health and Nutrition Examination Survey (NHANES) has shown differences in the prevalence of obesity among adults in the United States by sex, age, race, and Hispanic origin. By race and Hispanic origin, non-Hispanic black women (56.9%) have the highest prevalence of obesity compared to non-Hispanic white (39.8%) and Hispanic women (43.7%), while Hispanic men (45.7%) have the highest prevalence compared to non-Hispanic white men (44.7%).[2] The current prevalence of obesity is highest among Black (56.9%) and Mexican American women (43.7%) and Mexican American men (45.7%). Adults aged 40 to 59 years (44.8%) have a higher prevalence of obesity compared with adults aged 20 to 39 years (40.0%),

adults aged 60 years (42.8%) and adults aged 65 years and above (29.3%) among both men and women.[2]

## 1.2 Health Consequences of Obesity

Obesity is a significant public health concern, and it is estimated that obesity will surpass smoking as the leading cause of avoidable death in the United States in the upcoming decades.[5] While excess body weight is a risk factor for cardiovascular disease (CVD), it is also related to a cluster of health conditions and risk factors that can directly and indirectly contribute to the development of CVD. These diseases include type 2 diabetes, dyslipidemia, metabolic syndrome, and hypertension, with each potentially leading to adverse health consequences and increased mortality.[6,7,26,29]

Type 2 diabetes is a contributing risk factor for the development of CVD, and the increasing prevalence of diabetes has tracked a similar pattern to what is observed with obesity.[10,11] This is likely a result of obesity being associated with insulin resistance and the endocrine activity of adipose tissue, that can potentially result in diabetes.[12]

The substantial negative impact obesity has on overall health is clear and requires considerable attention as a public health burden. In the prevention and treatment of obesity it is critical to identify effective strategies that may be associated with a reduction in the risk of chronic diseases. Evidence has shown that weight loss of at least 5 percent can reduce disorders associated with obesity,[13,14] and modest weight loss of at least this magnitude can improve glycemic control, reduce blood pressure, and improve blood lipids.[13–16]

## 1.3 Contribution of Physical Activity to Weight Loss

Weight loss has been shown to attenuate insulin resistance, improve glucose tolerance, and reduce hyperglycemia and hyperinsulinemia.[15,17,18] Weight loss is also associated with elevated high-density lipoprotein (HDL) concentrations, the improvement of low-density lipoprotein (LDL) to high-density lipoprotein (HDL) ratio, and, in overweight individuals with hypertension, weight loss leads to decreased arterial blood pressure.[19–21]

Because weight loss has been associated with improvements in many cardiometabolic risk factors, there has been more advocation that individuals who are overweight and obese attempt weight loss. To achieve weight loss, several health organizations recommend physical activity as a vital component of an effective intervention strategy.[22–24] Of importance, physical activity appears to be a significant predictor of successful long-term weight loss maintenance. Thus, within the context of weight loss, physical activity may be an important intervention component.

Research supports that, with physical activity alone, the decrease in body weight is modest.[14,24–26] However, there is also evidence of a dose-response relationship with elevated levels of physical activity potentially resulting in enhanced weight loss.[27] The results of interventions that have examined various combinations of physical activity and dietary modification revealed that weight loss elicited through physical activity alone was significantly less when compared to other conditions that involved a reduction in dietary intake (i.e., diet alone, diet combined with physical activity).[28,29] Furthermore, several systematic reviews have revealed that when physical activity was performed alone without a prescribed reduction in dietary intake, initial body weight loss was less than 3 percent, and total decreases in weight was approximately 0.5 to 3.0 kg.[24] However, even though physical activity typically produces a modest amount of weight loss, studies

have reported improvements in cardiometabolic risk factors demonstrating that physical activity alone could be a potential beneficial for individuals with overweight or obesity.[23]

A reduction in dietary intake results in significantly greater weight loss than physical activity. However, weight loss that is accomplished with dietary restriction may be enhanced when combined with physical activity.[30–32] Evidence supports that the combination of physical activity and dietary restriction can increase weight loss by nearly 20% when compared to weight loss accomplished through dietary restriction alone.[33,34] Additionally, physical activity may be important for long-term weight loss and maintenance.[35]

### 1.4 Health Benefits of Physical Activity Independent of Obesity or Weight Loss

The risk of developing a variety of chronic conditions increases with physical inactivity.[9,36,37] Systematic reviews have found that participating in regular physical activity can reduce all-cause and cardiovascular mortality.[8,27,38,39] Additionally, regular physical activity improves several risk factors, such as cardiac performance, aerobic capacity, and inflammatory markers.[24,40,41] Therefore, it is critical to emphasize physical activity as one of the most important lifestyle-related components in the prevention of mortality of various chronic conditions.

A critical component of public health is quality of life, and it is important to consider effective strategies for attenuating functional decline and enhancing quality of life. Findings from several studies show that physical activity performed in higher doses is associated with improved health related quality of life.[27,42] Participating in physical activity improves gait and balance function, enhances basic activities of daily living, reduces depressive symptoms, and improves stroke impact scale domains related to quality of life.[43] Additionally, higher levels of physical

activity have been shown to be associated with an improved perception of quality of life among individuals with chronic health conditions and the elderly.[43] It is important to recognize the association between physical activity and quality of life because, from a public health perspective, physical activity may be one of the most important behaviors for eliciting better general and health-related quality of life outcomes.

Beyond its beneficial effects on body weight, there is considerable evidence which shows that many obesity-related health conditions can be substantially improved through physical activity independent of level of obesity or weight loss.[23] For example, physical activity in the absence of weight loss is associated with reduced risk for the development of, type 2 diabetes, and other chronic health conditions.[44,45] These findings suggest that a non–weight loss paradigm emphasizing the utility of regular physical activity can be a treatment strategy for individuals who are overweight or obese.

Furthermore, physical activity without weight loss affects both total and abdominal adiposity along with skeletal muscle composition.[44,45] Several studies have reported that physical activity without weight loss is associated with significant reductions in abdominal fat and skeletal muscle lipid concentration in both men and women with obesity.[12,26,44,45] Even without a corresponding change in body weight, participation in physical activity has shown to improve blood pressure, glucose intolerance, insulin resistance, elevated blood triglycerides and inflammatory markers.[23,26]

Additionally, the "fitness-fatness hypothesis" proposes that elevated cardiorespiratory fitness levels can significantly diminish the negative health consequences of obesity with morbidity and mortality independent of level of obesity. Numerous studies have investigated the combined association of cardiorespiratory fitness and fatness on mortality, and findings revealed

an independent effect of cardiorespiratory fitness on numerous health outcomes. For example, the findings from a meta-analysis comparing the joint association of fitness and fatness on mortality from all causes showed an increased risk of death for individuals defined as unfit compared to individuals defined as fit.[46] Normal-weight individuals defined as unfit with a chronic disease had the largest mortality risk (hazard ratio HR=3.55). When compared to their younger counterparts, older adults (≥50 y), of normal weight and defined as unfit also had a higher mortality risk (HR=3.35). Individuals classified as overweight and unfit, had a significantly higher mortality risk (HR=2.14). Individuals classified as obese and unfit, also had a significantly elevated mortality risk (HR=2.46). These results demonstrate that mortality risk can depend on one's cardiorespiratory fitness and indicate that significant health benefits can be elicited with regular physical activity participation in which a modest level of cardiorespiratory fitness is achieved.

### 1.5 Physical Activity Recommendations

The relationship between physical activity and health benefits has been well established.[16,27,42,47] Many studies have consistently demonstrated that engaging in regular physical activity on most days of the week elicits significant health benefits.[24,27,39,47] The dose–response relationship amongst physical activity and improved health has also been shown with all-cause mortality and numerous chronic health conditions. Systematic reviews support that greater volumes of physical activity and exercise lead to greater health benefits.[24,38,44] These findings have led to the current physical activity recommendations which promote volumes of at least 150 minutes per week of regular moderate to vigorous intensity physical activity.

Specifically, on most days of the week, individuals should achieve at least 30 minutes of moderate-to-vigorous physical activity to accumulate >150 minutes per week.

Over time, there has been a shift within physical activity recommendations. Initially, the guidelines allowed for the accumulation of short bouts of activity of 8-10 minutes in duration, rather than requiring longer continuous periods of physical activity, to achieve public health recommendations.[24,39] This aspect of the physical activity recommendations has continued with more contemporary versions of the guidelines, with further refinement to suggest that physical activity accumulated across even shorter periods of physical activity can result in health benefits.[24]

## 1.6 Considerations for Light Intensity Physical Activity

The current literature related to the health benefits of physical activity has emphasized the importance of moderate-to-vigorous intensity and bout duration as key components for health benefits. Although most studies support moderate-to-vigorous intensity physical activity to achieve health benefits, there is some evidence that physical activity performed at a lower intensity may also have health benefits.[48–51] For many individuals, light-intensity physical activity (LPA) comprises most of their daily physical activity. However, within the context of physical activity, the primary focus is on moderate to vigorous-intensity physical activity. The energy requirement for LPA is lower than what is required for moderate and vigorous physical activity. LPA is traditionally defined as < 3 metabolic equivalents of task (METs). Therefore, given the fact that individuals spend most of their time performing light intensity physical activity and it requires the least amount of effort, more research needs to be undertaken to explore its health benefits.

There is accumulating evidence that LPA is associated with reductions in cardiometabolic risk factors and reduced risk of mortality. Systematic reviews have shown LPA to be associated with lower all-cause mortality risk and reductions in some cardiometabolic risk factors including triglyceride levels and insulin.[50] Although current physical activity guidelines recommend only moderate-to-vigorous physical activity within the context of health benefits, light intensity physical activity may elicit additional health benefits. Therefore, the inclusion of LPA in the physical activity recommendations should be considered in the future, especially in circumstances where moderate-vigorous intensity physical activity is not viable.

## 1.7 Specific Aims and Hypotheses

1. To examine the cross-sectional associations of light-intensity physical activity with level of obesity, cardiorespiratory fitness, and selected cardiometabolic risk factors in inactive adults with obesity prior to engaging in a behavioral weight loss intervention.
    a. It was hypothesized that higher levels of light-intensity physical activity would be associated with lower body weight and body fatness;
    b. It was hypothesized that higher levels of light-intensity physical activity would be associated with higher levels of cardiorespiratory fitness;
    c. It was hypothesized that higher levels of light-intensity physical activity would be associated with lower resting blood pressure, total cholesterol, LDL cholesterol, triglycerides, glucose, insulin, and measures of inflammation (i.e., C-reactive protein [CRP]), and associated with higher HDL cholesterol.

2. To examine the association between change in light-intensity physical activity and change in level of obesity, fitness, and selected cardiometabolic risk factors in inactive adults with obesity in response to a behavioral weight loss intervention.
    a. It was hypothesized that a greater increase in light-intensity physical activity from baseline to 6 months and baseline to 12 months would be associated with a greater reduction in body weight and body fatness from baseline to 6 months and baseline to 12 months;
    b. It was hypothesized that a greater increase in light-intensity physical activity from baseline to 6 months and baseline to 12 months would be associated with a greater increase in cardiorespiratory fitness from baseline to 6 months and baseline to 12 months;
    c. It was hypothesized that a greater increase in light-intensity physical activity from baseline to 6 months and baseline to 12 months would be associated with a greater reduction in resting blood pressure, total cholesterol, LDL cholesterol, triglycerides, glucose, insulin, and CRP, and a greater increase in HDL cholesterol from baseline to 6 months and baseline to 12 months.

# 2.0 Review of the Literature

## 2.1 Overweight and Obesity

### 2.1.1 Prevalence of Obesity

The prevalence of obesity is particularly high in the United States and is increasing.[52–54] Individuals with a body mass index (BMI) of 30 kg/m$^2$ or more are classified as obese,[54] and almost two-thirds of U.S. adults aged 20 and older are classified with obesity.[4,55] Thus, the rise in excess body weight in the U.S. has become a major public health issue.

The prevalence of adult obesity in the United States has significantly increased over the past 60 years: from 13% in 1960–1962 to 23% in 1988 and 42.4% today.[2,4,52] The average BMI of U.S. adults aged between 20-74 years changed little between 1960-1962 and 1976-1980 but rapidly increased by 1.26 kg/m$^2$ between 1976-1980, and 1988-1994.[56] Data from the National Health Examination Survey (NHANES) reveal that median adult BMI rose 9.5% between 1976-1980 and 1999-2000.

The current age-adjusted data shows that among men, the prevalence of obesity is 40.3% among those aged 20–39 years, 46.4% among those aged 40–59 years, and 42.2% among those aged 60 years and over. Among women, the prevalence of obesity is 39.7% among those aged 20–39 years, 43.3% among those aged 40–59 years, and 43.3% among those aged 60 years and over.[2]

Current health statistics, stratified by race and Hispanic origin demonstrate that the prevalence of obesity is lowest among non-Hispanic Asian adults (17.4%) when compared with non-Hispanic white (42.2%), non-Hispanic black (49.6%), and Hispanic (44.8%) adults. Among

U.S. adults, non-Hispanic black adults have the highest prevalence of obesity when compared to all other race and Hispanic-origin groups.[2] Among men, the prevalence of obesity is lowest in non-Hispanic Asian (17.5%) compared with non-Hispanic white (44.7%), non-Hispanic black (41.1%), and Hispanic (45.7%) men. The prevalence of obesity is lowest among non-Hispanic Asian women (17.2%) compared with non-Hispanic white (39.8%), Hispanic (43.7%), and non-Hispanic black (56.9%) women, and the prevalence among non-Hispanic black women is higher than all other groups.[2]

The prevalence of obesity is not only a public health problem for U.S. adults, but also for children as well. The latest results from national survey data indicates that 19.3% of U.S. children and adolescents aged 2–19 years have obesity, and another 16.1% are overweight.[53,57,58] The prevalence of obesity is 13.4% among 2- to 5-year-olds, 20.3% among 6- to 11-year-olds, and 21.2% among 12- to 19- year-olds. When classified according to race and Hispanic origin, the obesity prevalence is 25.6% among Hispanic children, 24.2% among non-Hispanic Black children, 16.1% among non-Hispanic white children, and 8.7% among non-Hispanic Asian children.[53]

### 2.2 Association between Obesity and Chronic Health-Related Conditions

With the worldwide prevalence of obesity increasing substantially in recent decades, so have obesity-related chronic diseases.[36,52,59,60] Obesity leads to an excessive accumulation of adipose tissue and the excess adipose tissue can contribute to the development of obesity-related chronic diseases. There is accumulating evidence indicating that obesity is associated with an increased risk of chronic diseases such as CVD, type 2 diabetes, dyslipidemia, and hypertension.[9]

This section of the review will focus on obesity and the associations with obesity-related chronic diseases.

### 2.2.1 Obesity and Cardiovascular Disease

Cardiovascular disease is the leading cause of death in the United States and is a significant public health problem.[61] Among the leading causes of CVD mortality and morbidity is obesity. Several studies have demonstrated that obesity is associated with elevated CVD mortality. A study by Greenberg using data from NHANES I (1971–1975), NHANES II (1976–1980), and NHANES III (1988–1994) estimated mortality for obese Americans (BMI ≥30 kg/m$^2$).[1] Estimates from this study found that, when compared to the reference BMI (23 to <25 kg/m$^2$), mortality was likely to occur 9.44 years (95% confidence interval [CI]: 0.72, 18.16) earlier for those with obesity (BMI ≥30 kg/m$^2$). For overweight (25 to <30 kg/m$^2$), grade 1 obesity (BMI, 30 to <35) and grades 2–3 obesity (BMI, ≥35.0 kg/m$^2$), the mortality was likely to occur 4.40 (-3.90, 12.70), 6.69 (-2.06, 15.43), and 14.16(3.35, 24.97) years earlier, respectively, compared to those with the reference BMI. These estimates applied to American adults who were classified as healthy, nonsmoker, and aged 21–55 years. The findings suggest that obesity increases mortality.

Several large studies also have demonstrated increased CVD mortality among individuals with obesity. In the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, a large randomized controlled multicenter trial in the United States, the association of obesity with CVD mortality was investigated.[62] Data from this study showed that, when compared to participants of normal BMI (18.5–24.9 kg/m$^2$), participants classified as overweight, (BMI: 25.0–29.9 kg/m$^2$) were not at an increased risk for CVD mortality (hazard ratio [HR]=1.02 [95% CI:

0.92–1.13]). Increased CVD mortality was observed for participants of BMI 30.0–34.9 kg/m$^2$ (HR=1.29 [95% CI: 1.13– 1.48]), BMI 35.0–39.9 kg/m$^2$ (HR=1.87 [95% CL: 1.51–2.32]) and BMI 40.0+ kg/m$^2$ (HR= 2.21 [95% CI: 1.57– 3.21]) ($p<0.001$ for trend). Another study using data from the Framingham Heart Study, a large cohort study, examined the association of obesity with mortality over 24 years of weight history.[63] Results show CVD mortality had larger risks for overweight (HR= 1.22 [95% CI, 1.02-1.45]), for class I obesity (HR=1.66; [ 95% CI, 1.36-2.02]), and for class II obesity (HR=2.56 [ 95% CI, 2.00- 3.28]).

Evidence from a meta-analysis by McGee et al. examining BMI and mortality found CVD mortality to be elevated in individuals with overweight and obesity.[64] The data show that the relative risks among individuals in the highest BMI category for CVD are 1.48 when compared with the those within the lowest BMI category. Regarding CVD mortality, the relative risks for the female and male overweight groups, compared to the normal weight groups, are 1.03 (95% CI: 0.945–1.12) and 1.10 (95% CI: 1.034–1.16), respectively. The relative risks for the female and male obese groups, compared to the normal weight groups, are 1.53 (95% CI: 1.38–1.69) and 1.45 (95% CI: 1.327–1.59), respectively.

As obesity prevalence increases, so does the prevalence of its related morbidities. CVD morbidity has been shown to be elevated in individuals classified as overweight, particularly with central adiposity.[65] Obesity appears to be an independent risk for coronary heart disease (CHD) and CVD.[66] In a prospective cohort study, CHD risk was assessed in women.[66] During a 14-year follow-up, the risk of CHD for women with a BMI of 26 kg/m$^2$ is twice that of those with a BMI < 21 kg/m$^2$. Relative risks [RRs] and 95% confidence intervals (CIs) for CHD were 1.19 [95% CI 0.97 to 1.44] for a BMI of 21-22.9 kg/m$^2$, 1.46 [95% CI: 1.20 to 1.77] for a BMI of 23-24.9 kg/m$^2$, 2.06 [95% CI: 1.72 to 2.48] for a BMI of 25-28.9 kg/m$^2$, and 3.56 [95% CI: 2.96 to 4.29] for a

BMI of 29 kg/m$^2$ or more. Results from the follow up showed, women who gained weight were compared with those with stable weight (±5 kg) the analyses accounted for the same variables which included BMI at the age of 18. The RRs and CIs for CHD were 1.25 [95% CI: 1.01 to 1.55] for a 5-7.9-kg gain, 1.64 [95% CI: 1.33 to 2.04] for an 8-10.9-kg gain, 1.92 [95% CI: 1.61 to 2.29] for an 11-19-kg gain, and 2.65 [95% CI: 2.17 to 3.22] for a gain of 20 kg or more. For women within the BMI range of 18 -25 kg/m$^2$ the amount of weight gained after the age of 18 years was a strong predictor of CHD risk. These data provide evidence that higher levels of body weight appear to increase risks of CHD.

Also, there is evidence that obesity increases the risk of coronary artery disease (CAD). In the Asian Pacific Cohort Collaboration study, there was a 9% increase in heart disease per unit change in BMI.[67] When the risk of heart failure (HF) was evaluated in the Framingham study, the risk of HF was found to be twice as high in the obese group compared to the non-obese group.[63,68,69] For women, the hazard ratio was 2.12 [95% CI: 1.51 to 2.97]; for men, the hazard ratio was 1.90 [95% CI: 1.30 to 2.79]. The hazard ratios per BMI category for HF were 1.46 (95% CI: 1.23 to 1.72) for women and 1.37 (95% CI: 1.13 to 1.67) in men. There also is strong evidence from a systematic review and meta-analysis by Guh et al, on the incidence of comorbidities related to obesity and it was determined that significant associations with obesity were found with the incidence of multiple forms of CVD.[70] The pooled incidence rate ratios (IRR [95% CI]) estimates for hypertension across BMI categories for men were 1.28 (95% CI: 1.10–1.50) for overweight and 1.84 (95% CI: 1.51–2.24) for obesity. The pooled IRR [95% CI] estimates for congestive heart failure across categories of BMI for men were 1.31 (95% CI: 0.96– 1.79) for overweight and 1.79 (95% CI: 1.24–2.59) for obesity. The pooled ratios of proportions [RRP] estimates for females based on 3 studies were 1.27 (95% CI: 0.68–2.37) for overweight and 1.78 (95% CI: 1.07–2.95)

for obesity. The pooled RRP [95% CI] estimates for stroke across categories BMI for men were 1.23 (95% CI: 1.13–1.34) for overweight and 1.51 (95% CI: 1.33–1.72) for obesity. The corresponding results for females were 1.15 (95% CI: 1.00–1.32) and 1.49 (95% CI: 1.27–1.74). The incidence of multiple comorbidities is associated with individuals with overweight or obesity.

The association between overweight and obesity with CVD risk factors has been well documented. In a 10-year follow-up of data from the Nurses' Health Study and the Health Professionals Follow-up Study the health risks associated with overweight were examined.[71] The risk of developing chronic health conditions such as diabetes, hypertension, and CVD increased among men and women classified as overweight or obese. When compared with BMI between 18.5-24.9 kg/m$^2$, those with BMI ≥35.0 kg/m$^2$ were more likely to develop diabetes for women (RR=17.0 [95% CI: 14.2-20.5]) and for men (RR= 23.4; [95% CI, 19.4-33.2]. Women classified as overweight but not obese (BMI between 25.0 -29.9 kg/m$^2$) were also significantly more likely to develop hypertension (RR=1.7 [95% CI, 1.6-1.7]), high cholesterol level (RR=1.1 [95% CI, 1.1-1.2]), and heart disease (RR=1.4 [95% CI: 1.2-1.5]). These findings show that the incidence of chronic health conditions such as diabetes, hypertension, and CVD, increased in both men and women classified as overweight or obese.

It is evident that adults classified as overweight are at increased risk of developing chronic health conditions.[71] Evidence using data from national health surveys further supports the association between obesity and CVD risk factors. Data from the NHANES from 1999 through 2010 examined trends in cardiovascular risk factors by obesity level among adults in the United States.[10] Included among the CVD risk factors were diabetes, hypertension, and dyslipidemia. In 2007-2010, the prevalence's of diabetes, hypertension, and dyslipidemia were highest among those with obesity (18.5%, 35.7%, 49.7%, respectively), followed by those who were overweight (8.2%,

26.4%, 44.2%, respectively) and normal weight adults (5.4%, 19.8%, 28.6%, respectively). The trends from this study indicate that when compared to individuals with normal weight the prevalence of cardiovascular risk factors increases with obesity.

### 2.2.2 Obesity and Type 2 Diabetes

Type 2 diabetes prevalence has significantly increased over the last few decades, and more individuals with type 2 diabetes are also obese.[52] A cross-sectional survey led by the Centers for Disease Control and Prevention estimated the prevalence of obesity and diabetes among US adults.[7] Data from the 2001 Behavioral Risk Factor Surveillance System (BRFSS) examined the prevalence of obesity and diabetes. The prevalence of obesity (BMI ≥30 kg/m$^2$) was 20.9% compared to 19.8% in 2000. The prevalence of diabetes increased to 7.9% compared to7.3% in 2000. Overweight and obesity were significantly associated with diabetes. When compared with normal weight, adults with a BMI of ≤ 40 kg/m$^2$ had an odds ratio (OR) of 7.37[95% CI: 6.39-8.50] for diabetes. The findings show that obesity is strongly associated with increases in diabetes among U.S. adults.

Using data of 37,606 U.S. adults between the ages 20-74 from three U.S. national surveys (NHANES II, III, and NHANES 1999–2004), the diabetes prevalence was observed.[56] Results from these national survey data show that the prevalence of diabetes among adults increased from 5.08% in 1976–1980 to 8.83% in 1999–2004. Of the additional cases that occurred in 1999–2004 compared to 1976–1980, it was estimated that 27% were among those who were overweight (BMI: 25-30 kg/m$^2$); and 32%, 23%, and 26% among those with class I (BMI: 30-35 kg/m$^2$), class II (BMI: 35-40 kg/m$^2$), and class III obesity (BMI ≤40 kg/m$^2$), respectively. As compared to 1976–

1980, the additional diabetes cases that occurred in 1999–2004, 81% were obese (i.e., BMI ≤ 30 kg/m$^2$) and 49% had class II or III obesity (BMI ≤35 kg/m$^2$), a group that increased in prevalence from 4% to 13% of the overall adult population. Thus, providing evidence that the increases in diabetes prevalence is associated with the rise in obesity.

One of the links between type 2 diabetes and obesity is excess body fat. Several studies have targeted obesity as a risk factor, with elevated BMI increasing the risk of type 2 diabetes. A cohort study with a follow up examined weight as a risk for diabetes in U.S. women. During 8 years of follow-up, 873 cases were acknowledged among women diagnosed as non-diabetic.[72] The relative risk of diabetes was elevated for women with BMI greater than 22 kg/m$^2$ and was more pronounced for those with BMI greater than 25 kg/m$^2$. Among women with a BMI of 22-22.9 kg/m$^2$, the proportional hazards relative risk of diabetes is 2.1 (95% CI: 1.4-3.3) compared with that in women with a BMI less than 22 kg/m$^2$, and for women with a BMI of 23-23.9 kg/m$^2$, the proportional hazards relative risk was 3.5 (95% CI: 2.3-5.1). Findings from this study demonstrate that the risk of type 2 diabetes increases with elevated BMI. The National Longitudinal Survey of Youth cohort study evaluated the relation between excess BMI and risk for incident diabetes.[73] Elevated levels of BMI were associated with an increased risk of diabetes. Caucasian men aged 40 years with elevated BMI had 2.94 times (95% CI: 2.36-3.67) higher odds of developing diabetes. This study provided evidence supporting that individual have a higher risk of diabetes with elevated BMI. The risk of developing diabetes increases with BMI. Evidence suggests that the prevalence of diabetes increased from 2% to 8% to 13% in individuals with a BMI of 25 to 29.9 kg/m$^2$, 30 to 34.9 kg/m$^2$, and a BMI >35 kg/m$^2$ respectfully.[74]

#### 2.2.2.1 Body fat accompanied with obesity is a facilitator that links obesity and type 2 diabetes.

Visceral fat is important in this process due to the adipocytes releasing free fatty acids into the liver. These fatty acids can produce several adverse effects on glucose metabolism. Adipocyte's prompt, the release of free fatty acids into the blood circulation, which ultimately elevates the levels of free fatty acids in the liver and muscle.[75] The elevated free fatty acid levels increase insulin resistance by disrupting insulin signaling.[75] Insulin resistance in the liver elevates blood glucose levels. Insulin secretion increases in response to the elevated blood glucose levels.[12,75] The increased performance of the pancreas may damage the beta cells, which will impede glycemic control.[75] Insulin resistance, combined with impaired insulin secretion, lead to impaired glucose tolerance and to the development of type 2 diabetes. The association of obesity with diabetes has been shown in several studies.

### 2.2.3 Obesity and Hypertension

The association between obesity and hypertension has been recognized for several decades. Substantial evidence exists supporting the link between obesity and hypertension. In a large cohort study of U.S. female nurses, BMI was positively associated with hypertension. Results from this study revealed that BMI was associated with occurrence of hypertension (P for trend $< 0.001$). Long-term weight loss after the age of 18 was associated to significantly reduced risk for hypertension, and weight gain significantly increased the risk for hypertension (multivariate relative risks were 0.85 for a loss of 5.0 to 9.9 kg, 0.74 for a loss $\geq$ 10 kg, 1.74 for a gain of 5.0 to 9.9 kg, and 5.21 for a gain $\geq$ 25.0 kg). Findings from this study suggest that excess weight and

weight gain significantly increased risk for hypertension.[76] A study by Ryu et al. evaluated secular trends in the relationship between weight status and hypertension among American adults.[77] Data from the 1999–2014 National Health and Nutrition Examination Survey were used. The association between BMI and hypertension was significant (OR = 1.09 [95% CI: 1.08–1.09]), ($p < .001$). That is, for every 1 $kg/m^2$ increase in BMI, adults had 9% increased odds of being hypertensive. The association between obesity and hypertension was statistically significant (OR = 2.51 [95% CI = 2.27–2.76] $p<.001$). That is, on average, individuals with obesity had 2.51 times higher odds of being hypertensive when compared to adults with non-obesity. The association between overweight/obesity and hypertension was statistically significant (OR = 2.23 [95% CI = 2.03–2.44] $p<.001$). That is, on average, individuals with overweight and obesity had 2.23 higher odds of being hypertensive when compared to adults with non-overweight and obesity. Regarding the trend in the association between overweight/ obesity and hypertension, there was a statistically significant linear trend ($b = 0.02$, $p = .006$) indicating an increase in the odds ratios. These findings suggest that there is a strong association between obesity and hypertension over time.

Analysis from The Framingham Heart Study, a prospective study of CVD, demonstrated that an increase in blood pressure with increased weight occurred in both men and women.[55,68,69,76,78] The relative risk of hypertension in men and women classified as overweight were 1.46 and 1.75. Individuals with the highest BMI had a 16 mmHg higher systolic blood pressure and a 9 mmHg higher diastolic blood pressure than individuals with the lowest BMI.[78,79] Data from this study also showed, the systolic blood pressure increased 4 mmHg for each 4.5 kg of increased weight.[68,78,80] In the nationwide Community Hypertension Evaluation Clinic screening, the prevalence of hypertension in adults with overweight were examined.[81] Hypertension in adults classified as overweight between the ages of 20-39 was twice that of normal

weight and three times that of adults underweight. Among adult between the ages 40-64, the overweight group had overall a higher hypertension prevalence rate than the normal weight group. With each increase of blood pressure, the regularity of hypertension with adults classified as overweight was greater.

Obesity may also be a risk factor for the identification of hypertension. Gus et al explored the longitudinal association between different measurements of obesity and the incidence of hypertension in a population-based cohort of adults.[82] The hazard ratios for incidence of hypertension for individuals with a BMI higher than 30 kg/m$^2$ were 1.08 (95% CI: 0.52–2.24) P=.82) in men and 1.74 (95% CI: 0.93– 3.26) P=.08) in women. The hazard ratios for incidence of hypertension were 1.78 (95% CI: 0.76–4.09) (P=.18) for men with waist circumference $\geq$102 cm, and 1.72 (95% CI: 1.09–2.73) (P=.02) for women with a waist circumference of 88 cm. These results may suggest the need to consider abdominal adiposity, rather than BMI, when examining the risk for hypertension.

### 2.2.4 Obesity and Dyslipidemia

Dyslipidemia, defined by abnormal elevated cholesterol and increased triglycerides, is associated with obesity.[83] According to previous NHANES data from 1999-2004, the association between obesity and dyslipidemia is significant.[84] With the increase in adults with overweight and obesity, the prevalence of dyslipidemia increased (8.9% for normal weight to 19.0% for obesity). With individuals classified as normal weight as a reference, individuals with obesity had an odds ratio of 2.2 (95% CI 1.7 to 2.4) for dyslipidemia. It is evident that the prevalence of dyslipidemia significantly increases with increasing BMI.[84] Another study assessing the prevalence of obesity

and dyslipidemia amongst women, also shown a high prevalence between obesity/overweight and dyslipidemia.[85] The prevalence of overweight was 38.5%, obesity 20.7%, hypertriglyceridemia 34.1%, hypercholesterolemia 31.4%, low HDL 37.6%, and dyslipidemia 60.5%. BMI was shown to be correlated with total cholesterol (r=.246, P<.001; LDL r=.172, P=.024). Dyslipidemia was noticeably associated with obesity, and the prevalence increased as the prevalence of obesity increased.

There is a relationship between the visceral adipose tissue and rises in plasma triglyceride, reduced HDL cholesterol, and increased VLDL cholesterol.[86] Due to these components, dyslipidemia is critical with obesity, and ultimately can lead to the development of CVD. Shah et al determined the relationship of lipid profile in obese versus non-obese individuals and the frequency of dyslipidemia.[87] Findings from this study determined that individuals with obesity showed significant ($p \leq 0.05$) dyslipidemia. Thirty seven percent of individuals had total cholesterol >200 mg/dl, 46% had HDL cholesterol of 130 mg/dl and 51% had triglycerides (TG) >150 mg/dl. The mean values of total HDL cholesterol, total LDL cholesterol and TG in obese group were different significantly ($P<0.05$). There is significant evidence suggesting that dyslipidemia is strongly associated with obesity.

### 2.2.5 Obesity and Cancer

Cancer is one of the top leading causes of mortality in the U.S., according to the most recent World Cancer Report by the International Agency for Research on Cancer. The most prevalent cancers among men and women are lung, and colorectal.[75]

In a follow up study by Zhang et al., reported that compared to a waist circumference <28 inches the adjusted relative risks for obesity-related cancer were 1.21 (95% CI: 1.00-1.47) for waist circumference 28-29 inches, 1.18 (95% CI: 0.96-0.45) for waist circumference 30-31 inches, 1.30 (95% CI: 1.05-1.62) for waist circumference 32-34 inches, and 1.70 (95% CI: 1.31-2.20) for waist circumference >35 inches (P<0.001 for linear trend).[88] Findings from this study demonstrate that abdominal adiposity was strongly associated with cancer mortality.

Obesity is also associated with increased mortality from various cancers.[89,90] The increased risk of developing esophageal, pancreatic, rectal, and kidney cancer is also related to obesity.[75] It has been predicted that with the rise in obesity, there could be more than half a million cancer cases in the United States within the next 10 years.[75] Several mechanisms have illustrated the association between obesity and cancer, however according to the National Cancer Institute further research is needed.

### 2.2.6 Obesity and Inflammation:

As previously mentioned, obesity is associated with several chronic health conditions (i.e., hypertension, dyslipidemia, type 2 diabetes, etc.). The accumulation of excess adipose tissue that is characterized with obesity, is accompanied with inflammation.[19] With obesity the inflammatory response is compromised and shifted towards a proinflammatory state, categorized as a chronic low-grade inflammatory state. The inflammatory response is then upregulated, causing an elevation of the release of inflammatory markers such as tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), and C-reactive protein (CRP).[19,91]

It has been established that markers of inflammation are higher with individuals with obesity. For example, a study by Hotamisligl et al. found that when compared to individuals with lean body mass, higher amounts of TNF-α were present in individuals with obesity.[91] Additionally, the ATTICA study, which was based on a large population evaluated inflammatory markers in adults with obesity.[92] This study demonstrated that adiposity stimulates an inflammatory response promoting an excess of inflammatory markers such as TNF-α, IL-6, and CRP. When compared to individuals with normal fat distribution, individuals with elevated central fat had elevated C-reactive protein, TNF-α, and interleukin-6 levels (53%), (30%), (42%) respectively ($p< 0.05$). Thus, it is clear that the chronic long-term inflammatory response or low-grade inflammation is elevated with obesity.

Over the last few decades efforts have been made to examine the link between obesity and inflammation. Of particular interest has been C-reactive protein, which is a marker of systemic inflammation. Several studies have shown that obesity is associated with CRP. Brooks et al. evaluated abdominal adiposity in relation to CRP.[93] Findings from this study demonstrate that with an increase in abdominal adiposity there is an increase in systemic inflammation identified by CRP ($r =0.40-0.61$). Visser et al. examined CRP levels in adults with overweight and obesity.[94] Data from The National Health and Nutrition Examination Survey was used to determine if low-grade inflammation measured by CRP is associated with overweight and obesity. When compared to adults classified as normal weight, adults with overweight and obesity were more likely to have higher CRP levels. Odds ratio for CRP was (OR= 2.13[95% CI:1.56-2.61]) for men with obesity and (OR= 6.21[95% CI:4.94-7.81]) for women with obesity. Thus, illustrating that obesity is associated with CRP. A meta-analysis by Choi et al. identified that obesity was related directly to CRP. The correlation for BMI and CRP was (r=0.36 [95% CI: 0.30–0.42]) in adults and (r=0.37

[95% CI: 0.31–0.43]) in children. In adults, the correlation was greater in women than men by (0.24 [95% CI: 0.09–0.37]). Overall, there is evidence suggesting there is an association between obesity and systemic inflammation as it relates to CRP.

Weight loss has been shown to be an effective strategy for the treatment and prevention of obesity.[44] There is evidence to suggest that weight loss is associated with an improvement in proinflammatory markers (i.e., TNF-α, Il-6, CRP, etc.) and a decrease in inflammation. Hotamisligl et al showed that select proinflammatory makers were reduced after a weight loss intervention.[91] The expression of TNF-α decreased after weight loss, from 49 to 26 %, $p<0.001$. In a randomized trail examining the effect of weight loss on vascular inflammatory makers, results showed that reductions in body weight also reduced inflammation. When compared to control group, serum concentrations of inflammatory markers such as IL-6, interleukin 18 (IL-18), and CRP decreased with body weight reduction. IL-6 (−1.1 pg/mL; $P = .009$), IL-18 (−57 pg/mL; $P = .02$), and CRP (−1.6 mg/L; $P = .008$).[91] Nicklas et al. demonstrated that weight loss reduces inflammation. Findings showed that weight loss resulted in significant reductions in concentration of CRP ($p=0.01$), IL-6 ($p= 0.009$), and TNF-α ($p=0.007$).[95]

Additionally, a systematic review evaluating the effect of weight loss on CRP suggests that reductions in CRP are associated with weight loss. Results demonstrate for every 1 kg of body weight loss, the change in CRP was -0.13mg/L ($r =0.85$, weighted Pearson correlation).[96] A review by Forsythe et al. assessed the effects of weight loss as it relates to obesity and inflammation. Findings from this review conclude that inflammatory markers CRP, TNF-a, and IL-6 improve with weight loss.[97] Another review examined inflammation related genes with weight loss. Based on the evidence, it was reported that weight loss improves inflammation through a decrease of

proinflammatory markers such as CRP, IL-6 and TNF-α and an increase of anti-inflammatory markers. Thus, highlighting the beneficial effect of weight loss on inflammation.

### 2.3 Weight Loss for Prevention and Treatment for Chronic Health-Related Conditions

Clearly, obesity has many adverse effects on health, particularly on CVD risk factors. As previously mentioned, obesity has shown to increase the risk for several CVD risk factors, including hypertension, dyslipidemia, type 2 diabetes, and inflammation. Thus, weight loss has been a major emphasis in strategies that both treat and prevent obesity-associated chronic health conditions.[44] It has been well established that an initial body weight loss of 5-10 percent can be effective in the reduction of several obesity-associated chronic health conditions.[16,42] According to the most recent National Heart, Lung and Blood Institute, established clinical guidelines about body weight control, a loss of ≥5 percent of initial body weight in adults with overweight and obesity reduces numerous obesity-associated chronic health conditions and decreases morbidity and mortality.[23]

The effect of weight loss on the various obesity-associated chronic health conditions has been examined by several investigators and systematic reviews. For example, a systematic review by Goldstein evaluated the effects of at least 10 percent weight loss on non-insulin-dependent diabetes, hypertension, hyperlipidemia, hypercholesterolemia, and CVD.[13] This review found that weight loss was shown to reduce blood pressure, reduce total cholesterol, and assist with improving glycemic control. Wing et al investigated the benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes.[26]

This study examined the associations between the degree of weight loss and the degree of improvement in glycemic control, blood pressure, and lipid levels at 1 year in a cohort. The degree of weight loss at 1 year was strongly (P <, 0.0001) associated with improvements in glycemia, blood pressure, triglycerides, and HDL cholesterol (P = 0.79). When compared with participants with stable weight, participants that lost 5-10% (7.25- 6 2.1 kg) of their initial body weight had elevated odds of a 0.5% point reduction in HbA1c (OR=3.52 [95% CI 2.81–4.40]), a 5-mmHg decrease in diastolic blood pressure (OR=1.48 [95% CI: 1.20–1.82]), a 5-mmHg decrease in systolic blood pressure (OR=1.56 [95% CI: 1.27–1.91]), a 5 mg/dL increase in HDL cholesterol (OR=1.69 [95% CI: 1.37–2.07]), and a 40 mg/dL decrease in triglycerides (OR=2.20 [95% CI: 1.71–2.83]). The odds of clinically significant improvements in most risk factors were greater in participants that lost 10–15 percent of their body weight. It was concluded that modest weight loss (5-10%) was associated with improvements in cardiovascular risk factors, and greater weight loss had even more benefits.

The association between obesity and type 2 diabetes is well known.[10] Weight loss is recommended because it is an effective strategy in improving insulin resistance, glucose tolerance, and reduce hyperinsulinemia. Even though weight loss can be a successful strategy for glycemic control in individuals with type 2 diabetes, investigators have examined whether type 2 diabetes can be "reversible" via lifestyle interventions. Gregg et al. examined the association of a long-term intensive weight-loss intervention with the frequency of remission from type 2 diabetes.[98] Secondary observational analysis of The Look AHEAD (Action for Health for Diabetes) study, one of the largest randomized controlled trial of an intensive lifestyle intervention among adults with type 2 diabetes was used. Intensive lifestyle intervention (ILI) participants lost more weight than the diabetes support and education control condition (DSE) participants at year 1 (net

difference, 7.9% [95% CI: 8.3% to 7.6%]) and at year 4 (3.9% [95% CI: 4.4% to 3.5%]) and had greater fitness increases at year 1 (net difference, 15.4% [95% CI: 13.7%-17.0%]) and at year 4 (6.4% [95% CI: 4.7%- 8.1%]) (P.001 for each). The ILI group was significantly more prone to experience remission, with prevalence's of 11.5% (95% CI: 10.1%-12.8%) during the first year and 7.3% (95% CI: 6.2%-8.4%) at year 4, compared with the DSE group at year 1 (2.0% [95% CI:1.4%-2.6%]) and year 4 (2.0% [95% CI:1.5%-2.7%] (P<.001). Among ILI participants, 9.2% (95% CI:7.9%-10.4%), 6.4% (95% CI: 5.3%-7.4%), and 3.5% (95% CI: 2.7%-4.3%) had remission for at least 2, at least 3, and 4 years, respectively, compared to DSE for at least 2 years (1.7% [95% CI: 1.2%-2.3%]), for at least 3 years (1.3% [95% CI: 0.8%-1.7%]), or 4 years (0.5% [95% CI: 0.2%-0.8%]). These findings indicated that the intensive lifestyle interventions were associated with an increased possibility of partial remission of type 2 diabetes.

In terms of long-term glycemic control, weight loss has a positive affect even if ideal body weight is not achieved.[16] Watts et al evaluated glycemic control in responders or non-responders in individuals with diabetes and obesity.[99] This was a retrospective study in which obese individuals with diabetes lost a minimum of 10 percent of initial body weight within the first four years of investigation. Results from this study show that responders had significant improvement in both glycemic control and plasma glucose after losing 10 percent of initial body weight. The improvement following weight loss could be predicted by a plasma glucose level of 10.0 mmol/L or lower after 2.3-kg and 4.5-kg weight loss (62%, 79% positive predictive value respectively). It was concluded that moderate weight loss is critically important regarding glycaemia control.

In a study of hyperinsulinemia in obesity, Numata et al. found that insulin and C-peptide secretions were increased before weight loss and were significantly decreased following weight loss for 8-12 wks. Findings from this study suggest that weight loss has a positive impact on

insulin, which ultimately can lead to improved glycemic control. Also, findings from this study are in line with results from large, randomized control trials.[100] Evidence-based studies such as The Diabetes Prevention Program have demonstrated that modest weight loss achieved through lifestyle changes resulted in a 58% reduction in the incidence type 2 diabetes in obese individuals with impaired glucose tolerance.[101]

Obesity is important in the development of hypertension.[102] The direct relationship between changes in body weight and blood pressure has been supported by several studies. Recent studies have shown that weight loss has an antihypertensive effect in the absence of sodium restriction.[103] Weinsier et al. found that the independent role of weight loss is attributed to changes in blood volume, and cardiac output.[104] Additionally, ideal body weight was not required to achieve the beneficial changes in blood pressure. In individuals with overweight/obesity and hypertension weight loss has shown to lead to a reduction in arterial pressure.[83,105] A study by Ramsey et al predicted that with every kg of weight loss there will be a reduction of 1.5-2.5 mmHg in systolic blood pressure.[106] The Trials of Hypertension Prevention, Phase I results show that a loss of only 10 percent of initial body weight reduces blood pressure significantly in overweight and obese adults.[107] Similarly Phase II of the Trial of Antihypertensive Interventions and Management demonstrated that there can be long-term effects of weight loss on blood pressure maintenance.

The excess adipose tissue that contributes to obesity has been associated with lipid abnormalities (i.e., dyslipidemia).[19] Mechanisms linking dyslipidemia and obesity include decreased high-density-lipoprotein, increased triglycerides, and increased cholesterol.[19] Wood et al. demonstrated that with modest weight loss there is an association with the increase in high-density-lipoprotein and improvements in cholesterol.[108] These changes to blood lipids occurred

when weight loss was elicited by physical activity or dietary restriction. Meta- analysis performed by Dattilo et al showed that weight loss is associated with significant decreases in total, low-density-lipoprotein, and very-low-lipoprotein cholesterol along with triglycerides.[21] For every kg of body weight lost, the high-density-lipoprotein increased by 0.009 mmol/L, total cholesterol decreased by 0.05 mmol/L, low-density-lipoprotein decreased by 0.02 mmol/L, and triglycerides decreased by 0.015 mmol/L. These results support that moderate weight loss is beneficial in individuals with obesity and dyslipidemia. Seim et al reported that a weight loss of 5.8 percent of initial weight could reduce total cholesterol by 16 percent and low-density-lipoprotein by 12 percent and increase high-density- lipoprotein by 18 percent at six weeks.[109] Benefits have been shown to continue after one year. Waki et al., examined the long-term differences in blood serum lipids in healthy women with obesity following weight loss.[110] Results from the follow-up at 17 months did show significant decreases in body weight, total cholesterol, and low-density-lipoprotein. The levels of triglycerides also significantly decreased, also the ratio of high-density-lipoprotein to total cholesterol when compared to baseline significantly increased. Even when weight loss has been modest (5-10% initial body weight) improvement to total cholesterol and low-density-lipoprotein have been demonstrated.

### 2.4 Physical Activity as an Important Lifestyle Behavior

Much of the adults in the U.S. are classified as overweight or obese.[2] This presents a significant public health issue because obesity is associated with the increased prevalence of chronic health conditions, including CVD, type 2 diabetes, hypertension, and certain cancers.[36,111] Therefore, it is important to develop interventions are that will be effective for individuals to both

attain and maintain a healthy body weight. To induce weight loss, physical activity is recommended as a critical component to a weight loss program.[27,44] In this section of the review, the role of Physical activity as an important lifestyle behavior will be examined.

#### 2.4.1.1 Physical Activity Alone and Weight Loss

Physical activity plays a critical role in lifestyle behaviors aimed at reducing body weight. However, physical activity alone within the context of weight loss is meager. The effect of physical activity alone on inducing weight loss are modest. According to evidence from the Physical Activity Guidelines Committee Report, weight change via physical activity alone results in <3% of initial body weight, with weight loss ranging from 0.5 to 3.0 kg.[24] Findings of numerous published meta-analyses and reviews have concluded that physical activity alone is related with weight loss an average of 0.6–3.0 kg.[112,113]

A systematic review of studies with at least a 1-year follow-up suggested that participants who used physical activity alone for weight reduction experienced minimal weight loss.[114] Results revealed a mean weight loss of 5-8.5 kg was observed from interventions involving a dietary restriction and/or weight-loss medications. In contrast, physical activity-alone groups experienced weight loss of 1.9±3.6 kg. Garrow et al. performed a meta-analysis evaluating the effect of physical activity with or without dieting on overweight individuals. Findings showed that aerobic physical activity without dietary restriction elicited a weight loss of 3 kg among men in 30 weeks compared to controls and 1.4 kg of weight loss in 12 weeks among women.[25] This evidence supports that aerobic physical activity only produces a modest weight loss.

Another review by Wing et al. assessed the effect of lifestyle intervention over 2 years. At 6 months into the lifestyle intervention, weight losses in the diet and diet combined with physical activity groups were significantly greater than in the physical activity alone and control groups.[14]

The diet group lost 9.1 kg during the first 6 months of the program, and the diet-plus-physical activity group lost 10.3 kg. Weight changes in the physical activity group (-2.1 kg) and the control condition (-1.5 kg) were significant and modest. Foster-Schubert et al. conducted a year-long, group-based lifestyle intervention to examine the effects of physical activity and dietary weight loss on body weight and body composition among postmenopausal women with overweight and obesity.[28] The average weight loss at 12 months was −8.5% for the diet group ($P < 0.0001$), −2.4% for the physical activity group ($P = 0.03$), and −10.8% for the combined diet and physical activity group ($P < 0.0001$). Results show the most change came from the combined intervention, with modest weight loss coming from physical activity alone group.

Many other studies have examined strategies for weight loss and shown that physical activity alone does not produce the same magnitude of weight loss when compared to dietary restriction. In a randomized, controlled trial by Slentz et al, physical activity alone for weight loss was highlighted.[29] Individuals who jogged/ran for 20 miles (32.0 km)/wk lost 3.5 kg at the end of 8 months of training while individuals that walked 12 miles (19.2 km)/wk lost only 1.1 kg. Church et al. reported no significant weight changes in adults with diabetes participating in the aerobic training group only (0.8%) compared to a control group (1.0% weight gain) for 9 months.[115] In a study of men classified as overweight and sedentary, Wood et al. indicated that weight loss induced by a dietary intervention at 7 and 12 months was 7.6 and 7.2 kg, which was significantly more than weight loss induced by physical activity alone which was 3.0 and 4.0kg.[108] Donnelly et al. evaluated the impact of 18 months (3 times/week, 30 min/session) of continuous versus intermittent endurance training (5 times/week, 15 min/session) in participants with overweight and obesity.[116] The results showed small reductions in body weight (2.0%) in the continuous training group and no significant change in intermittent groups after the intervention.

Although there is substantial evidence that suggests that physical activity alone only produces modest amounts of weight loss compared to weight loss with dietary restrictions, it has been shown that when the energy deficit is constant and other factors are controlled, physical activity can elicit significant weight loss. Donnelly et al. demonstrated weight loss with physical activity alone in a group of men and women with overweight and obesity (BMI ≥31 kg/m$^2$) in the Midwest Exercise Trial 2.[22] Physical Activity was supervised for 10 months with a physical activity calorie-equivalent reduction of either 400 or 600 calories 5 days per week. Weight losses for the 400 and 600 kcal/session groups were 3.9 ± 4.9 and 5.2 ± 5.6 kg, respectively when compared to weight gain for controls of 0.5 ± 3.5kg (0.5%) ($p<0.05$). This demonstrated that significant weight loss for both men and women can be accomplished with an equivalent energy expenditure and physical activity.

In a randomized, controlled trial of men with obesity, Ross et al. demonstrated with energy intake remaining constant, a body weight decreases of 7.5 kg over 3 months in the physical activity alone group that was comparable to the calorie-restricted group.[117] Duration of physical activity was established on the goal of a daily 700-calorie energy expenditure (60 min/day), suggesting that performing physical activity may be able to elicit meaningful weight loss. Weiss et al. showed effective weight loss (7% over 17weeks) with physical activity alone in men and women classified as overweight and sedentary.[118]

#### 2.4.1.2 Physical Activity in Combination with Dietary Modification

As previously mentioned, it has been recommended that adults with overweight or obesity reduce initial body weight by 5-10%.[23] The optimal strategy for promoting weight loss is the combination of dietary restriction and physical activity. Several randomized control trials and meta-analyses have examined the impact of weight loss programs composed of both dietary

restriction and physical activity and have shown greater weight loss compared to programs composed of physical activity only.

A meta-analysis by Johns et al. observed a 5.3 kg (95% CI -7.61 to -3.04) greater weight loss in combined diet and physical activity programs compared to diet alone for interventions that were 3–6 months long.[30] For interventions that were 12–18 months, there was a 6.3 kg (95% CI -7.33 to -5.25) greater weight loss with combined dietary and physical activity programs compared to dietary alone programs. A systematic review by Washburn et al. investigated studies that were at least 1 year in length.[32] Dietary restrictions combined with physical activity elicited significantly greater weight loss than dietary restrictions alone in more than half of trials. Thus, it was concluded that the combination of physical activity and dietary restrictions induce more weight loss than dietary restrictions alone. The weight loss median range was 6.9% in dietary groups and 8.8% in dietary restrictions combined with physical activity groups.

In a meta-analysis of 6 studies, Curioni et al. greater weight loss occurred with dietary restrictions and physical activity programs compared to dietary only in adults with overweight and obesity.[34] Dietary restrictions associated with physical activity elicited a 20% greater initial weight loss. (13 kg vs 9.9 kg; z=1.86—p=0.063, 95%CI). The combined intervention also elicited in a 20% greater weight loss after 1 year (6.7 kg vs 4.5 kg; p=0.058) than dietary restriction alone. Messier et al. compared the impact of 18 months of dietary restriction only (800–1000 kcal/day), physical activity (3 days/week, strength training [20 min] and walking [15 min]) or a combination of both interventions in older adults with overweight and obesity.[31] Participants in the dietary restriction alone (9.5%) and the combination (11.3%) programs had greater weight loss compared to the physical activity only group (2.0%). The authors also observed greater fat mass loss in both diet groups (diet only−4.8 kg, diet + physical activity−6.5 kg) compared to the physical activity

only group (−0.4 kg). Similarly, Hagan et al suggested that weight loss for men and women induced by physical activity alone was significantly less when compared to dietary restrictions alone and compared to the combination of dietary restriction and physical activity for a 12 wk intervention.[33] These data appear to suggest that physical activity can produce more weight loss when combined with dietary restrictions.

#### 2.4.1.3 Physical Activity and Long-Term Weight Loss and Maintenance

Dietary restriction combined with physical activity have been shown to be successful for inducing weight loss. However, physical activity appears to be critical for long-term weight management.[39,44] A study by Jeffery et al. showed that higher levels of physical activity (ie, 2500 kcal/wk) maintained greater weight losses at 12 months and 18 months than lower physical activity level (ie,1000 kcal/wk).[112] Cumulative weight losses at 6, 12, and 18 months in the high physical activity group were 9.0 ± 7.1, 8.5 ± 7.9, and 6.7 ± 8.1 kg, respectively. In the lower physical activity group, the corresponding weight losses were 8.1 ± 7.4, 6.1 ± 8.8, and 4.1 ± 7.3 kg, respectively. Weight loss were significant at 12 and 18 months between-group differences. These results suggest that higher levels of physical activity are important for long-term weight loss. Similarly, Jakicic et al. have reported that higher doses of physical activity are important for long-term weight loss and maintenance.[35] A secondary analysis of data from a study of adult women, showed that physical activity of 275 min/wk above baseline was performed by those with weight loss of 10% of initial body weight and was maintained at 24 months.

The most recent position stand by the American College of Sports Medicine recommends that adults need to obtain at least 200–300 min of moderate physical activity per week to promote weight maintenance, which is the equivalent to 60 min of physical activity on most days of the week. Additionally, The National Weight Control Registry (NWCR), is a registry of individuals

who self-reported to have lost at least 30 pounds and have maintained weight loss for a 1 year, has produced important data related to individuals who have successfully maintained significant weight loss. Klem et al. reported that individuals in the NWCR participate in 2,800 kcal/week of physical activity to maintain weight loss.[119] Gormally and Rardin compared individuals that regained weight to individuals that maintained weight loss and found that individuals that maintained weight loss reported participating in regular physical activity.[120]

Another study Jakicic by evaluated the impact of intermittent home-based physical activity on weight maintenance in women with overweight/obesity and classified as sedentary.[121] Participants were assigned to a long bout (5 days/week, 40 min), short bout (5 days/week, 40 min divided into multiple 10-min bouts) or short bout plus home physical activity equipment group (treadmill provided for home use). The initial weight loss at 6 months was 7–10 kg without significant differences between groups. Analyses evaluating weight maintenance at 18 months showed that weight loss at 18 months was significantly greater in individuals exercising more than 200 min/wk throughout the intervention (−13.1 [8.0] kg) compared with individuals exercising 150 to 200 min/wk (−8.5 [5.8] kg) or less than 150 min/wk (−3.5 [6.5] kg) ($P<.05$). Fogelholm et al reviewed weight-reduction studies that had a prospective follow-up of more than 1 year and found that most results were consistent: reported that a large amount of physical activity at follow-up was associated with less weight regain after weight reduction.[114] There was a trend towards less weight regain with physical activity compared with control: the mean weight regain was 0.28 kg/month with physical activity versus 0.33 kg/month without physical activity. Overall, higher overall amounts of physical activity indicate greater weight maintenance.

A Secondary analysis of the data from a study performed by Schoeller et al. were performed to determine the amount of physical activity that elicits maximum differentiation between gainers

and maintainers.[122] Based on this analysis, it was determined that individuals that are classified as sedentary should participate in 80 min per day of moderate-intensity physical activity or 35 min per day of vigorous physical activity to prevent weight regain. These studies also aided in the 2001 recommendations by American College of Sports Medicine (ACSM) of 200–300 min per wk of moderate-intensity physical activity for long-term weight loss. Unick et al. evaluated the impact of physical activity level on weight maintenance in a sub-set from the Look AHEAD study in which accelerometry was performed in years 1 and 4.[123] Higher amounts of moderate to vigorous physical activity (150 to250 min/week, 12% weight loss; 250 min/week, 13% weight loss) were associated with greater weight maintenance compared to 50 min/week (7% weight loss) at year 1. At year 4, individuals that participated in ≥250 min/week of moderate to vigorous physical activity had greater weight maintenance (8.3% [95% CI: 6.1 to 10.4]) compared to those who had 50-150 min/week (5.5% [95% CI: 3.7 to 7.4]) or 50 min/week (5.8% [95% CI: 4.0 to7.6]). Most important for greater weight maintenance at year 4 included weight change at year 1 ($p<0.001$) and quantity of year 4 moderate to vigorous physical activity ($p = 0.006$). Moderate to vigorous physical activity seems to be the recommended intensity for weight loss and maintenance.

#### 2.4.1.4 Physical Activity and Inflammation

The current study has data available to examine CRP, and therefore this literature review is focused primarily on CRP, and an important inflammatory marker. A systematic review by Kasapis assessed the effects of physical activity on CRP and other inflammatory markers. Findings from this review revealed that with engagement in physical activity, CRP levels were lower in cross-sectional studies.[124] Additionally, a study examined the relationship between physical activity and inflammation identified by CRP.[125] Data from The National Health and Nutrition Examination Survey was used to examine the association of physical activity and CRP. Results

from this study demonstrated that physical activity was associated with reduced odds of elevated CRP. When compared with individuals participating in physical activity up to 3 times /month, the odds of elevated CRP were reduced among individuals participating in physical activity up to 21 times/ month (OR=0.77 [95% CI: 0.58-1.02]) and above 22 times /month (OR=0.63[95% CI: 0.43-0.93]) (*P* for trend, .02). Some evidence would suggest that physical activity is associated with the reduction in inflammation as identified by CRP, however there is accumulating evidence alluding to the notion that physical activity is not directly associated with reductions in inflammation identified by CRP.

A study by Stewart et al evaluated physical activity doses on CRP among women. Findings from this study showed that improvements in oxygen consumption and fitness in a response to physical activity did not elicit significant changes in CRP.[126] Nevertheless, weight change was associated with changes in CRP. This demonstrates that reduction in CRP may be more associated with body weight reduction rather than physical activity. Furthermore, the INFLAME study, investigated the effect of exercise on elevated CRP levels.[127] The significance of this particular study is it was designed specifically with the primary outcome being change in CRP. Results showed no change in CRP between control and exercise intervention groups (0.0 [−0.5, 0.9] vs. 0.0 [−0.8, 0.7] mg/L, p=0.4), although change in weight was correlated with change in CRP. Based on the evidence, it appears that reductions in CRP may be associated with reductions in body weight rather than physical activity.

#### 2.4.1.5 Physical Activity and Cardiometabolic Risk Factors

While the achievement of significant weight loss is important, the cardiometabolic benefits elicited from weight loss are particularly important in the treatment of individuals with overweight or obesity. An examination of participants in prospective studies that were able to achieve mean

levels of weight loss of at least 5% suggests that improvements in several cardiometabolic risk factors (i.e., body fat, lipids, and insulin sensitivity) are observed for aerobic physical activity in combination with weight loss compared to aerobic physical activity alone.[128] Swift et al. evaluated the effect of aerobic training on clinically significant weight loss (>5%), modest weight loss (3 to 5%) and a group that did not achieve either (<3% weight loss) on cardiovascular risk factors in postmenopausal women in the DREW study.[18] Both the clinically significant weight loss and modest weight loss groups had a significant increase in insulin sensitivity compared to the no weight loss group. The findings found that the clinically significant weight loss group had greater reductions in fasting insulin and waist circumference compared to the no weight loss group. Modest weight loss as low as 2–3% has been shown to be associated with cardiovascular benefits. Donnelly et al. randomized females classified as sedentary, with obesity to 18 months of either continuous or intermittent physical activity.[116] After 18 months of physical activity, weight loss was 2% in the continuous group and 1% in the intermittent group. Although there was minimal weight loss, both groups had significant improvements in HDL and reduced insulin area under the curve after an oral glucose tolerance test was administered. In the Healthy Women Study, when physical activity increased by ≥300 kcal/wk there was shown to be no change in HDL over a 3-year period. When decreased physical activity by ≥300 kcal/wk there was shown to be a 1.9 mg dL decrease in HDL over a 3- year period.[129] Weight loss with physical activity is critical to elicit positive changes in cardiometabolic risk factors.

#### 2.4.1.6 Light-Intensity Physical Activity

Much of the literature examining the influence of physical activity on body weight has reported primarily on moderate-to-vigorous physical activity (MVPA). The above sections summarize key findings from these studies. Currently there is little to no research evaluating the

influence of LPA on body weight. However, there are data to suggest that light-intensity physical activity may be a significant contributor to weight loss within the context of a behavioral weight loss intervention. For example, in a 6-month intervention that focused on behavior modification, reduced energy intake, and increased physical activity, Jakicic et al. reported that increasing light-intensity physical activity was one of the significant factors that was associated with weight loss.[49]

There are a few meta-analysis and systematic reviews examining LPA and cardiometabolic risk factors. A systematic review by Chastin et al. assessed the relationship between time spent in LPA and cardiometabolic health and mortality in adults.[51] Studies showed that small bouts of light-intensity activity during the day attenuated postprandial glucose (−17.5% [95% CI: −26.2 to −8.7]) and insulin (−25.1% [95% CI: −31.8 to –18.3]) concentrations when compared to uninterrupted sitting. Several of the prospective observational studies that were entered in the meta-analysis reported that more time spent in daily light physical activity reduced risk of all-cause mortality (pooled HR=0.71 [95% CI: 0.62 to 0.83]). These findings suggest that LPA could potentially improve cardiometabolic health and reducing mortality risk.

A meta-analysis by Fuezeki et al. assessing the association of accelerometer-measured LPA with modifiable health outcomes in adults and older adults. LPA was positively associated with obesity, mortality, and lipid and glucose metabolism.[48] Amagasa et al. performed a systematic review to summarize existing epidemiological evidence on associations of objectively measured LPA with health outcomes in adults. LPA was negatively associated with all-cause mortality.[50] Results reported a significant decrease in mortality risk in those who accomplished at least 4 hr per day of LPA.

Thus, although there is little evidence on LPA and body weight and cardiometabolic risk factors, the current evidence is promising and warrants further investigation. Therefore, the focus

of this study will further examine the potential contributions of LPA on weight loss and cardiometabolic health in adults with overweight or obesity within the context of a behavioral weight loss intervention.

# 3.0 Methods

Data for this study were obtained from a parent randomized clinical trial that was designed to compare different behavioral weight loss interventions on cardiovascular health in adults with overweight or obesity (R01 HL096770). Results of the primary outcomes of this study are currently under review for publication. Thus, presented here are secondary analyses to examine the specific aims and hypotheses of this study. Where appropriate components of the primary study are presented with additional description of the approach that is being undertaken within the secondary analyses for this study.

## 3.1 Methods from the Parent Study

### 3.1.1 Participants

The parent study recruited and randomized 383 adults with overweight or obesity (age=45.6±7.9 years; BMI=32.4±3.8 kg/m$^2$). To be eligible for the parent study, participants self-reported not engaging in regular structured exercise that exceeded 60 min/week. In addition, the following eligibility/ineligibility criteria were used for subject selection as previously reported.[130]

Eligibility Criteria

1. Age between 18 to 55 years;

2. Body mass index (BMI) of 25.0 to <40.0 kg/m$^2$;

3. Ability to provide informed consent prior to participation in this study;

4. Ability to provide consent from their personal physician to participate in this study.

Exclusion Criteria

1. Self-reporting ≥60 min/wk of structured moderate-to-vigorous intensity physical activity;
2. Weight loss of ≥5% within the prior 6 months or a history of bariatric surgery;
3. History of cardio-metabolic disease, type 2 diabetes, or cancer;
4. Taking medication that could affect heart rate or blood pressure;
5. Taking medication that could influence body weight;
6. Treatment for psychological conditions that included medication or counselling;
7. Currently pregnant, pregnant within the prior 6 months, or planning a pregnancy within the next 12 months;
8. Planning on geographical relocation outside of the region within 12 months;
9. Inability to comply with the components of the interventions.

### 3.1.2 Study Recruitment and Informed Consent

Participants were recruited using a variety of recruitment methods that included direct mailing of advertisements, research registries, and other media such as television advertisements. Individuals interested in participation in this study were provided a telephone number to contact the investigators, and study staff conducted a brief telephone screening to determine initial eligibility. Those individuals who appeared to be eligible based on the telephone screening were invited to an orientation to receive more detailed information about the study, and these orientation sessions were conducted by the Principal Investigator or a designated Co-Investigator. Individuals interested in participating in the parent study after attending an orientation session provided written

informed consent and medical clearance from their primary care physician prior to further engaging in the study. The University of Pittsburgh's Institutional Review Board and Human Research Protection Office approved all procedures.

### 3.1.3 Study Design of the Parent Study

Participants eligible for the parent randomized clinical trial were randomized to one of three behavioral weight loss interventions. These included the following:

1. Diet only weight loss intervention (DIET).
2. DIET plus progression to 150 minutes of prescribed physical activity (DIET+PA150).
3. DIET plus progression to 250 minutes of prescribed physical activity (DIET+PA250).

The details of the intervention are presented below.

Outcomes measures for the parent study, which include the measures used for these secondary analyses, were collected at baseline, 6 months, and 12 months of the intervention. Details of the outcome measures pertinent to these secondary analyses are presented below.

### 3.1.4 Behavioral Weight Loss Program

Intervention Sessions: Participants in all intervention conditions received weekly weight loss group sessions for weeks 1-24 and approximately every other week during weeks 25-52 as previously described.[131] Groups were closed to only those participants randomly assigned to a particular intervention condition (DIET, DIET+PA150, DIET+PA250). Intervention sessions focused on behavioral strategies to reduce energy intake. For DIET+PA150 and DIET+PA250, sessions also focused on increasing physical activity that was consistent with the intervention

protocol. A variety of professionals that included exercise physiologists and nutritionists led these intervention sessions. If a group session was missed a brief individual make-up session was offered to allow the content to be shared with the subject. Body weight was measured at each of the intervention sessions to determine responsiveness of the subject to the weight loss program and to provide ongoing feedback. Participants who were unable to attend either the group session or the make-up session were mailed intervention materials that were distributed to the other participants at the intervention session.

In addition to the group intervention sessions as described above, participants received an individual (approximately 10 minutes in duration) telephone contact from a member of the intervention staff approximately twice per month during weeks 25-52 on weeks when an in-person session was not scheduled. The interventionist used a standardized script to direct the approach and content of this telephone contact.

Diet Intervention: As previously described,[131] the same dietary intervention was provided to all participants regardless of randomization assignment (DIET, DIET+PA150, DIET+PA250). Participants were prescribed to consume 1,200-1,800 kcal per day, and to reduce their dietary fat intake to 20-30 percent of their total daily energy intake. Energy intake was determined based on baseline body weight, with additional adjustments made based on weight loss response across the intervention. Registered dietitians developed meal plans that were provided to participants to facilitate adoption and compliance with these dietary recommendations. Participants were encouraged to self-monitor their dietary intake in a diary that was returned to the intervention staff at each intervention session. The intervention staff reviewed these diaries and provided written feedback to the subject in an effort to enhance dietary compliance.

Physical Activity Intervention: The physical activity prescription differed between randomized intervention conditions as previously described.[131] By study design, the DIET group did not receive a prescription for physical activity.

Participants in the DIET+PA150 intervention were instructed to engage in moderate intensity physical activity 5 days per week. The total duration per day began at 20 minutes per day and gradually progressed to at least 30 minutes per day. Physical activity was progressed in a gradual manner (5 min/day in 4-week intervals) to maximize adherence and minimize the onset of musculoskeletal injuries. Moderate intensity prescribed using the Borg 15-point Rating of Perceived Exertion (RPE) scale, with the range set at 13-15 on this scale.

Participants in the DIET+PA250 intervention were instructed to engage in moderate intensity physical activity 5 days per week. The total duration per day began at 20 minutes per day and gradually progressed to at least 50 minutes per day. Physical activity was progressed in a gradual manner (5 min/day in 4-week intervals) to maximize adherence and minimize the onset of musculoskeletal injuries. Moderate intensity was prescribed using the Borg 15-point Rating of Perceived Exertion (RPE) scale, with the range set at 13-15 on this scale.

All participants prescribed physical activity were encouraged to engage in brisk walking, or other activities similar in intensity to brisk walking, to achieve their prescribed physical activity goals. Participants self-monitored physical activity behaviors in a weekly diary. Participants returned the diary to the intervention staff, and the intervention staff provided written feedback on the diary.

### 3.1.5 Outcome Assessments

Physical Activity

Physical activity was assessed with an activity monitor (SenseWear Armband) worn for 7 days with participants maintaining their regular activity prior to initiating the intervention. Data were considered valid if the activity monitor was worn for ≥10 hours per day on at least 4 days. These data from the activity monitor were analyzed in proprietary algorithms developed by the manufacturer to identify periods of sedentary behavior (awake time, <1.5 metabolic equivalent task [METs], light-intensity physical activity (1.5 to <3.0 METs), and MVPA (≥3.0 METs).

Weight, Height, and BMI

Weight, height, and BMI were measured as previously described.[130,131] Weight was assessed to the nearest 0.1 kg with the subject clothed in a hospital gown or lightweight clothing, with duplicate measures differing by <0.2 kg. Height was assessed using a wall-mounted stadiometer, with shoes removed, to the nearest 0.1 cm with duplicate measures differing by ≤0.5 cm. BMI was computed from weight and height as $kg \cdot m^{-2}$.

Cardiorespiratory Fitness

A submaximal graded exercise test performed on a motorized treadmill was used to assess cardiorespiratory fitness as previously described.[130] A constant speed of 80.4 $m \cdot min^{-1}$ was sustained on the treadmill, with a beginning grade of 0% and increasing by 1% per minute until the point of test termination. Test termination criteria occurred at the point where the subject achieved 85% of their age-predicted maximal heart rate (predicted maximal heart rate = 220 minus age). Heart rate was obtained using a 12-lead ECG at one-minute intervals and immediately upon termination of the exercise test. For safety purposes, blood pressure was obtained during each even minute (2 min, 4, min, 6 min etc.) and immediately upon termination of the exercise test.

Each test was evaluated by a physician to ensure that exercise training during the study was not contraindicated.

Indirect calorimetry using a metabolic cart (Carefusion Vmax Encore, Yorba Linda, CA) was used to measure oxygen consumption ($L \cdot min^{-1}$ and $mL \cdot kg^{-1} \cdot min^{-1}$). Submaximal fitness was represented by oxygen consumption achieved during the final 20 seconds prior to test termination.

Body Composition

Body composition was assessed using dual-energy x-ray absorptiometry from a total body scan (GE Lunar iDXA, Madison, WI). Participants were clothed in a light-weight hospital gown, and metal (e.g., jewelry) was removed. Female participants completed a urine pregnancy test just prior to this assessment to confirm non-pregnancy. Participants with a positive urine pregnancy test were ineligible for further participation in this study.

Girth measures of the waist and hip were taken using a Gulick anthropometric measuring tape, with measures taken to the nearest 0.1 cm with duplicate measures differing by ≤1.0 cm. Waist circumference was measured horizontally at both the umbilicus and the iliac crest. Hip circumference was measured at the widest visual protrusion of the buttocks. For girth measures, participants were clothed in a lightweight hospital gown.

Resting Blood Pressure and Heart Rate

Resting blood pressure and heart rate were measured in duplicate following a 5-min seated resting period using an automated system (DINAMAP V100, GE Medical System Technologies; Milwaukee, WI). The mean values of duplicate measures of systolic blood pressure that differed by ≤10 mmHg and diastolic blood pressure that differed by ≤6 mmHg were used to represent resting blood pressure. Participants with systolic blood pressure of ≥140 mmHg or diastolic blood pressure ≥ 90 mmHg were referred to their physician for follow-up evaluation.

Blood Samples

Participants were instructed to fast with the exception of water, abstain from exercise, and abstain from alcohol and smoking for at least 12 hours prior to collection of blood samples. Adherence to these directions were confirmed via self-report prior to blood collection. Blood samples were collected in the morning, between approximately 7:00 AM and 11:00 AM. Participants underwent a brief 5-minute rest period prior to blood collection after arriving at the laboratory. Blood was collected into evacuated tubes, processed in a refrigerated centrifuge, and pipetted into 2.0 mL cryovials prior to storage at -80$^{o}$C. For this study, blood samples were analyzed for lipids (total cholesterol, HDL cholesterol, triglycerides), C-reactive protein (CRP), glucose, and insulin, with LDL cholesterol calculated using the Friedwald equation (15) at a CLIA certified laboratory at the University of Pittsburgh using standardized procedures.

### 3.1.6 Data Analysis

Descriptive baseline data were expressed as either mean and standard deviation or median (25th, 75th percentile) for continuous variables and as frequencies for categorical variables. For baseline cross-sectional analyses all participants with data of interest were included. To examine the association between change in light-intensity physical activity and the outcomes of interest (weight, body composition, cardiorespiratory fitness, selected cardiometabolic risk factors) only those participants with complete data were examined. Therefore, descriptive analyses compared those participants providing and not providing data for analyses for the change in light-intensity physical activity. Prior to analysis, data were checked for normality. If data were not normally distributed, where appropriate non-parametric statistics were used, or log transformations were implemented in an effort to normalize the data prior to analysis.

To examine Specific Aim 1, linear regression was performed to assess the association between light-intensity physical activity and measures of weight, body composition, cardiorespiratory fitness, and cardiometabolic risk factors which include: resting blood pressure, total cholesterol, LDL cholesterol, triglycerides, HDL cholesterol, glucose, insulin, and C-reactive protein [CRP]. Separate analyses were conducted for each dependent variable. These analyses controlled for age, sex, race, ethnicity, and baseline level of MVPA. Cardiorespiratory fitness expressed as minutes was used as a secondary measure of cardiorespiratory fitness.

To examine Specific Aim 2, linear regression was performed to assess the association between change in light-intensity physical activity and change in measures of weight, body composition, cardiorespiratory fitness, and cardiometabolic risk factors including, resting blood pressure, total cholesterol, LDL cholesterol, triglycerides, HDL cholesterol, glucose, insulin, and CRP. Separate analyses were conducted for each dependent variable. These analyses controlled for age, sex, race, ethnicity, baseline level of light-intensity physical activity, change in MVPA, and randomized intervention condition. These analyses were performed assessing the change from baseline to 6 months and baseline to 12 months. The change scores were computed as follows: 6 months minus baseline and 12 months minus baseline. Cardiorespiratory fitness expressed as minutes was used as a secondary measure of cardiorespiratory fitness.

To perform the proposed analyses, physical activity was defined as MET-minutes per week (MET-min/week) of light-intensity physical activity, with light intensity physical activity identified by minutes where metabolic equivalents (METS) were between 1.5 to < 3.0 METS.

Age, sex, race, and ethnicity were included as covariates. Age was included as a covariate given the data to support that obesity prevalence may vary by age.[33] Sex was included as a covariate because prior data suggests that weight loss may differ for men and women in response

to a behavioral intervention.[131] Moreover, both race and ethnicity were included as covariates because data suggests that obesity prevalence and weight loss may vary by race and ethnicity.[33,132]

For the analyses examining change in the proposed outcome variables, additional covariates were included. Moderate-to-vigorous physical activity and baseline light-intensity physical activity were included as covariates. Moderate-to-vigorous physical activity was included as a covariate given the data to support that weight loss may vary in response to doses of physical activity.[39] Baseline light-intensity physical activity was included as a covariate because initial light-intensity physical activity level may differ prior to a behavioral intervention.[130] In addition, randomized group assignment was included as a covariate given that intervention assignment may have influenced the response in the variables examined.

The sample size of the parent study was determined to test the hypotheses of detecting differences in primary outcomes between the randomized intervention conditions. The overall sample available from the parent study is available for the secondary data analysis to test the hypotheses for this study, which are focused on examining associations between LPA and selective outcome variables. Examination of the data indicates that approximately 375 participants will contribute data for baseline analyses, 320 participants will contribute data for analyses of the change from baseline to 6 months, and 301 participants will contribute data for the analyses of the change from baseline to 12 months. Based on these available participants a power analysis was conducted to determine the magnitude of the correlation that would be detectable, and for these estimates power was set at 0.95 with alpha set at 0.05 for a two-tailed test. These power analyses indicated that correlations of r=0.185, r=0.200, and r=0.206 would be detected for the baseline, change from baseline to 6 months, and change from baseline to 12 months analyses, respectively.

# 4.0 Results

The primary aim of this study was to examine the associations between LPA and cardiometabolic risk factors at baseline and throughout a behavioral weight loss intervention in adults with overweight or obesity. This was a secondary data analysis of a 12-month randomized weight loss study with assessments performed at baseline, 6 months, and 12 months. All study procedures which include physical assessments, blood collection, and behavioral intervention were performed at the University of Pittsburgh Physical Activity and Weight Management Research Center.

## 4.1 Participants

Three-hundred eighty-three participants who were enrolled and randomized into the parent study provided data for these secondary analyses. However, due to dropout or missing data for select assessments, data for up to 375 (97.9%) provided data for baseline analyses, 320 (83.6%) of participants provided data for 6-month analyses, and 301 (78.6%) of participants provided data for 12-month analyses. Baseline characteristics are shown in Table 1 for those included in analysis of baseline data, change at 6 months, and change at 12 months. The characteristics of the participants in general are the same.

## 4.2 Outcome Variables

Baseline, the change from baseline to 6 months, and the change from baseline to 12 months for outcome variables are shown in Table 2. Body weight, body mass index, and percent body fat showed significant reduction at both 6 months and 12 months ($p<0.001$). Fitness significantly increased at 6 months and 12 months ($p<0.001$). Resting systolic blood pressure, diastolic blood pressure, total cholesterol, LDL cholesterol, triglycerides, glucose, insulin, and c-reactive protein significantly decreased at both 6 months and 12 months ($p<0.001$). There was no significant change in HDL cholesterol at 6 months ($p=0.459$), however, HDL cholesterol significantly increased at 12 months ($p<.001$). LPA and MVPA both significantly increased at 6 months and 12 months ($p<0.001$).

**Table 1. Demographic characteristsics of study participants included in analyses**

| | Randomized (N=383) | Included in Baseline Analyses (N=375)* | Included in Month 6 Analysis (N=320)* | Included in Month 12 Analysis (N=301)* |
|---|---|---|---|---|
| Age (years) | 45.6±8.0 | 45.8±7.8 | 46.1±7.7 | 45.9±7.8 |
| Wt (kg) | 90.9±13.7 | 90.9±13.7 | 90.8±14.0 | 91.1±14.1 |
| BMI ($kg/m^2$) | 32.4±3.8 | 32.2±3.8 | 32.2±3.8 | 32.3±3.8 |
| Sex (Female) | 304 (79.4%) | 298 (79.5%) | 251 (78.4) | 234 (77.7) |
| Race (Caucasian/White) | 279 (72.8%) | 275 (73.3%) | 240 (75.0) | 227 (75.4%) |
| Ethnicity (Hispanic/Latino) | 13 (3.4%) | 13 (N=3.5%) | 9 (2.8) | 9 (3.0%) |

*Indicates the N is based on data available for weight and physical activity data.

### 4.3 Change in Variables throughout the 12-month Intervention

Analysis of Body Weight

Analyses were conducted to examine the baseline association between LPA and body weight (Table 3). Unadjusted analysis showed that body weight was not significantly associated with LPA (β=-.0008; p=0.171). However, after adjustment for covariates, LPA was positively associated with body weight (β=.0016; p=0.008), suggesting that participants with higher amounts of LPA had a higher body weight.

Analyses were conducted to examine the association between the change from baseline to 6 months for change in LPA and change in body weight (Table 3). Unadjusted analysis showed a significant negative association between change in LPA and change in body weight (β=-.0010; p<0.001), and the association remained significant after adjustment for covariates (β=-.0008; p=0.006). Similar patterns of results were observed for the change in LPA and body weight at 12 months for both unadjusted (β=-.0017; p<0.001) and adjusted (β=-.0014; p=0.003) analyses (Table 3). These findings suggest that a greater increase in LPA was associated with a greater reduction in body weight at both 6 and 12 months.

**Table 2. Summary data for baseline change from baseline to 6 months, and change from baseline to 12 months for outcome measures.**

| Dependent Variable | | Baseline | Change from baseline to 6 months* | | Change from baseline to 12 months** | |
|---|---|---|---|---|---|---|
| | | mean ± standard deviation | estimate [95% confidence interval | P-value# | estimate [95% confidence interval] | P-value# |
| Body Weight (kg) | | 90.9±13.7<br>N=375 | -9.2 [-9.8, -8.2]<br>N=320 | <0.001 | -10.3 [-11.1, -9.4]<br>N=301 | <0.001 |
| Body Mass Index ($kg/m^2$) | | 32.3±3.8<br>N=375 | -3.2 [-3.4, -3.0]<br>N=320 | <0.001 | -3.5 [-3.9 -3.2]<br>N=300 | <0.001 |
| Percent Body Fat (%) | | 43.2±5.5<br>N=375 | -4.7 [-5.1, -4.4]<br>N=320 | <0.001 | -5.5 [-6.1, -5.0]<br>N=300 | <0.001 |
| Fitness | ml/kg/min | 22.6±4.4<br>N=374 | 2.6 [2.3, 3.0]<br>N=311 | <0.001 | 3.0 [2.5, 3.4]<br>N=292 | <0.001 |
| | Minutes | 7.7±3.0<br>N=375 | 2.0 [1.8, 2.3]<br>N=318 | <0.001 | 1.9 [1.7, 2.2]<br>N=296 | <0.001 |
| Resting Systolic Blood Pressure (mmHg) | | 120.3±11.7<br>N=375 | -5.2 [-6.3, -4.2]<br>N=320 | <0.001 | -5.0 [-6.4, -3.7]<br>N=300 | <0.001 |
| Resting Diastolic Blood Pressure (mmHg) | | 72.3±8.8<br>N=375 | -2.9 [-3.6, -2.2]<br>N=320 | <0.001 | -2.7 [-3.6, -1.8]<br>N=300 | <0.001 |
| Total Cholesterol (mg/dl) | | 198.7±33.7<br>N=374 | -11.5 [-14.3, -8.7]<br>N=317 | <0.001 | -7.2 [-10.2, -4.3]<br>N=298 | <0.001 |
| LDL Cholesterol (mg/dl) | | 120.7±28.2<br>N=374 | -6.5 [-8.9, -4.2]<br>N=317 | <0.001 | -5.2 [-7.8, -2.5]<br>N=298 | <0.001 |
| HDL Cholesterol (mg/dl) | | 53.4±12.0<br>N=374 | -0.27 [-1.0, 0.5]<br>N=317 | 0.459 | 3.4 [2.9, 4.5]<br>N=298 | <0.001 |
| Triglycerides (mg/dl) | | 123.3±3.5<br>N=374 | -23.3 [-29.0, -17.5]<br>N=317 | <0.001 | -28.6 [-34.0, -23.2]<br>N=298 | <0.001 |
| Glucose (mg/dl) | | 95.1±12.9<br>N=374 | -2.5 [-3.5, -1.4]<br>N=317 | <0.001 | -3.1 [-4.1, -2.1]<br>N=298 | <0.001 |
| Insulin (μIU/mL) | | 16.3±9.2<br>N=374 | -3.5 [-4.2, -2.8]<br>N=317 | <0.001 | -3.6 [-4.3, -2.8]<br>N=298 | <0.001 |
| CRP (mg/L) | | 4.3±4.6<br>N=374 | -1.3 [-1.7, -0.9]<br>N=317 | <0.001 | -1.2 [-1.8, -0.7]<br>N=298 | <0.001 |
| LPA (MET-minutes per week) | | 2720.0±1225.0<br>N=375 | 358.0 [222.3, 493.7]<br>N=320 | <0.001 | 421.2 [294.4, 548.0]<br>N=301 | <0.001 |
| MVPA (MET-minutes per week) | | 1336.0±1471.9<br>N=375 | 557.1 [420.9, 693.3]<br>N=320 | <0.001 | 767.9 [601.5, 34.2]<br>N=301 | <0.001 |

*Change score computed as 6-month score minus baseline score.

**Change score computed as 12-month score minus baseline score.

#P-value based on dependent t-test.

LDL = low-density lipoprotein; HDL = high-density lipoprotein; CRP = c-reactive protein; LPA= light-intensity physical activity; MVPA= moderate-to-vigorous physical activity

**Table 3. Association between LPA and body weight at baseline and change in weight at 6 and 12 months**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Body Weight (kg) | Intercept | 93.03603 | 1.7261 | <.001 | .0050 | 182.6708 | 7.3997 | <.001 | .3528 |
| | Baseline LPA (MET-minutes per week) | -.0008 | .0006 | 0.171 | | .0016 | .0006 | .008 | |
| | *Age (years) | ----- | ----- | ----- | | -.3211 | .0754 | .001 | |
| | *Sex (female) | ----- | ----- | ----- | | -20.8781 | 1.6059 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | .3952 | 1.3345 | .767 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.4691 | 3.1761 | .883 | |
| | *[$]Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -6.6351 | .7272 | <.001 | |
| | | | | | | | | | |
| Change in Body Weight (kg) from Baseline to 6 months | Intercept | -8.9606 | .3374 | <.001 | .0453 | -12.9752 | 2.7153 | <.001 | .2185 |
| | Change in LPA (MET-minutes per week) | -.0010 | .0003 | <.001 | | -.0008 | .0003 | .006 | |
| | *Age (years) | ----- | ----- | ----- | | -.0071 | .0397 | .858 | |
| | *Sex (female) | ----- | ----- | ----- | | 4.0433 | .7654 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -2.6936 | .7035 | <.001 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.7665 | 1.8302 | .676 | |
| | *Treatment Group 1 | | | | | -.2395 | .7466 | .749 | |
| | *Treatment Group 2 | | | | | .2408 | .7515 | .749 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0008 | .0003 | .003 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0002 | .0003 | .554 | |
| | | | | | | | | | |
| Change in Body Weight (kg) from Baseline to 12 months | Intercept | -9.5190 | .4698 | <.001 | .0613 | -6.7630 | 3.8249 | .078 | .1868 |
| | Change in LPA (MET-minutes per week) | -.0017 | .0004 | <.001 | | -.0014 | .0005 | .003 | |
| | *Age (years) | ----- | ----- | ----- | | -.0472 | .0550 | .391 | |
| | *Sex (female) | ----- | ----- | ----- | | 1.9911 | 1.0716 | .064 | |
| | *Race (white) | ----- | ----- | ----- | | -2.7930 | 1.0003 | .006 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -2.1654 | 2.4742 | .382 | |
| | *Treatment Group 1 | | | | | .5456 | 1.0405 | .600 | |
| | *Treatment Group 2 | | | | | 1.2960 | 1.0228 | .206 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0012 | .0003 | .001 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0007 | .0004 | .112 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
[$]Indicates that the data were log-transformed.
LPA= light-intensity physical activity
MVPA= moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET + PA250

Analysis of Body Mass Index (BMI)

Analyses to examine the association between LPA and BMI are shown in Table 4. Unadjusted analysis for baseline data showed that BMI was significantly associated with LPA (β= -.0006; p<.001). However, after adjustment for covariates, analysis of baseline data showed that LPA was not associated with BMI (β=.0002; p=0.310).

Analyses were conducted to examine the association between the change from baseline to 6 months for LPA and BMI (Table 4). A significant negative association between change in LPA and change in BMI was shown in the unadjusted analysis (β=-.0004; p<0.001), and after adjustment for covariates the association remained significant (β=-.0004; p<0.001). Unadjusted analysis showed that BMI change was not significantly associated with LPA change at 12 months (β=.0000; p=0.901). However, after adjustment for covariates, LPA change was negatively associated with BMI change (β=-.0005; p=<.001).

**Table 4. Associatin between LPA and body mass index (BMI) at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline BMI ($kg/m^2$) | Intercept | 33.9846 | .4689 | <.001 | .0388 | 49.8668 | 2.3167 | <.001 | .1736 |
| | Baseline LPA (MET-minutes per week) | -.0006 | .0002 | <.001 | | .0002 | .0002 | .310 | |
| | *Age (years) | ----- | ----- | ----- | | -.0935 | .0236 | <.001 | |
| | *Sex (female) | ----- | ----- | ----- | | -1.6602 | .5028 | .001 | |
| | *Race (white) | ----- | ----- | ----- | | .0783 | .4178 | .851 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | .4960 | .9944 | .618 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -1.6294 | .2277 | <.001 | |
| | | | | | | | | | |
| Change in BMI ($kg/m^2$) from Baseline to 6 months | Intercept | -3.0908 | .1115 | <.001 | .0716 | -3.3420 | .9276 | <.001 | .1877 |
| | Change in LPA (MET-minutes per week) | -.0004 | .0001 | <.001 | | -.0004 | .0001 | <.001 | |
| | *Age (years) | ----- | ----- | ----- | | .0001 | .0136 | .993 | |
| | *Sex (female) | ----- | ----- | ----- | | .7399 | .2615 | .005 | |
| | *Race (white) | ----- | ----- | ----- | | -.9217 | .2403 | <.001 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.5451 | .6252 | .384 | |
| | *Treatment Group 1 | | | | | -.1601 | .2551 | .531 | |
| | *Treatment Group 2 | | | | | .0235 | .2567 | .927 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0003 | .0000 | .002 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0001 | .0001 | .467 | |
| | | | | | | | | | |
| Change in BMI ($kg/m^2$) from Baseline to 12 months | Intercept | -3.5529 | .3759 | <.001 | .0000 | -.9575 | 1.3410 | .476 | .1660 |
| | Change in LPA (MET-minutes per week) | .0000 | .0001 | .901 | | -.0005 | .0017 | <.001 | |
| | *Age (years) | ----- | ----- | ----- | | -.0113 | .0193 | .559 | |
| | *Sex (female) | ----- | ----- | ----- | | -.1083 | .3757 | .773 | |
| | *Race (white) | ----- | ----- | ----- | | -1.0471 | .3525 | .003 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.8022 | .8674 | .356 | |
| | *Treatment Group 1 | | | | | .1439 | .3648 | .693 | |
| | *Treatment Group 2 | | | | | .4243 | .3598 | .239 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0004 | .0001 | <.001 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0003 | .0001 | .077 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA= light-intensity physical activity
MVPA= moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

Analysis of Percent Body Fat

Analyses to examine the association between LPA and percent body fat are shown in Table 5. Unadjusted analysis for baseline data showed that percent body fat was significantly negatively associated with LPA (β=-.0013; p<.001). However, after adjustment for covariates, analysis of baseline data showed that LPA was not associated with percent body fat (β=-.0002; p=0.337).

Analyses were conducted to examine the association between the change from baseline to 6 months for change in LPA and change in percent body fat (Table 5). A significant negative association between change in LPA and change in percent body fat (β=-.0007; p<0.001) was shown in the unadjusted analysis, and after adjustment for covariates (β=-.0007; p<.001) the association remained significant. Patterns remained similar in results observed for the change in LPA and percent body fat at 12 months for both unadjusted (β=-.0014; p<0.001) and adjusted (β=-.0013; p<.001) analyses (Table 5).

**Table 5. Association between LPA and percent body fat at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Percent Body Fat | Intercept | 46.8932 | .6625 | <.001 | .0899 | 36.1084 | 2.6230 | <.001 | .4957 |
| | Baseline LPA (MET-minutes per week) | -.0013 | .0002 | <.001 | | -.0002 | .0002 | .337 | |
| | *Age (years) | ----- | ----- | ----- | | .0149 | .0267 | .576 | |
| | *Sex (female) | ----- | ----- | ----- | | 7.7404 | .5692 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | 1.2332 | .4730 | .010 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.0792 | 1.1258 | .338 | |
| | *[$]Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -1.1755 | .2578 | .001 | |
| | | | | | | | | | |
| Change in Percent Body Fat from Baseline to 6 months | Intercept | -4.5013 | .0001 | <.001 | .0656 | -5.3516 | 1.4936 | <.001 | .2596 |
| | Change in LPA (MET-minutes per week) | -.0007 | .0001 | <.001 | | -.0007 | .0002 | <.001 | |
| | *Age (years) | ----- | ----- | ----- | | -.0033 | .0219 | .882 | |
| | *Sex (female) | ----- | ----- | ----- | | 2.0222 | .4210 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -1.4090 | .3870 | <.001 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.8888 | 1.0067 | .378 | |
| | *Treatment Group 1 | | | | | -.2960 | .4107 | .472 | |
| | *Treatment Group 2 | | | | | -.0601 | .4134 | .884 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0005 | .0001 | <.001 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0004 | .0002 | .008 | |
| | | | | | | | | | |
| Change in Percent Body Fat from Baseline to 12 months | Intercept | -4.9399 | .2755 | <.001 | .1036 | -1.4347 | 2.1708 | .509 | .2684 |
| | Change in LPA (MET-minutes per week) | -.0014 | .0002 | <.001 | | -.0013 | .0003 | <.001 | |
| | *Age (years) | ----- | ----- | ----- | | -.0370 | .0312 | .236 | |
| | *Sex (female) | ----- | ----- | ----- | | .8524 | .6082 | .162 | |
| | *Race (white) | ----- | ----- | ----- | | -1.6102 | .5706 | .005 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -2.0516 | 1.4042 | .145 | |
| | *Treatment Group 1 | | | | | .6780 | .5905 | .252 | |
| | *Treatment Group 2 | | | | | .5526 | .5825 | .344 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0008 | .0002 | <.001 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0007 | .0002 | .005 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
[$]Indicates that the data were log-transformed.
LPA= light-intensity physical activity
MVPA= moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

Analysis of Cardiorespiratory Fitness

Analyses were conducted to examine the baseline association between LPA and cardiorespiratory fitness (Table 5a). Unadjusted analysis showed that cardiorespiratory fitness (ml/kg/min) was positively associated with LPA (β=.00107; p<.001). After adjustment for covariates, there was a trend for LPA to remain significantly positively associated with cardiorespiratory fitness (ml/kg/min) (β=.0004; p=.057). A similar pattern was observed when cardiorespiratory fitness was expressed as minutes until termination time (Table 5b).

Analyses were conducted to examine the association between the change from baseline to 6 months for change in LPA and change in cardiorespiratory fitness (Table 5a). Unadjusted analysis showed a significant association between change in LPA and change in cardiorespiratory fitness (ml/kg/min) (β=.0005; p=.002), there was a trend for this to remain significant after adjustment for covariates (β=.0003; p=0.065). A similar pattern was observed when cardiorespiratory fitness was expressed as minutes until termination time (Table 5b). However, after adjustment for covariates, neither the change in cardiorespiratory fitness expressed as ml/kg/min or minutes until termination time were significantly associated with change in LPA at 12 months (Tables 5a and 5b).

**Table 5a. Association between LPA and cardiorespiratory fitness (ml/kg/min) at baseline and at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Fitness (ml/kg/min) | Intercept | 19.6691 | .5262 | <.001 | .0900 | 28.6906 | 2.2896 | <.001 | .3858 |
| | Baseline LPA (MET-minutes per week) | .00117 | .0002 | <.001 | | .0004 | .0002 | .057 | |
| | *Age (years) | ----- | ----- | ----- | | -.0822 | .0234 | <.001 | |
| | *Sex (female) | ----- | ----- | ----- | | -4.6345 | .4969 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | 1.0217 | .4132 | .014 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.8663 | .9827 | .058 | |
| | *[$]Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | .6267 | .2251 | .006 | |
| | | | | | | | | | |
| Change in Fitness (ml/kg/min) from Baseline to 6 months | Intercept | 2.4477 | .1970 | <.001 | .0306 | 3.5862 | 1.6042 | .026 | .1887 |
| | Change in LPA (MET-minutes per week) | .0005 | .0002 | .002 | | .0003 | .00027 | .065 | |
| | *Age (years) | ----- | ----- | ----- | | -.0092 | .0235 | .695 | |
| | *Sex (female) | ----- | ----- | ----- | | -1.6422 | .4497 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | 1.3740 | .4162 | .001 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 2.0350 | 1.0674 | .058 | |
| | *Treatment Group 1 | | | | | .7538 | .4418 | .089 | |
| | *Treatment Group 2 | | | | | 1.0465 | .4468 | .020 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | .0005 | .0002 | .003 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0001 | .0002 | .502 | |
| | | | | | | | | | |
| Change in Fitness (ml/kg/min) from Baseline to 12 months | Intercept | 2.7345 | .2283 | <.001 | .0290 | -.4191 | 1.8501 | .821 | .1673 |
| | Change in LPA (MET-minutes per week) | .0006 | .0002 | .004 | | .0004 | .0002 | .127 | |
| | *Age (years) | ----- | ----- | ----- | | .0184 | .0264 | .486 | |
| | *Sex (female) | ----- | ----- | ----- | | -.1157 | .5213 | .825 | |
| | *Race (white) | ----- | ----- | ----- | | .5717 | .4912 | .245 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 2.7331 | 1.2425 | .029 | |
| | *Treatment Group 1 | | | | | 1.3146 | .5029 | .009 | |
| | *Treatment Group 2 | | | | | .6390 | .4942 | .197 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | .0006 | .0001544 | <.001 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0004 | .0002053 | .077 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
[$]Indicates that the data were log-transformed.
LPA= light-intensity physical activity
MVPA= moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 5b. Association between LPA and cardiorespiratory fitness (minutes) at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Fitness (minutes) | Intercept | 5.8491 | .3642 | <.001 | .0761 | 11.3322 | 1.6424 | <.001 | .3354 |
| | Baseline LPA (MET-minutes per week) | .0007 | .0001 | <.001 | | .0002 | .0001 | .098 | |
| | *Age (years) | ----- | ----- | ----- | | -.0487 | .0167 | .004 | |
| | *Sex (female) | ----- | ----- | ----- | | -2.9362 | .3564 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | .7931 | .2962 | .008 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.4739 | .7050 | .037 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | .3925 | .1614 | .016 | |
| | | | | | | | | | |
| Change in Fitness (minutes) from Baseline to 6 months | Intercept | 1.9649 | .1348 | <.001 | .0254 | 2.4392 | 1.1659 | .037 | .0725 |
| | Change in LPA (MET-minutes per week) | .0003 | .0001 | .004 | | .0003 | .0001 | .032 | |
| | *Age (years) | ----- | ----- | ----- | | -.0003 | .0171 | .987 | |
| | *Sex (female) | ----- | ----- | ----- | | -.7286 | .3289 | .027 | |
| | *Race (white) | ----- | ----- | ----- | | .1169 | .3036 | .701 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | .2877 | .7853 | .714 | |
| | *Treatment Group 1 | | | | | .4898 | .3209 | .128 | |
| | *Treatment Group 2 | | | | | .4696 | .3239 | .148 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | .0002 | .0001 | .121 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0001 | .0001 | .037 | |
| | | | | | | | | | |
| Change in Fitness (minutes) from Baseline to 12 months | Intercept | 1.7878 | .1546 | <.001 | .0245 | 1.5081 | 1.2851 | .242 | .1080 |
| | Change in LPA (MET-minutes per week) | .0004 | .0001 | .007 | | .0002 | .0002 | .136 | |
| | *Age (years) | ----- | ----- | ----- | | .0024 | .0185 | .897 | |
| | *Sex (female) | ----- | ----- | ----- | | -.5437 | .3621 | .134 | |
| | *Race (white) | ----- | ----- | ----- | | .2247 | .3441 | .514 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.1357 | .8276 | .171 | |
| | *Treatment Group 1 | | | | | .6297 | .3499 | .073 | |
| | *Treatment Group 2 | | | | | .3254 | .3455 | .308 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | .0003 | .0001 | .004 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0016 | .0001 | .275 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

Analysis of Resting Systolic and Diastolic Blood Pressure

Baseline LPA was not significantly associated with either resting systolic blood pressure (Table 6) or diastolic blood pressure (Table 7) for either unadjusted or adjusted analyses. Moreover, the change in LPA at both 6 and 12 months was not significantly associated with the change in either systolic or diastolic blood pressure (Tables 6 and 7).

Analysis of Total Cholesterol

Results of the analyses to examine the association between LPA and total cholesterol are shown in Table 8. At baseline, unadjusted (β=.0018; p=.211) and adjusted analyses (β=.0011; p=.533) showed that LPA was not significantly associated with total cholesterol. For the change from baseline to 6 months, LPA was negatively associated with total cholesterol in unadjusted (β=-.0045; p<0.001) and adjusted analyses (β=-.0038; p=0.007). However, for the change from baseline to 12 months, there was a trend for a negative association between LPA and total cholesterol in the unadjusted analysis (β=-.0024; p=.068) with the association in the adjusted analysis not being statistically significant (β=-.0008; p=0.633).

Analysis of LDL Cholesterol

Results of the analyses to examine the association between LPA and LDL cholesterol are shown in Table 9. At baseline, unadjusted (β=.0018; p=.129) and adjusted analyses (β=.0015; p=.303) showed that LPA was not significantly associated with LDL cholesterol. For the change from baseline to 6 months, LPA was negatively associated with LDL cholesterol in unadjusted (β=-.0035; p<0.001) and adjusted analyses (β=-.0030; p=0.011). However, for the change from baseline to 12 months, LPA was negatively associated with LDL cholesterol in the unadjusted analysis (β=-.0030; p=0.011) but not in the adjusted analyses (β=-.0014; p=0.349).

**Table 6. Association between LPA and resting systolic blood pressure at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Resting Systolic Blood Pressure (mmHg) | Intercept | 119.29 | 1.4734 | <.001 | .0016 | 131.2381 | 7.3905 | <.001 | .1132 |
| | Baseline LPA (MET-minutes per week) | .0004 | .0005 | .436 | | .0007 | .0006 | .273 | |
| | *Age (years) | ----- | ----- | ----- | | .2827 | .0753 | <.001 | |
| | *Sex (female) | ----- | ----- | ----- | | -8.1169 | 1.6039 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -2.5041 | 1.3328 | .061 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -1.8267 | 3.1722 | .565 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -1.3668 | .7263 | .061 | |
| | | | | | | | | | |
| Change in Resting Systolic Blood Pressure (mmHg) from Baseline to 6 months | Intercept | -5.1005 | .5728 | <.001 | .0024 | -5.4560 | 4.8808 | .264 | .0849 |
| | Change in LPA (MET-minutes per week) | -.0004 | .0004 | .378 | | -.0001 | .0005 | .806 | |
| | *Age (years) | ----- | ----- | ----- | | -.0785 | .0714 | .272 | |
| | *Sex (female) | ----- | ----- | ----- | | 3.8015 | 1.3759 | .006 | |
| | *Race (white) | ----- | ----- | ----- | | -4.1813 | 1.2646 | .001 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | .1136 | 3.2897 | .972 | |
| | *Treatment Group 1 | | | | | .6568 | 1.3421 | .625 | |
| | *Treatment Group 2 | | | | | .4499 | 1.3508 | .739 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0007 | .0005 | .173 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0001 | .0005 | .863 | |
| | | | | | | | | | |
| Change in Resting Systolic Blood Pressure (mmHg) from Baseline to 12 months | Intercept | -4.8892 | .7179 | <.001 | .0012 | -6.6214 | 6.1223 | .280 | .0522 |
| | Change in LPA (MET-minutes per week) | -.0004 | .0006 | .546 | | -.0002 | .0008 | .837 | |
| | *Age (years) | ----- | ----- | ----- | | .0553 | .0883 | .531 | |
| | *Sex (female) | ----- | ----- | ----- | | 2.3428 | 1.7136 | .173 | |
| | *Race (white) | ----- | ----- | ----- | | -4.1785 | 1.6003 | .009 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -1.5314 | 3.9569 | .699 | |
| | *Treatment Group 1 | | | | | -.2250 | 1.6639 | .893 | |
| | *Treatment Group 2 | | | | | -.5161 | 1.6416 | .753 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0006 | .0005 | .260 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0004 | .0007 | .516 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis
$Indicates that the data were log-transformed.
LPA= light-intensity physical activity
MVPA= moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 7. Association between LPA and resting diastolic blood pressure at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Resting Diastolic Blood Pressure (mmHg) | Intercept | 70.2780 | 1.1079 | <.001 | .0102 | 84.3140 | 5.4355 | <.001 | .1613 |
| | Baseline LPA (MET-minutes per week) | .0007 | .0004 | .051 | | .0002 | .0004 | .689 | |
| | *Age (years) | ----- | ----- | ----- | | .0709 | .0554 | .202 | |
| | *Sex (female) | ----- | ----- | ----- | | -8.2290 | 1.1796 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -3.1293 | .9803 | .002 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -3.1418 | 2.3330 | .179 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | .2089 | .5342 | .696 | |
| | | | | | | | | | |
| Change in Resting Diastolic Blood Pressure (mmHg) from Baseline to 6 months | Intercept | -2.9850 | .3977 | <.001 | .0003 | -7.3189 | 3.3720 | .031 | .0917 |
| | Change in LPA (MET-minutes per week) | .0001 | .0003 | .771 | | .0002 | .0004 | .670 | |
| | *Age (years) | ----- | ----- | ----- | | -.0211 | .0494 | .669 | |
| | *Sex (female) | ----- | ----- | ----- | | 3.7594 | .9506 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -2.0374 | .8737 | .020 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.7839 | 2.2728 | .730 | |
| | *Treatment Group 1 | | | | | 1.2602 | .9272 | .175 | |
| | *Treatment Group 2 | | | | | -.3000 | .9332 | .748 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0003 | .0003 | .433 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0000 | .0004 | .973 | |
| | | | | | | | | | |
| Change in Resting Diastolic Blood Pressure (mmHg) from Baseline to 12 months | Intercept | -2.9112 | .4877 | <.001 | .0035 | -6.767 | 4.1125 | .101 | .0756 |
| | Change in LPA (MET-minutes per week) | .0004 | .0004 | .309 | | .0007 | .0005 | .181 | |
| | *Age (years) | ----- | ----- | ----- | | .0455 | .0593 | .444 | |
| | *Sex (female) | ----- | ----- | ----- | | 2.6468 | 1.1511 | .022 | |
| | *Race (white) | ----- | ----- | ----- | | -2.4143 | 1.0749 | .025 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -1.9539 | 2.6580 | .463 | |
| | *Treatment Group 1 | | | | | .2438 | 1.1177 | .828 | |
| | *Treatment Group 2 | | | | | -1.2034 | 1.1027 | .276 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0006 | .0003 | .091 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0002 | .0005 | .738 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 8. Associaton between LPA and total cholesterol at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Total Cholesterol (mg/dl) | Intercept | 193.875 | 4.2452 | <.001 | .2114 | 133.3574 | 21.7595 | <.001 | .0772 |
| | Baseline LPA (MET-minutes per week) | .0018 | .0014 | .211 | | .0011 | .0018 | .533 | |
| | *Age (years) | ----- | ----- | ----- | | 1.0575 | .2219 | <.001 | |
| | *Sex (female) | ----- | ----- | ----- | | 1.1706 | 4.7218 | .804 | |
| | *Race (white) | ----- | ----- | ----- | | 3.9809 | 3.9267 | .311 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -13.8994 | 9.3386 | .138 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | 1.4026 | 2.1438 | .513 | |
| | | | | | | | | | |
| Change in Total Cholesterol (mg/dl) from Baseline to 6 months | Intercept | -9.5158 | 1.4883 | <.001 | .0425 | -24.6881 | 12.8560 | .056 | .0925 |
| | Change in LPA (MET-minutes per week) | -.0045 | .0012 | <.001 | | -.0038 | .0014 | .007 | |
| | *Age (years) | ----- | ----- | ----- | | .1056 | .1884 | .575 | |
| | *Sex (female) | ----- | ----- | ----- | | 6.8691 | 3.6214 | .059 | |
| | *Race (white) | ----- | ----- | ----- | | -4.7101 | 3.3606 | .162 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -4.0009 | 8.6519 | .644 | |
| | *Treatment Group 1 | | | | | 7.5286 | 3.5390 | .034 | |
| | *Treatment Group 2 | | | | | 2.4684 | 3.5769 | .491 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0025 | .0013 | .054 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0001 | .0013 | .914 | |
| | | | | | | | | | |
| Change in Total Cholesterol (mg/dl) from Baseline to 12 months | Intercept | -6.1752 | 1.5946 | <.001 | .0112 | -24.5557 | 13.6591 | .073 | .0500 |
| | Change in LPA (MET-minutes per week) | -.0024 | .0013 | .068 | | -.0008 | .0017 | .633 | |
| | *Age (years) | ----- | ----- | ----- | | .2074 | .1956 | .290 | |
| | *Sex (female) | ----- | ----- | ----- | | 3.8088 | 3.8334 | .321 | |
| | *Race (white) | ----- | ----- | ----- | | -2.5135 | 3.5970 | .485 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -7.0132 | 8.8015 | .426 | |
| | *Treatment Group 1 | | | | | 6.2017 | 3.7206 | .097 | |
| | *Treatment Group 2 | | | | | 2.2469 | 3.6673 | .541 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0026 | .0011 | .022 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0011 | .0015 | .484 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 9. Association between LPA and LDL cholesterol at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline LDL Cholesterol (mg/dl) | Intercept | 115.7846 | 3.5449 | <.001 | .0062 | 80.1715 | 18.1844 | <.001 | .0788 |
| | Baseline LPA (MET-minutes per week) | .0018 | .0012 | .129 | | .0015 | .0015 | .303 | |
| | *Age (years) | ----- | ----- | ----- | | .9203 | .0015 | <.001 | |
| | *Sex (female) | ----- | ----- | ----- | | -3.7507 | 3.9460 | .342 | |
| | *Race (white) | ----- | ----- | ----- | | -.3003 | 3.2815 | .927 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -5.7034 | 7.8043 | .465 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | .2078 | 1.7916 | .908 | |
| | | | | | | | | | |
| Change in LDL Cholesterol (mg/dl) from Baseline to 6 months | Intercept | -4.8756 | 1.2498 | <.001 | .0397 | -17.8481 | 10.8527 | .101 | .0076 |
| | Change in LPA (MET-minutes per week) | -.0035 | .0010 | <.001 | | -.0030 | .0012 | .011 | |
| | *Age (years) | ----- | ----- | ----- | | .0601 | .1590 | .706 | |
| | *Sex (female) | ----- | ----- | ----- | | 6.0380 | 3.0571 | .049 | |
| | *Race (white) | ----- | ----- | ----- | | -.4904 | 2.8369 | .863 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -3.1536 | 7.3037 | .666 | |
| | *Treatment Group 1 | | | | | 5.0328 | 2.9875 | .076 | |
| | *Treatment Group 1 | | | | | .0719 | 3.0195 | .981 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0019 | .0011 | .075 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0004 | .0011 | .759 | |
| | | | | | | | | | |
| Change in LDL Cholesterol (mg/dl) from Baseline to 12 months | Intercept | -3.905779 | 1.424575 | .006 | .0216 | -9.1190 | 12.2447 | .457 | .0535 |
| | Change in LPA (MET-minutes per week) | -.0030 | .0012 | .011 | | -.0014 | .0015 | .349 | |
| | *Age (years) | ----- | ----- | ----- | | .0393 | .1753 | .823 | |
| | *Sex (female) | ----- | ----- | ----- | | -.0098 | 3.4364 | .998 | |
| | *Race (white) | ----- | ----- | ----- | | .2291 | 3.2245 | .943 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -4.8686 | 7.8901 | .538 | |
| | *Treatment Group 1 | | | | | 5.1937 | 3.3354 | .121 | |
| | *Treatment Group 2 | | | | | 1.6110 | 3.2875 | .624 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0027 | .0010 | .009 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0010 | .0014 | .471 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA= moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

Analysis of HDL Cholesterol

Results of the analyses to examine the association between LPA and HDL cholesterol are shown in Table 10. At baseline, unadjusted (β=-.0014; p=.007) and adjusted analyses (β=-.0012; p=.039) showed that LPA was negatively associated with HDL cholesterol. For the change from baseline to 6 months, LPA was not significantly associated with HDL cholesterol in unadjusted (β=-.0005; p=0.128) or adjusted analyses (β=-.0003; p=0.478). However, for the change from baseline to 12 months, LPA was positively associated with HDL cholesterol in the unadjusted (β=.0008; p=0.021) and the adjusted analyses (β=.0009; p=0.038).

Analysis of Triglycerides

Results of the analyses to examine the association between LPA and triglycerides are shown in Table 11. At baseline, unadjusted analyses (β=.0001; p=0.010) showed that LPA was negatively associated with triglycerides, but this association with no longer significant in the adjusted analysis (β=.0000; p=0.192). For the change from baseline to 6 months, LPA was negatively associated with triglycerides in both the unadjusted (β=-.0045; p<0.001) and adjusted analyses (β=-.0038; p=0.007). However, for the change from baseline to 12 months, there was a trend for LPA to be negatively associated with triglycerides in the unadjusted analysis (β=-.0024; p=0.068) but not in the adjusted analyses (β=-.0008; p=0.633).

**Table 10. Association between LPA and HDL cholesterol at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline HDL Cholesterol (mg/dl) | Intercept | 57.0954 | 1.5033 | <.001 | .0194 | 20.2962 | 7.3554 | .006 | .1651 |
| | Baseline LPA (MET-minutes per week) | -.0014 | .0005 | .007 | | -.0012 | .0006 | .039 | |
| | *Age (years) | ----- | ----- | ----- | | .1388 | .07501 | .065 | |
| | *Sex (female) | ----- | ----- | ----- | | 11.8238 | 1.5961 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | .2000 | 1.3273 | .880 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -5.5649 | 3.1567 | .079 | |
| | *[$]Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | 1.3322 | .7247 | .067 | |
| | | | | | | | | | |
| Change in Total HDL (mg/dl) from Baseline to 6 months | Intercept | -.1423 | .3870 | .713 | .0074 | 4.6159 | 3.2520 | .157 | .1070 |
| | Change in LPA (MET-minutes per week) | -.0005 | .0003 | .128 | | -.0003 | .0004 | .478 | |
| | *Age (years) | ----- | ----- | ----- | | -.0072 | .0476 | .880 | |
| | *Sex (female) | ----- | ----- | ----- | | -3.6370 | .9161 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -1.5417 | .8501 | .071 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.0441 | 2.1885 | .634 | |
| | *Treatment Group 1 | | | | | 1.9760 | .8952 | .028 | |
| | *Treatment Group 2 | | | | | 2.6263 | .9048 | .004 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0000 | .0003 | .880 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0006 | .0003 | .078 | |
| | | | | | | | | | |
| Change in HDL Cholesterol (mg/dl) from Baseline to 12 months | Intercept | 3.3270 | .4281 | <.001 | .0179 | -1.4370 | 3.6105 | .691 | .0851 |
| | Change in LPA (MET-minutes per week) | .0008 | .0004 | .021 | | .0009 | .0005 | .038 | |
| | *Age (years) | ----- | ----- | ----- | | .1072 | .0517 | .039 | |
| | *Sex (female) | ----- | ----- | ----- | | -1.5778 | 1.0133 | .121 | |
| | *Race (white) | ----- | ----- | ----- | | -.5886 | .9508 | .536 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | .2193 | 2.3265 | .925 | |
| | *Treatment Group 1 | | | | | 1.2741 | .9835 | .196 | |
| | *Treatment Group 2 | | | | | 1.6913 | .9694 | .082 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | .0003 | .0003 | .255 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0007 | .0004 | .089 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
[$]Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 11. Association between LPA and triglycerides at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Triglycerides (mg/dl) | Intercept | 4.5477 | .0612 | <.001 | .0179 | 5.0005 | .3119 | <.001 | .0999 |
| | Baseline LPA (MET-minutes per week) | .0001 | .0000 | .010 | | .0000 | .0000 | .192 | |
| | *Age (years) | ----- | ----- | ----- | | -.0003 | .0032 | .937 | |
| | *Sex (female) | ----- | ----- | ----- | | -.2649 | .0677 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | .1786 | .0563 | .002 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.0661 | .1339 | .622 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0060 | .0307 | .845 | |
| | | | | | | | | | |
| Change in Triglycerides (mg/dl) from Baseline to 6 months | Intercept | -9.5158 | 1.4883 | <.001 | .0452 | -24.6881 | 12.8560 | .056 | .0925 |
| | Change in LPA (MET-minutes per week) | -.0045 | .0012 | <.001 | | -.0038 | .0014 | .007 | |
| | *Age (years) | ----- | ----- | ----- | | .1056 | .1884 | .575 | |
| | *Sex (female) | ----- | ----- | ----- | | 6.8691 | 3.6214 | .059 | |
| | *Race (white) | ----- | ----- | ----- | | -4.7101 | 3.3606 | .162 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -4.0009 | 8.6519 | .644 | |
| | *Treatment Group 1 | | | | | 7.5286 | 3.5390 | .034 | |
| | *Treatment Group 2 | | | | | 2.4684 | 3.5769 | .491 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0025 | .0013 | .054 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0001 | .0013 | .914 | |
| | | | | | | | | | |
| Change in Triglycerides (mg/dl) from Baseline to 12 months | Intercept | -6.1752 | 1.5946 | <.001 | .0112 | -24.5557 | 13.6591 | .073 | .0500 |
| | Change in LPA (MET-minutes per week) | -.0024 | .0013 | .068 | | -.0008 | .0017 | .633 | |
| | *Age (years) | ----- | ----- | ----- | | .2074 | .1956 | .290 | |
| | *Sex (female) | ----- | ----- | ----- | | 3.8088 | 3.8334 | .321 | |
| | *Race (white) | ----- | ----- | ----- | | -2.5135 | 3.5970 | .485 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -7.0132 | 8.8015 | .426 | |
| | *Treatment Group 1 | | | | | 6.2017 | 3.7206 | .097 | |
| | *Treatment Group 2 | | | | | 2.2469 | 3.6673 | .541 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0027 | .0011 | .022 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0011 | .0015 | .484 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity; MVPA=moderate-to-vigorous physical activity; Treatment Group 1 = DIET +PA150; Treatment Group 2 = DIET +PA250

Analysis of Glucose

Results of the analyses to examine the association between LPA and glucose are shown in Table 12. At baseline, LPA was not significantly associated with glucose in either unadjusted (β=.0006; p=0.290) or adjusted analyses (β.0004; p=0.550). At 6 months, the change in LPA was not associated with the change in glucose in unadjusted (β=.0000; p=0.924) or adjusted analyses (β=.0005; p=0.292). While the change in LPA at 12 months was negatively associated with the change in glucose in the unadjusted analysis (β=-.0009; p=0.049), it was not significant in the adjusted analysis (β=-.0009; p=0.150).

Analysis of Insulin

Results of the analyses to examine the baseline association between LPA and insulin are shown in Table 13. At baseline, LPA and insulin were not significantly associated in either the unadjusted (β=-.0000; p=0.521) or adjusted analyses (β.0004; p=0.625). For the change from baseline to 6 months there was a negative association between LPA and insulin for both the unadjusted (β=-.0012; p<0.001) and adjusted analyses (β=-.0008; p=0.038). However, the change in LPA and insulin at 12 months for both unadjusted (β-.0002; p=.540) and adjusted (β=-.0001; p=.740) analyses showed no significant association.

Analysis of CRP

The results of the analyses to examine the association between LPA and CRP are shown in Table 14. Unadjusted analysis showed that CRP was negatively associated with LPA (β=-.0001; p=0.009) at baseline; however, after adjustment for covariates, LPA was not associated with CRP (β=-.0000; p=0.941). When examining the association between change in LPA and change in CRP, the associations were not statistically significant for analyses at 6 months (unadjusted: β=.0001;

p=0.507; adjusted: β=.0001; p=0.456) or 12 months (unadjusted: β=-.0001; p=0.654; adjusted: β=-.0002; p=0.481).

**Table 12. Association between LPA and glucose at baseline and change at 6 and 12 months.**

*Indicates these variables were forced in the model as covariates for the adjusted analysis.

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Glucose (mg/dl) | Intercept | 93.4828 | 1.6302 | <.001 | .0030 | 106.8531 | 8.3333 | <.001 | .0827 |
| | Baseline LPA (MET-minutes per week) | .0006 | .0005 | .290 | | .0004 | .0007 | .550 | |
| | *Age (years) | ----- | ----- | ----- | | .1756 | .0850 | .040 | |
| | *Sex (female) | ----- | ----- | ----- | | -8.8223 | 1.8083 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -.5817 | 1.5038 | .699 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.2056 | 3.5764 | .954 | |
| | *[$]Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.6980 | .8210 | .396 | |
| | | | | | | | | | |
| Change in Glucose (mg/dl) from Baseline to 6 months | Intercept | -2.8119 | .5101 | <.001 | .0000 | -7.3886 | 4.3863 | .093 | .0582 |
| | Change in LPA (MET-minutes per week) | .0000 | .0004 | .924 | | .0005 | .0005 | .292 | |
| | *Age (years) | ----- | ----- | ----- | | -.0786 | .0643 | .222 | |
| | *Sex (female) | ----- | ----- | ----- | | 4.0509 | 1.2356 | .001 | |
| | *Race (white) | ----- | ----- | ----- | | -1.1103 | 1.1466 | .334 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | .0586 | 2.9519 | .984 | |
| | *Treatment Group 1 | | | | | .6492 | 1.2074 | .591 | |
| | *Treatment Group 2 | | | | | 1.3505 | 1.2204 | .269 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0008 | .0004 | .087 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0005 | .0005 | .260 | |
| | | | | | | | | | |
| Change in Glucose (mg/dl) from Baseline to 12 months | Intercept | -2.6983 | .5504 | <.001 | .0130 | 1.4835 | 4.6935 | .752 | .0603 |
| | Change in LPA (MET-minutes per week) | -.0009 | .0005 | .049 | | -.0009 | .0006 | .150 | |
| | *Age (years) | ----- | ----- | ----- | | -.1279 | .0672 | .058 | |
| | *Sex (female) | ----- | ----- | ----- | | 1.8283 | 1.3173 | .166 | |
| | *Race (white) | ----- | ----- | ----- | | -2.5048 | 1.236 | .044 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -2.8112 | 3.0243 | .353 | |
| | *Treatment Group 1 | | | | | 1.3579 | 1.2785 | .289 | |
| | *Treatment Group 2 | | | | | .6267 | 1.2602 | .619 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0001 | .0004 | .880 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0001 | .0005 | .904 | |

[$]Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 13. Association between LPA and insulin at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline Insulin (uU/ml) | Intercept | 2.7101 | .0593 | <.001 | .0011 | 3.9937 | .3061 | <.001 | .0629 |
| | Baseline LPA (MET-minutes per week) | -.0000 | .0000 | .521 | | .0000 | .0000 | .625 | |
| | *Age (years) | ----- | ----- | ----- | | -.0081 | .0031 | .010 | |
| | *Sex (female) | ----- | ----- | ----- | | -.2478 | .0664 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -.1409 | .0552 | .011 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | .0030 | .1314 | .982 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0643 | .0302 | .034 | |
| | | | | | | | | | |
| Change in Insulin (uU/ml) from Baseline to 6 months | Intercept | -3.0705 | .4008 | <.001 | .0428 | -14.5680 | 3.4318 | <.001 | .1062 |
| | Change in LPA (MET-minutes per week) | -.0012 | .0003 | <.001 | | -.0008 | .00041 | .038 | |
| | *Age (years) | ----- | ----- | ----- | | .0784 | .0503 | .120 | |
| | *Sex (female) | ----- | ----- | ----- | | 3.7925 | .9667 | <.001 | |
| | *Race (white) | ----- | ----- | ----- | | -.8472 | .8971 | .346 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.5915 | 2.3096 | .491 | |
| | *Treatment Group 1 | | | | | .3151 | .9447 | .739 | |
| | *Treatment Group 2 | | | | | .9254 | .9548 | .333 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0005 | .0003 | .119 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | .0005 | .0004 | .130 | |
| | | | | | | | | | |
| Change in Insulin (uU/ml) from Baseline to 12 months | Intercept | -3.4845 | .4094 | <.001 | .0013 | -9.9835 | 3.4537 | .004 | .0691 |
| | Change in LPA (MET-minutes per week) | -.0002 | .0003 | .540 | | -.0001 | .0004 | .740 | |
| | *Age (years) | ----- | ----- | ----- | | .0447 | .0495 | .367 | |
| | *Sex (female) | ----- | ----- | ----- | | 3.0064 | .9693 | .002 | |
| | *Race (white) | ----- | ----- | ----- | | -.7271 | .9095 | .425 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -1.0859 | 2.2254 | .626 | |
| | *Treatment Group 1 | | | | | .4670 | .9408 | .620 | |
| | *Treatment Group 2 | | | | | 1.2813 | .9273 | .168 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0004 | .0003 | .166 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0002 | .0004 | .550 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

**Table 14. Association between LPA and CRP at baseline and change at 6 and 12 months.**

| Dependent Variable | Variable | Unadjusted Analysis | | | | Adjusted Analysis | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Beta | S.E. | p-value | Model $r^2$ | Beta | S.E. | p-value | Model $r^2$ |
| Baseline CRP µg/ml | Intercept | 1.3029 | .1199 | <.001 | .0182 | 2.2985 | .6138 | .001 | .0943 |
| | Baseline LPA (MET-minutes per week) | -.0001 | .0000 | .009 | | -.0000 | .0001 | .941 | |
| | *Age (years) | ----- | ----- | ----- | | -.01567 | .0063 | .013 | |
| | *Sex (female) | ----- | ----- | ----- | | .2919 | .1332 | .029 | |
| | *Race (white) | ----- | ----- | ----- | | -.2219 | .1108 | .046 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.1653 | .2634 | .531 | |
| | *$Baseline MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.1362 | .0605 | .025 | |
| | | | | | | | | | |
| Change in CRP µg/ml from Baseline to 6 months | Intercept | -1.2116 | .1971 | <.001 | .0014 | -.7594 | 1.7224 | .660 | .0283 |
| | Change in LPA (MET-minutes per week) | .0001 | .0002 | .507 | | .0001 | .0002 | .456 | |
| | *Age (years) | ----- | ----- | ----- | | .0298 | .0252 | .239 | |
| | *Sex (female) | ----- | ----- | ----- | | -.9102 | .4852 | .062 | |
| | *Race (white) | ----- | ----- | ----- | | -.3332 | .4502 | .460 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | 1.3509 | 1.1592 | .245 | |
| | *Treatment Group 1 | | | | | .0893 | .4741 | .851 | |
| | *Treatment Group 2 | | | | | .3881 | .4792 | .419 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0001 | .0002 | .406 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0000 | .0002 | .870 | |
| | | | | | | | | | |
| Change in CRP µg/ml from Baseline to 12 months | Intercept | -1.2037 | .2811 | <.001 | .0007 | -3.5592 | 2.4099 | .141 | .0380 |
| | Change in LPA (MET-minutes per week) | -.0001 | .0002 | .654 | | -.0002 | .0003 | .481 | |
| | *Age (years) | ----- | ----- | ----- | | .07945 | .0345 | .022 | |
| | *Sex (female) | ----- | ----- | ----- | | -.6337 | .6763 | .350 | |
| | *Race (white) | ----- | ----- | ----- | | .4130 | .6346 | .516 | |
| | *Ethnicity (non-Hispanic) | ----- | ----- | ----- | | -.4653 | 1.5529 | .765 | |
| | *Treatment Group 1 | | | | | .7954 | .6564 | .227 | |
| | *Treatment Group 2 | | | | | .6475 | .6470 | .318 | |
| | *Change in MVPA (MET-minutes per week) | ----- | ----- | ----- | | -.0002 | .0002 | .304 | |
| | *Baseline LPA (MET-minutes per week) | ----- | ----- | ----- | | -.0003 | .0003 | .305 | |

*Indicates these variables were forced in the model as covariates for the adjusted analysis.
$Indicates that the data were log-transformed.
LPA=light-intensity physical activity
MVPA=moderate-to-vigorous physical activity
Treatment Group 1 = DIET +PA150
Treatment Group 2 = DIET +PA250

## 4.4 Summary of Results

This study involved a secondary analysis of data from a weight loss intervention study to examine the associations between LPA and weight, body fatness, fitness, cardiometabolic risk factors, and inflammation. A summary of the associations is shown in Table 15. The results of this study show few significant associations between LPA and outcome measures at baseline. It appears that the change in LPA from baseline to either 6 months or 12 months was most consistently associated with change in body weight and percent body fat. The change in other outcomes variables examined appear to be most consistently associated with change in LPA from baseline to 6 months compared to the change from baseline to 12 months.

Within the adjusted analyses, it appears that MVPA may be a confounding factor that needs consideration, and this may be most apparent when considering the outcome variables of BMI, percent body fat, and cardiorespiratory fitness. For these variables there are examples where LPA was associated with the outcome variable of interest in the unadjusted analysis, but in the adjusted analysis when MVPA was shown to also be significant, LPA was no longer significantly associated with the outcome. For example, LPA was associated with BMI at baseline in the unadjusted analysis ($\beta$=-.0006; p=<0.001), but in the adjusted analysis LPA was no longer significantly associated with BMI ($\beta$=.0002; p=0.310) when MVPA was shown to be significant in the model. A similar pattern of findings was shown for baseline percent body fat and cardiorespiratory fitness at baseline and for change at both 6 and 12 months. This is a potentially important finding given

that MVPA is a modifiable behavioral variable, in addition to LPA, whereas the other variables considered (age, sex, race, and ethnicity) are not modifiable. However, in some of the adjusted analyses these other factors (age, sex, race, and ethnicity) are associated with the various dependent variables, even though not consistently associated, which may imply that these may be important factors to consider both in combination and independent of LPA. The potential implications of these findings are further addressed in the Discussion Section.

**Table 15. Summary of the associations between LPA and outcome variables at baseline, change from baseline to 6 months and change from baseline to 12 months.**

| Dependent Variable | Association between Baseline LPA and Baseline Dependent Variable | Association between the Change in LPA and the Change in the Dependent Variable from Baseline to 6 Months | Association between the Change in LPA and the Change in the Dependent Variable from Baseline to 12 Months |
|---|---|---|---|
| Body Weight | **+ (p=0.008)** | **- (p=0.006)** | **- (p=0.003)** |
| Body Mass Index | + (p=0.310) | **- (p<0.001)** | **- (p<0.001)** |
| Percent Body Fat | - (p=0.337) | **- (p<0.001)** | **- (p<0.001)** |
| Fitness | | | |
| ml/kg/min | + (p=0.057) | + (p=0.065) | + (p=0.127) |
| Minutes | + (p=0.098) | **+ (p=0.032)** | + (p=0.136) |
| Resting Systolic Blood Pressure | + (p=0.273) | - (p=0.806) | - (p=0.837) |
| Resting Diastolic Blood Pressure | + (p=0.681) | + (p=0.670) | + (p=0.181) |
| Total Cholesterol | + (p=0.533) | **- (p=0.007)** | - (p=0.633) |
| LDL Cholesterol | + (p=0.303) | **- (p=0.011)** | - (p=0.349) |
| HDL Cholesterol | **- (p=0.039)** | - (p=0.478) | **+ (p=0.038)** |
| Triglycerides | + (p=0.192) | **- (p=0.007)** | - (p=0.633) |
| Glucose | + (p=0.550) | + (p=0.202) | - (p=0.150) |
| Insulin | - (p=0.625) | **- (p=0.038)** | - (p=0.740) |
| CRP | - (p=0.941) | + (p=0.456) | - (p=0.481) |

+ indicates a positive association, - indicates a negative association
P-values presented based on adjusted analysis

# 5.0 Discussion

The present study was conducted to examine the association between LPA and cardiometabolic risk factors in adults with overweight and obesity who participated in a behavioral weight loss intervention. This study is of importance for several reasons. Currently, limited evidence exists examining the influence of LPA on health outcomes. Evidence related to health benefits are primarily based on MVPA.[24] Additionally, very few studies have investigated the association between LPA and measures of obesity and weight loss, as research has focused primarily on the influence of MVPA.[121] Thus, the role LPA has on measures of obesity and weight loss has not been fully examined.

## 5.1 Effects of the Intervention on Key Outcome Variables

The 2018 physical activity guidelines report suggest that inactive individuals gradually progress to engaging in 150 minutes per week of MVPA.24 The interventions implemented in this study resulted in a mean increase of 557.1 MET-minutes per week at 6 months and 767.9 MET-minutes per week at 12 months. Assuming a conservative intensity of 3 METs to represent MVPA, this would equate to MVPA increasing by approximately 186 minutes per week at 6 months and 256 minutes per week at 12 months. Thus, the mean improvement in MVPA resulting from the intervention in this study meets or exceeds the current physical activity recommendations for physical activity, which may suggest that this would result in health improvements. This may also

partially explain why MVPA, either alone or in combination with LPA, was associated with any of the observed improvements in weight, body composition, fitness, or other outcomes that were examined. This may also partially explain why there was an observed reduction in the association of LPA with selected outcomes in this study when MVPA was included along with LPA in the statistical analysis that were conducted, suggesting that MVPA may be a confounding factor to consider. The other key outcome in this study was the change in body weight, which was a target of all the interventions in the parent study. The mean weight loss achieved was 9.2 kg (10.1% of baseline body weight) at 6 months, and 10.3 kg (11.3% of baseline body weight) at 12 months. Thus, the magnitude of weight loss achieved in this study appears to be consistent with other behavioral weight loss interventions.[14,35] This magnitude of weight loss has also been shown to be associated with improvements in numerous health outcomes,[16,26] and we observed improvements in the cardiometabolic risk factors in this study as well.

### 5.2 Body Weight, BMI, and Body Fat

This study showed that LPA was positively associated with body weight at baseline prior to entry into a behavioral weight loss intervention. The 2018 Physical Activity Guidelines Advisory Report concluded that physical activity contributes to prevention of weight gain and a lower body weight.[24] However, the evidence to support this conclusion was based primarily on MVPA. Thus, the results of this study does not support that LPA also is associated with a lower body weight; however, further research is needed in this area to support this association.

The results also support that the change in LPA was associated with the change in body weight. LPA was shown to be associated with body weight change from baseline to 6 months and

12 months. This is consistent with the hypothesis as stated in the specific aims, that LPA would be associated with a greater reduction in body weight at both 6 months and 12 months.

While neither baseline BMI nor percent body fat were significantly associated with baseline LPA in the adjusted analyses, the change in BMI and percent body fat were associated with change in LPA at both 6 and 12 months. This supports the hypothesis that a greater increase in LPA is associated with a greater reduction in body weight within the context of a behavioral intervention. However, these results should be reviewed with caution and do not suggest that the focus of obesity interventions should be on LPA alone. Rather, within the adjusted analyses for measures of weight and body fatness, a greater increase in MVPA was also associated with a greater reduction in these measures of weight and fat loss. These findings may suggest that it is the combination of increases in both LPA and MVPA that contribute to weight loss within the context of a behavioral intervention. These findings are similar to other studies that have shown that both MVPA and LPA contribute to weight loss in adults with overweight or obesity.[49]

There is an abundance of scientific literature to support that physical activity contributes to a decrease in body weight.[13,14,24,26] The present study further supports these findings, though the findings of body weight, BMI, and body composition may need to be interpreted with caution, and not over interpreted, given the high likelihood of collinearity between these outcome measures. While the precise mechanism by which physical activity contributes to weight loss cannot be determined from the results of this study, it is highly likely that one pathway is through enhanced energy expenditure. Thus, LPA contributes to increased energy expenditure, which may explain its contribution to weight and fat loss observed in this study. This study showed that for every 100 MET-minutes per week of LPA there was an additional 0.08 kg of mean weight loss at 6 months and 0.14 kg of mean weight loss at 12 months. However, additional studies are needed to fully

understand the pathways by which LPA may contribute to weight loss in adults with overweight or obesity.

### 5.3 LPA and Cardiorespiratory Fitness

Data from this study show that in adjusted analyses, there was a trend for LPA to be associated with cardiorespiratory fitness prior to initiating the weight loss intervention. This finding may be consistent with the hypothesis that a higher level of LPA will be associated with a higher level of cardiorespiratory fitness. This finding may be of importance given that participants recruited into the parent study providing data for these analyses self-reported engaging in less than 60 minutes of structured physical activity per week. Thus, these findings may suggest that there is some cardiorespiratory fitness benefit resulting from LPA, and this may suggest that underactive adults may benefit from engagement in LPA even if their engagement in structure physical activity is less than optimal. Literature on the impact of LPA on cardiorespiratory fitness are consistent with the findings from this study.[133,134] McGure et al, demonstrated that cardiorespiratory fitness improves significantly with light intensity physical activity.[134]

The results from this study also suggest that the increase in LPA from baseline to 6 months may be associated with an increase in cardiorespiratory fitness during this same time period of the intervention, which supports one of the hypotheses stated for this study. However, the increase in LPA from baseline to 12 months was not statistically associated with the increase in cardiorespiratory fitness during this same period of the intervention, which does not support the stated hypothesis. The reason for this pattern of findings is unclear and warrants further investigation. However, one explanation for this could be that LPA may have an initial influence

on improving cardiorespiratory fitness in underactive adults with overweight or obesity; however, after the initial improvements in cardiorespiratory fitness are observed the influence of LPA to result in further improvements in fitness is minimized. Rather, after the initial increase in cardiorespiratory fitness, MVPA rather than LPA may play a more prominent role. For example, while not the primary focus of this study, MVPA was examined in the fully adjusted statistical models. For the change from baseline to 12 months, LPA was not significantly associated with the change in cardiorespiratory fitness, but MVPA was positively associated with this measure of cardiorespiratory fitness. This may suggest that while engagement in greater amounts of LPA during the initial phases of a weight loss intervention may contribute to improvements in cardiorespiratory fitness, MVPA may need to be recommended to result in sustained or further improvements in cardiorespiratory fitness. This warrants further investigation.

The importance of intensity of physical activity to improve cardiorespiratory fitness within the context of a behavioral weight loss intervention has been demonstrated previously. For example, in a study of equally prescribed amounts of physical activity, Jakicic et al. showed that a higher intensity of physical activity resulted in greater improvements in cardiorespiratory fitness compared to less intense physical activity.[135] Thus, this may suggest that even if the total volume of LPA and MVPA were equal, MVPA may result in a greater improvement in cardiorespiratory fitness compared to LPA. Thus, appropriately designed studies to directly compare the influence of LPA versus MVPA on cardiorespiratory fitness, when total volume of activity is held constant, are needed to further understand these potential effects.

## 5.4 LPA and Cardiometabolic Risk Factors

This study also examined the association between LPA and cardiometabolic risk factors that included resting blood pressure, total cholesterol, LDL cholesterol, triglycerides, HDL cholesterol, glucose, insulin, and CRP. As summarized in Table 15 and presented in the Results Section, the results from the baseline adjusted analyses did not support the hypotheses that LPA would be significantly associated negatively with resting blood pressure, total cholesterol, LDL cholesterol, triglycerides, glucose, insulin, or CRP. While HDL cholesterol was significant associated with LPA, the association was opposite of what was expected (e.g., higher LPA was associated with lower HDL cholesterol).

The explanation for these findings is unclear but, given the lack of data in the literature on the association between LPA and these risk factors, these findings may have valuable clinical implications. For example, healthcare providers may need to caution when encouraging engagement in LPA with an intent to reduce health risk through improvement in cardiometabolic risk factors such as those examined in this study. Rather, this may suggest that healthcare provides still need to encourage patience to progressively increase their engagement in levels of physical activity that are consistent with the current public health recommendation, which primarily focus on MVPA.[24]

This study showed no significant association between LPA with either resting systolic blood pressure or diastolic blood pressure within the adjusted analyses, which is not consistent with the hypothesized associations. This is not consistent with the effects that MVPA has been shown to have on reductions in resting blood pressure.[24,136] This may suggest that MVPA rather than LPA, or that a higher threshold of LPA needs to be achieved, to impact resting blood pressure. However, the findings from this study are similar to other studies that have shown no associations

between LPA and blood pressure.[137–139] For example, Buman et al, demonstrated that blood pressure was not associated with LPA compared to other biomarkers.[139] An explanation for the results found in this study, is the possibility that the selection criteria used for this study limited the ability to detect significant associations between LPA and resting blood pressure. This study recruited relatively healthy adults with overweight or obesity, and this resulted in the exclusion of individuals with hypertension. Thus, studies of patients with hypertension may result in different effects of LPA on resting blood pressure that what was observed in this study, and this warrants further examination.

The analyses for change in LPA from baseline to 6 months showed significant negative associations with change in total cholesterol, LDL cholesterol, and triglycerides. These findings are consistent with the hypothesized negative associations with LPA. Moreover, these findings are consistent with other studies of physical activity that have shown that an increase in physical activity can result in a reduction in these cardiometabolic risk factors.[136] For example, this prior systematic review concluded that aerobic and resistance exercise reduce non-HDL cholesterol and LDL cholesterol, and the findings from this current study suggests that LPA may also contribute to reductions in the measures of blood lipids.[136] However, the prior systematic review also concluded that the effect of physical activity on triglycerides is inconsistent across studies, whereas the current study found that the 6-month change in LPA was associated with a concurrent reduction in triglycerides. The inconsistent findings of the effects of physical activity, including LPA, on triglycerides warrants further investigation.

The significant associations observed between the change in LPA and the change in total cholesterol, LDL cholesterol, and triglycerides at 6 months were not observed when examining the change from baseline to 12 months. The specific cause of this lack of association for the baseline

to 12-month changes is unknown. However, it is possible that LPA may have an initial short-term influence of selected cardiometabolic risk factors that is not sustainable long-term, and this warrants further investigation.

For the change in HDL cholesterol, this study did not support the hypothesis that there is an association between HDL cholesterol and LPA for the change from baseline to 6 months. This finding is consistent with conclusions from a systematic review of aerobic physical activity that found no consistent association between physical activity and HDL cholesterol.[136] However, we also found that the association between change in LPA was positively associated with a change in HDL at 12 months. This may suggest that while LPA may not significantly influence HDL across a 6-month period, the longer-term effects of LPA on HDL cholesterol may be more promising. Thus, future studies should consider both the short and long-term effect of LPA on blood lipids, which includes HDL cholesterol.

Data from this study show that neither baseline nor change in glucose at either 6 or 12 months were significantly associated with LPA in the adjusted analyses. While these findings do not support the study's hypotheses, this also is not consistent with the literature that physical activity has been shown to have a favorable impact on glucose tolerance.[140] These results may suggest that LPA has little influence on fasting blood glucose levels in adults with overweight or obesity, but this warrants confirmation in additional studies specifically designed to examine LPA and its effects on fasting glucose. Moreover, the lack of a significant association between LPA and fasting glucose may be a due to the characteristics of the study sample given that participants selected for this study were relatively healthy and did not have a diagnosis of type 2 diabetes. An additional consideration is that this study examined fasting glucose, but a different finding may have been present if glucose was measured in more than a fasting state such as what could be

achieved with the use of continuous glucose monitoring. For example, Healey et al, found LPA to associated with reductions in 2-hour plasma glucose, which is not consistent with the findings of this study.[141] These factors should be considered in future studies of LPA and its potential influence on blood glucose.

This study showed that LPA was associated with a greater reduction in insulin at 6 months, but this effect was not observed with the change at 12 months. Thus, these results only partially support the hypothesis that LPA would be associated with lower levels of insulin. By comparison, the existing literature supports that physical activity, typically of moderate-to-vigorous intensity, is associated with greater insulin sensitivity.[140] An important consideration is that the current study examined fasting insulin, while other studies have examined measures of insulin resistance. This may also suggest that LPA is not sufficient to influence fasting insulin long-term, whereas physical activity of a higher intensity may be necessary to have a long-term influence on insulin. Thus, these factors should be considered when further examining the potential influence of LPA on insulin in adults with overweight or obesity.

Results did not reveal that LPA was significantly associated CRP at baseline or across changes at 6 or 12 months. Thus, these results do not support the hypothesis that LPA would be associated with lower CRP. However, these results are consistent with other studies that have examined the effect of physical activity on CRP. For example, the INFLAME study found that CRP was not impacted by physical activity.[127] Rather, the INFLAME study found that weight loss, rather than physical activity, was associated with observed changes in CRP. This may suggest that LPA should not be an intervention target for reducing markers of inflammation in adults with overweight or obesity.

## 5.5 Limitations and Future Directions

The results of this study may have clinical implications for the potential benefits of adults with overweight or obesity to engage in LPA prior to and within the context of a behavioral weight loss intervention. However, the implications of these findings should be considered with the context of potential limitations of this study, which provide opportunities for future research to study the potential health benefits of LPA. These limitations and future directions include the following:

1. The present study was a secondary analysis of data collected from a parent randomized clinical trial, and the parent study was not specifically designed to examine the effects of LPA on the outcomes examined. Thus, there is a need for appropriately designed and powered studies to specifically examine the health benefits of LPA. For example, the current study design allowed for examination of the associations between LPA and selected health outcomes; however, this design did not allow for the study of causality, and it was not designed to control for confounding. Rather, to examine causality and to reduce confounding, a randomized clinical trial design will be needed, that include additional design considerations to examine efficacy or effectiveness. Additional designs to assess acute effects of LPA may include laboratory-based studies that may involve randomization or cross-over methodology.

2. This participants in this study largely consisted of non-Hispanic/white females. Thus, this study was not designed to specifically examine the effects that sex/gender, race, or ethnicity may have on the health benefits of engagement in LPA. Thus, appropriately designed studies that specifically include adequate representation from sex/gender, race, and ethnicity are needed to examine the health benefits of LPA.

3. The inclusion criteria for this study included an age range of 18-55 years. This limits the ability of this study to examine the health benefits of LPA across a wider age range that include both older adults and younger individuals (e.g., children and adolescents). Future studies should consider a wider age range to allow for examination of the health benefits of physical activity across the lifespan.

4. This study adults with overweight or obesity who were otherwise healthy with no know metabolic or other chronic health conditions. Therefore, whether LPA may have different effects on health outcomes with existing chronic health conditions is not able to be examined in this study. Studies are needed to examine the potential benefits of LPA on a variety of health outcomes in individual with existing metabolic and other chronic health conditions.

5. Within the current study, physical activity was objectively assessed three times, each for a period of one week (one week at baseline, one week at 6 months, one week at 12 months). While this is consistent with research methodology of other clinical trials that have examined physical activity, these weeks may not necessarily represent a typical week of physical activity and may not reflect the day-to-day or week-to-week variability in physical activity that may influence health benefits. Thus, if feasible, future studies should consider objective assessment of physical activity throughout the entire study period.

6. Within the context of the interventions that were implemented for this study, MVPA rather than LPA was prescribed. This may have limited the improvements observed in LPA resulting from the intervention, and this may have influenced the associations with health outcomes that were observed. Future studies may need to be designed to specifically target improving LPA to better understand the potential health-related benefits of LPA.

## 5.6 Strengths

While the present study has limitations, the strengths of the study should also be considered. These strengths include the following:

1. The present study had a relatively large sample size from a randomized clinical trial. This allowed sufficient power to detect an approximate correlation of r=0.200 between LPA and the other outcome variables with the significant level set at $p \leq 0.05$ and power set at 0.95. Thus, there appears to be an adequate sample size to conduct this study of associations between LPA and other outcome variables and to detect small to moderate associations between these variables.

2. The research methodology used in this current study was conducted with rigor. For, example, measurements were conducted using calibrated equipment and certified laboratories. Moreover, this study included objective assessments of physical activity, which allowed for the study of both LPA and MVPA.

3. The present study is one of the few studies to examine the associations of between LPA and weight, fitness, or cardiometabolic risk factors. Thus, this study provides novel results that are important for public health and clinical approaches to the benefits of physical activity.

## 5.7 Conclusions and Clinical Implications

This study provides evidence that, within the context of a behavioral weight loss intervention, LPA is significantly associated with reductions in body weight, body fat, and a trend towards increasing cardiorespiratory fitness. However, these results may not be sustained with

LPA alone, with the combination of both LPA and MVPA contributing to short- and long-term weight loss. Moreover, physical activity of a higher intensity may be needed to contribute to the initial and sustained improvements in cardiorespiratory fitness.

An additional aim of this study was to examine the associations between LPA and cardiometabolic risk factors, and the results from this study do not support an association between LPA and all of the cardiometabolic risk factors that were examined. The results suggest that LPA may have a positive short-term impact on total cholesterol, LDL cholesterol, HDL, and insulin in adults with obesity. This could suggest that LPA may be an important contributor to some short-term health benefits for adults with overweight or obesity but requires additional investigation.

The findings from this study provides implications for additional research to fully evaluate the role LPA has on cardiometabolic risk factors, which may provide insight into how the contribution of LPA can positively impact cardiometabolic risk factors but also elicit increased health benefits. These findings may have important implications for adults with overweight or obesity who are unable, for various reasons, to engage in sufficient amounts of MVPA but for whom LPA may be more feasible. These findings suggest that, even in the absence of MVPA, LPA may have modest but clinically important influences on some health-related outcomes in adults with overweight or obesity.

## Bibliography


1. Greenberg JA. Obesity and early mortality in the United States. *Obesity*. 2013;21(2):405-412.

2. Hales CM, Carroll M, Fryar C, Ogden C. Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017-2018. *National Center for Health Statistics; 2017*.

3. Ruhm CJ. Current and future prevalence of obesity and severe obesity in the United States. *Forum for Health Economics and Policy*.2007;10(2).

4. Fryar C, Carroll M, Ogden C. Prevalence of Overweight, Obesity, and Severe Obesity Among Adults Aged 20 and Over: United States, 1960-1962 Through 2015-2016. Hyattsville, MD: NCHS Health Statistics, CDC Stacks Public Health Publications; 2018.

5. Kelly T, Yang W, Chen C-S, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. *International Journal of Obesity*. 2008;32(9):1431-1437.

6. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *Journal of the American College of Cardiology*. 2009;53(21):1925-1932.

7. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *Journal of the American Medical Association.* 2003;289(1):76-79.

8. Aronne LJ, Brown WV, Isoldi KK. Cardiovascular disease in obesity: A review of related risk factors and risk-reduction strategies. *Journal of Clinical Lipidology*. 2007;1(6):575-582.

9. Barroso TA, Marins LB, Alves R, Gonçalves ACS, Barroso SG, Rocha G de S. Association of central obesity with the incidence of cardiovascular diseases and risk factors. *International Journal of Cardiovascular Science*. 2017; 30:416-424.

10. My Saydah S, Bullard KM, Cheng Y, et al. Trends in cardiovascular disease risk factors by obesity level in adults in the United States, NHANES 1999-2010. *Obesity*. 2014;22(8):1888-1895.

11. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. *Obesity Reviews*. 2014;15(6):504-515.

12. Van Gaal LF, Mertens IL, Christophe E. Mechanisms linking obesity with cardiovascular disease. *Nature*. 2006;444(7121):875-880.

13. Goldstein DJ. Beneficial health effects of modest weight loss. International Journal of Obesity and Related Metabolic Disorders*: Journal of the International Association for the Study of Obesity*. 1992;16(6):397-415.

14. Wing RR, Venditti E, Jakicic JM, Polley BA, Lang W. Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes Care*. 1998;21(3):350-359.

15. Hughes TA, Gwynne JT, Switzer BR, Herbst C, White G. Effects of caloric restriction and weight loss on glycemic control, insulin release and resistance, and atherosclerotic risk in obese patients with type II diabetes mellitus. *Journal of the American Medical Association*. 1984;77(1):7-17.

16. Pasanisi F, Contaldo F, De Simone G, Mancini M. Benefits of sustained moderate weight loss in obesity. *Nutrition, Metabolism and Cardiovascular Diseases*. 2001;11(6):401-406.

17. Henry R, Wallace P, Olefsky J. Effects of weight loss on mechanisms of hyperglycemia in obese non-insulin-dependent diabetes mellitus. *Diabetes*. 1986;35(9):990-998.

18. Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Blair SN, Church TS. Effects of clinically significant weight loss with exercise training on insulin resistance and cardiometabolic adaptations. *Obesity*. 2016;24(4):812-819.

19. Jung UJ, Choi M-S. Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. *International Journal of Molecular Sciences*. 2014;15(4):6184-6223.

20. Brehm A, Pfeiler G, Pacini G, Vierhapper H, Roden M. Relationship between serum lipoprotein ratios and insulin resistance in obesity. *Clinical Chemistry*. 2004;50(12):2316-2322.

21. Dattilo AM, Kris-Etherton P. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *The American Journal of Clinical Nutrition*. 1992;56(2):320-328.

22. Donnelly JE, Honas JJ, Smith BK, et al. Aerobic exercise alone results in clinically significant weight loss for men and women: midwest exercise trial 2. *Obesity*. 2013;21(3):E219-E228.

23. Expert Panel Members, Jensen MD, Ryan DH, et al. Executive summary: guidelines (2013) for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society published by the Obesity Society and American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Based on a systematic review from the The Obesity Expert Panel, 2013. *Obesity*. 2014;22(S2):S5-S39.

24. 2018 Physical Activity Guidelines Advisory Committee. 2018 physical activity guidelines advisory committee scientific report.Washington, DC: U.S. Department of Health and Human Services,2018.

25. Garrow J, Summerbell C. Meta-analysis: effect of exercise, with or without dieting, on the body composition of overweight subjects. *European Journal of Clinical Nutrition*. 1995;49(1):1-10.

26. Wing RR, Lang W, Wadden TA, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care*. 2011;34(7):1481-1486.

27. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and Science in Sports and Exercise*. 2009;41(2):459-471.

28. Foster-Schubert KE, Alfano CM, Duggan CR, et al. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. *Obesity*. 2012;20(8):1628-1638.

29. Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE—a randomized controlled study. *Archives of Internal Medicine.* 2004;164(1):31-39.

30. Johns DJ, Hartmann-Boyce J, Jebb SA, Aveyard P, Group BWMR. Diet or exercise interventions vs combined behavioral weight management programs: a systematic review and meta-analysis of direct comparisons. *The Journal of the Academy of Nutrition and Dietetics*. 2014;114(10):1557-1568.

31. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *Journal of the American Medical Association.* 2013;310(12):1263-1273.

32. Washburn RA, Szabo AN, Lambourne K, et al. Does the method of weight loss effect long-term changes in weight, body composition or chronic disease risk factors in overweight or obese adults? A systematic review. *PLOS One*. 2014;9(10).

33. Hagan RD, Upton SJ, Wong L, Whittam J. The effects of aerobic conditioning and/or caloric restriction in overweight men and women. *Medicine and Science in Sports and Exercise*. 1986;18(1):87-94.

34. Curioni C, Lourenco P. Long-term weight loss after diet and exercise: a systematic review. *International Journal of Obesity*. 2005;29(10):1168-1174.

35. Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. *Archives of Internal Medicine*. 2008;168(14):1550-1559.

36. Calza S, Decarli A, Ferraroni M. Obesity and prevalence of chronic diseases in the 1999–2000 Italian National Health Survey. *BMC Public Health*. 2008;8(1):1-9.

37. Chrostowska M, Szyndler A, Hoffmann M, Narkiewicz K. Impact of obesity on cardiovascular health. *Best Practice and Research Clinical Endocrinology and Metabolism*. 2013;27(2):147-156.

38. Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *Journal of the American Dietetic Association.* 2007;107(10):1755-1767.

39. Jakicic JM, Clark K, Coleman E, et al. Appropriate intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and Science in Sports and Exercise.* 2001;33(12):2145-2156.

40. Gill JM, Malkova D. Physical activity, fitness and cardiovascular disease risk in adults: interactions with insulin resistance and obesity. *Clinical Science*. 2006;110(4):409-425.

41. Akbartabartoori M, Lean M, Hankey C. The associations between current recommendation for physical activity and cardiovascular risks associated with obesity. *European Journal of Clinical Nutrition*. 2008;62(1):1-9.

42. Pan H-J, Cole BM, Geliebter A. The benefits of body weight loss on health-related quality of life. *Journal of the Chinese Medical Association*. 2011;74(4):169-175.

43. Fontaine K, Barofsky I. Obesity and health-related quality of life. *Obesity Reviews*. 2001;2(3):173-182.

44. Jakicic JM, Otto AD. Treatment and prevention of obesity: what is the role of exercise? *Nutrition Reviews*. 2006;64(1):57-61.

45. Jakicic JM. The effect of physical activity on body weight. *Obesity*. 2009;17(3):34-38.

46. Barry VW, Baruth M, Beets MW, Durstine JL, Liu J, Blair SN. Fitness vs. fatness on all-cause mortality: a meta-analysis. *Progress in Cardiovascular Diseases*. 2014;56(4):382-390.

47. Blackburn G. Effect of degree of weight loss on health benefits. *Obesity Research*. 1995;3(2):211-216.

48. Fuezeki E, Engeroff T, Banzer W. Health benefits of light-intensity physical activity: a systematic review of accelerometer data of the National Health and Nutrition Examination Survey (NHANES). *Sports Medicine*. 2017;47(9):1769-1793.

49. Jakicic JM, King WC, Marcus MD, et al. Short-term weight loss with diet and physical activity in young adults: The IDEA study. *Obesity*. 2015;23(12):2385-2397.

50. Amagasa S, Machida M, Fukushima N, et al. Is objectively measured light-intensity physical activity associated with health outcomes after adjustment for moderate-to-vigorous physical activity in adults? A systematic review. *International Journal of Behavioral Nutrition and Physical Activity*. 2018;15(1):1-13.

51. Chastin SF, De Craemer M, De Cocker K, et al. How does light-intensity physical activity associate with adult cardiometabolic health and mortality? Systematic review with meta-analysis of experimental and observational studies. *British Journal of Sports Medicine*. 2019;53(6):370-376.

52. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960–1994. *International Journal of Obesity*. 1998;22(1):39-47.

53. Fryar C, Carroll M, Afful J. Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: United States, 1963–1965 through 2017–2018. *National Center for Health Statistics*. 2020.

54. Baskin ML, Ard J, Franklin F, Allison DB. Prevalence of obesity in the United States. *Obesity Reviews*. 2005;6(1):5-7.

55. Yu Y. Four decades of obesity trends among non-Hispanic whites and blacks in the United States: analyzing the influences of educational inequalities in obesity and population improvements in education. *PLOS One*. 2016;11(11).

56. Gregg EW, Cheng YJ, Narayan KV, Thompson TJ, Williamson DF. The relative contributions of different levels of overweight and obesity to the increased prevalence of diabetes in the United States: 1976–2004. *Preventive Medicine*. 2007;45(5):348-352.

57. Ogden CL, Carroll MD, Fryar CD, Flegal KM. Prevalence of obesity among adults and youth: United States, 2011-2014.2015.

58. Anderson SE, Whitaker RC. Prevalence of obesity among US preschool children in different racial and ethnic groups. *Archives of Pediatrics and Adolescent Medicine*. 2009;163(4):344-348.

59. Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in US population aged 20–74 yr. *Diabetes*. 1987;36(4):523-534.

60. Clark JM, Brancati FL. The challenge of obesity-related chronic diseases. *Journal of General Internal Medicine*. 2000;15(11):828.

61. Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. *Metabolism*. 2019; 92:98-107.

62. Jiang J, Ahn J, Huang W-Y, Hayes RB. Association of obesity with cardiovascular disease mortality in the PLCO trial. *Preventive Medicine*. 2013;57(1):60-64.

63. Xu H, Cupples LA, Stokes A, Liu C-T. Association of obesity with mortality over 24 years of weight history: findings from the Framingham Heart Study. *Journal of the American Medical Association*. 2018;1(7).

64. McGee DL, Diverse Populations Collaboration. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. *Annals of Epidemiology*. 2005;15(2):87-97.

65. Kissebah AH, Krakower GR. Regional adiposity and morbidity. *Physiological Reviews*. 1994;74(4):761-811.

66. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women: risk within the'normal'weight range. *Journal of the American Medical Association.* 1995;273(6):461-465.

67. Woodward M, Barzi F, Martiniuk A, et al. Cohort profile: the asia pacific cohort studies collaboration. *Internal Journal of Epidemiology*. 2006;35(6):1412-1416.

68. Higgins M, Kannel W, Garrison R, Pinsky J, Stokes III J. Hazards of obesity-the Framingham experience. *Acta Medica Scandinavica*. 1987;222(723):23-36.

69. Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Archives of Internal Medicine.* 2002;162(16):1867-1872.

70. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health*. 2009;9(1):1-20.

71. Field AE, Coakley EH, Must A, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. *Archives of Internal Medicine.* 2001;161(13):1581-1586.

72. Colditz GA, Willett WC, Stampfer MJ, et al. Weight as a risk factor for clinical diabetes in women. *American Journal of Epidemiology*. 1990;132(3):501-513.

73. Lee JM, Gebremariam A, Vijan S, Gurney JG. Excess body mass index–years, a measure of degree and duration of excess weight, and risk for incident diabetes. *Archives of Pediatrics and Adolescent Medicine*. 2012;166(1):42-48.

74. Harris MI. Impaired glucose tolerance in the US population. *Diabetes Care*. 1989;12(7):464-474.

75. Hakkak R, Bell A. Obesity and the link to chronic disease development. *Journal of Obesity and Chronic Disease*. 2016;1(1):1-3.

76. Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. *Annals of Internal Medicine*. 1998;128(2):81-88.

77. Ryu S, Frith E, Pedisic Z, Kang M, Loprinzi PD. Secular trends in the association between obesity and hypertension among adults in the United States, 1999–2014. *European Journal of Internal Medicine*. 2019; 62:37-42.

78. Aronow WS. Association of obesity with hypertension. *Annals of Translational Medicine*. 2017;5(17).

79. Mikhail N, Golub MS, Tuck ML. Obesity and hypertension. *Progress in Cardiovascular Diseases*. 1999;42(1):39-58.

80. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983;67(5):968-977.

81. Stamler R, Stamler J, Riedlinger WF, Algera G, Roberts RH. Weight and blood pressure: findings in hypertension screening of 1 million Americans. J*ournal of the American Medical Association.* 1978;240(15):1607-1610.

82. Gus M, Fuchs SC, Moreira LB, et al. Association between different measurements of obesity and the incidence of hypertension. *American Journal of Hypertension*. 2004;17(1):50-53.

83. Brown CD, Higgins M, Donato KA, et al. Body mass index and the prevalence of hypertension and dyslipidemia. *Obesity Research*. 2000;8(9):605-619.

84. Nguyen NT, Magno CP, Lane KT, Hinojosa MW, Lane JS. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the National Health and Nutrition Examination Survey, 1999 to 2004. *Journal of the American College of Surgeons*. 2008;207(6):928-934.

85. Osuji C, Nzerem B, Meludu S, Dioka C, Nwobodo E, Amilo G. The prevalence of overweight/obesity and dyslipidemia amongst a group of women attending" August" meeting. *Nigerian Medical Journal*. 2010;51(4):155.

86. Pouliot M, Després J, Moorjani S, et al. Regional variation in adipose tissue lipoprotein lipase activity: association with plasma high density lipoprotein levels. *European Journal of Clinical Investigation*. 1991;21(4):398-405.

87. Shah S, Devrajani B, Devrajani T, Bibi I. Frequency of dyslipidemia in obese versus non-obese in relation to body mass index (BMI), waist hip ratio (WHR) and waist circumference (WC). *Pakistan Journal of Science*. 2010;62(1):27-31.

88. Zhang C, Rexrode KM, Van Dam RM, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. *Circulation*. 2008;117(13):1658-1667.

89. Basen-Engquist K, Chang M. Obesity and cancer risk: recent review and evidence. *Current Oncology Reports*. 2011;13(1):71-76.

90. Wild C, Weiderpass E, Stewart BW. *World Cancer Report: Cancer Research for Cancer Prevention*. IARC Press; 2020.

91. Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM. Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance. *Journal of Clinical Investigation*. 1995;95(5):2409-2415.

92. Panagiotakos DB, Pitsavos C, Yannakoulia M, Chrysohoou C, Stefanadis C. The implication of obesity and central fat on markers of chronic inflammation: The ATTICA study. *Atherosclerosis*. 2005;183(2):308-315.

93. Brooks GC, Blaha MJ, Blumenthal RS. Relation of C-reactive protein to abdominal adiposity. *American Journal of Cardiology*. 2010;106(1):56-61.

94. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. *Journal of the American Medical Association.* 1999;282(22):2131-2135.

95. Nicklas BJ, Ambrosius W, Messier SP, et al. Diet-induced weight loss, exercise, and chronic inflammation in older, obese adults: a randomized controlled clinical trial. *American Journal of Clinical Nutrition*. 2004;79(4):544-551.

96. Selvin E, Paynter NP, Erlinger TP. The effect of weight loss on C-reactive protein: a systematic review. *Archives of Internal Medicine*. 2007;167(1):31-39.

97. Forsythe LK, Wallace JM, Livingstone MBE. Obesity and inflammation: the effects of weight loss. *Nutrition Research Reviews*. 2008;21(2):117-133.

98. Gregg EW, Chen H, Wagenknecht LE, et al. Association of an intensive lifestyle intervention with remission of type 2 diabetes. *Journal of the American Medical Association*. 2012;308(23):2489-2496.

99. Watts NB, Spanheimer RG, DiGirolamo M, et al. Prediction of glucose response to weight loss in patients with non–insulin-dependent diabetes mellitus. *Archives of Internal Medicine*. 1990;150(4):803-806.

100. Numata K, Tanaka K, Saito M, Shishido T, Inoue S. Very low-calorie diet-induced weight loss reverses exaggerated insulin secretion in response to glucose, arginine and glucagon in obesity. *International Journal of Obesity and Related Metabolic Disorders.* 1993;17(2):103-108.

101. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care*. 2002;25(12):2165-2171.

102. Diaz M. Hypertension and obesity. *Journal of Human Hypertension*. 2002;16(1):18-22.

103. Davis BR, Blaufox MD, Oberman A, et al. Reduction in long-term antihypertensive medication requirements: effects of weight reduction by dietary intervention in overweight persons with mild hypertension. *Archives Internal Medicine*. 1993;153(15):1773-1782.

104. Weinsier RL, James LD, Darnell BE, et al. Lipid and insulin concentrations in obese postmenopausal women: separate effects of energy restriction and weight loss. *American Journal of Clinical Nutrition*. 1992;56(1):44-49.

105. Berchtold P, Jörgens V, Kemmer FW, Berger M. Obesity and hypertension: cardiovascular response of weight reduction. *Hypertension*. 1982;4(5).

106. Ramsay L, Ramsay M, Hettiarachchi J, Davies D, Winchester J. Weight reduction in a blood pressure clinic. *British Medical Journal*. 1978;2(6132):244-245.

107. Trials of Hypertension Prevention Collaborative Research Group. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels: Results of the Trials of Hypertension Prevention, phase I. J*ournal of the American Medical Association*. 1992; 267:1213-1220.

108. Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *New England Journal of Medicine.* 1988;319(18):1173-1179.

109. Seim H, Holtmeier K. Effects of a six-week, low-fat diet on serum cholesterol, body weight, and body measurements. *Family Practice Research Journal*. 1992;12(4):411-419.

110. Waki M, Heshka S, Heymsfield S. Long-term serum lipid lowering, behavior modification, and weight loss in obese women. *Nutrition*. 1993;9(1):23-28.

111. Castro AVB, Kolka CM, Kim SP, Bergman RN. Obesity, insulin resistance and comorbidities–Mechanisms of association. *Arquivos Brasileros de Endocrinologia and Metabologia*. 2014; 58:600-609.

112. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *American Journal of Clinical Nutrition*. 2003;78(4):684-689.

113. Svetkey LP, Stevens VJ, Brantley PJ, et al. Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. *Journal of the American Medical Association.* 2008;299(10):1139-1148.

114. Fogelholm M, Kukkonen-Harjula K. Does physical activity prevent weight gain–a systematic review. *Obesity Reviews*. 2000;1(2):95-111.

115. Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *Journal of the American Medical Association*. 2010;304(20):2253-2262.

116. Donnelly J, Jacobsen D, Heelan KS, Seip R, Smith S. The effects of 18 months of intermittent vs continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *International Journal of Obesity*. 2000;24(5):566-572.

117. Ross R, Dagnone D, Jones PJ, et al. Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: a randomized, controlled trial. *Annals of Internal Medicine*. 2000;133(2):92-103.

118. Weiss EP, Jordan RC, Frese EM, Albert SG, Villareal DT. Effects of weight loss on lean mass, strength, bone, and aerobic capacity. *Medicine and Science in Sports and Exercise*. 2017;49(1):206.

119. Klem ML, Wing RR, McGuire MT, Seagle HM, Hill JO. A descriptive study of individuals successful at long-term maintenance of substantial weight loss. *American Journal of Clinical Nutrition*. 1997;66(2):239-246.

120. Gormally J, Rardin D. Weight loss and maintenance and changes in diet and exercise for behavioral counseling and nutrition education. *Journal of Counseling Psychology*. 1981;28(4):295.

121. Jakicic JM, Winters C, Lang W, Wing RR. Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *Journal of the American Medical Association*. 1999;282(16):1554-1560.

122. Schoeller DA, Shay K, Kushner RF. How much physical activity is needed to minimize weight gain in previously obese women? *American Journal of Clinical Nutrition*. 1997;66(3):551-556.

123. Unick JL, Gaussoin SA, Hill JO, et al. Objectively assessed physical activity and weight loss maintenance among individuals enrolled in a lifestyle intervention. *Obesity*. 2017;25(11):1903-1909.

124. Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *Journal of the American College of Cardiology*. 2005;45(10):1563-1569.

125. Abramson JL, Vaccarino V. Relationship between physical activity and inflammation among apparently healthy middle-aged and older US adults. *Archives of Internal Medicine*. 2002;162(11):1286-1292.

126. Stewart LK, Earnest CP, Blair SN, Church TS. Effects of different doses of physical activity on C-reactive protein among women. *Medicine and Science in Sports and Exercise*. 2010;42(4):701.

127. Church TS, Earnest CP, Thompson AM, et al. Exercise without weight loss does not reduce C-reactive protein: the INFLAME study. *Medicine and Science in Sports and Exercise*. 2010;42(4):708.

128. Wing RR, Goldstein MG, Acton KJ, et al. Behavioral science research in diabetes: lifestyle changes related to obesity, eating behavior, and physical activity. *Diabetes Care*. 2001;24(1):117-123.

129. Owens JF, Matthews KA, Wing RR, Kuller LH. Can physical activity mitigate the effects of aging in middle-aged women? *Circulation*. 1992;85(4):1265-1270.

130. Rogers RJ, Schelbert EB, Lang W, Fridman Y, Yuan N, Jakicic JM. Association of fitness and body fatness with left ventricular mass: The heart health study. *Obesity Science and Practice*. 2020;6(1):19-27.

131. Collins K, Jakicic J, Rogers R, Davis K, Ambrosio F. Change in Circulating Klotho in Response to Weight Loss, with and without Exercise, in Adults with Overweight or Obesity.2019 (Doctoral dissertation, University of Pittsburgh).

132. Davis KK, Tate DF, Lang W, et al. Racial differences in weight loss among adults in a behavioral weight loss intervention: role of diet and physical activity. *Journal of Physical Activity and Health*. 2015;12(12):1558-1566.

133. Kozey Keadle S, Lyden K, Staudenmayer J, et al. The independent and combined effects of exercise training and reducing sedentary behavior on cardiometabolic risk factors. *Applied Physiology Nutrition and Metabolism*. 2014;39(7):770-780.

134. McGuire KA, Ross R. Incidental physical activity is positively associated with cardiorespiratory fitness. *Medicine and Science in Sports and Exercise*. 2011;43(11):2189-2194.

135. Jakicic JM, Marcus BH, Gallagher KI, Napolitano M, Lang W. Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *Journal of the American Medical Association. 2003;290(10):1323-1330*.

136. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2014;63(25 Part B):2960-2984.

137. Sjöros T, Vähä-Ypyä H, Laine S, et al. Both sedentary time and physical activity are associated with cardiometabolic health in overweight adults in a 1-month accelerometer measurement. *Scientific Reports*. 2020;10(1):1-11.

138. Whitaker KM, Pettee Gabriel K, Buman MP, et al. Associations of accelerometer-measured sedentary time and physical activity with prospectively assessed cardiometabolic risk factors: the CARDIA study. *Journal of the American Heart Association*. 2019;8(1).

139. Buman MP, Winkler EA, Kurka JM, et al. Reallocating time to sleep, sedentary behaviors, or active behaviors: associations with cardiovascular disease risk biomarkers, NHANES 2005–2006. *American Journal of Epidemiology*. 2014;179(3):323-334.

140. Ross R, Freeman JA, Janssen I. Exercise alone is an effective strategy for reducing obesity and related comorbidities. *Exercise and Sports Sciences Reviews*. 2000;28(4):165-170.

141. Healy GN, Dunstan DW, Salmon J, et al. Objectively measured light-intensity physical activity is independently associated with 2-h plasma glucose. *Diabetes Care*. 2007;30(6):1384-1389.

142. Akil L, Ahmad HA. Relationships between obesity and cardiovascular diseases in four southern states and Colorado. *Journal of Health Care for the Poor Underserved*. 2011;22(4):61.

143. American Diabetes Association. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. *Diabetes Care*. 2007;30(6):1374-1383.

144. Barnes AS. Obesity and sedentary lifestyles: risk for cardiovascular disease in women. *Texas Heart Institute Journal*. 2012;39(2):224.

145. Brancati FL, Wang N-Y, Mead LA, Liang K-Y, Klag MJ. Body weight patterns from 20 to 49 years of age and subsequent risk for diabetes mellitus: the Johns Hopkins Precursors Study. *Archives of Internal Medicine*. 1999;159(9):957-963.

146. Catenacci VA, Wyatt HR. The role of physical activity in producing and maintaining weight loss. *Nature Clinical Practice Endocrinology and Metabolism*. 2007;3(7):518-529.

147. Choi J, Joseph L, Pilote L. Obesity and C-reactive protein in various populations: a systematic review and meta-analysis. *Obesity Reviews*. 2013;14(3):232-244.

148. Cossrow N, Falkner B. Race/ethnic issues in obesity and obesity-related comorbidities. *Journal of Clinical Endocrinology and Metabolism*. 2004;89(6):2590-2594.

149. Coughlin J, Brantley P, Champagne C, et al. Weight Loss Maintenance Collaborative Research G. The impact of continued intervention on weight: five-year results from the weight loss maintenance trial. *Obesity Silver Spring*. 2016; 24:1046-1053.

150. Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the US population: National Health and Nutrition Examination Survey 1999–2002. *Diabetes Care*. 2006;29(6):1263-1268.

151. Czernichow S, Kengne A, Stamatakis E, Hamer M, Batty GD. Body mass index, waist circumference and waist–hip ratio: which is the better discriminator of cardiovascular disease mortality risk? Evidence from an individual-participant meta-analysis of 82 864 participants from nine cohort studies. *Obesity Reviews*. 2011;12(9):680-687.

152. Després J-P. Obesity and lipid metabolism: relevance of body fat distribution. *Current Opinion Lipidology*. 1991;2(1):5-15.

153. Després J-P, Moorjani S, Pouliot M-C, et al. Correlates of plasma very-low-density lipoprotein concentration and composition in premenopausal women. *Metabolism*. 1990;39(6):577-583.

154. Dixon JB. The effect of obesity on health outcomes. *Molecular and Cellular Endocrinology*. 2010;316(2):104-108.

155. Ebbert JO, Elrashidi MY, Jensen MD. Managing overweight and obesity in adults to reduce cardiovascular disease risk. *Current Atherosclerosis Reports*. 2014;16(10):445.

156. Esposito K, Pontillo A, Di Palo C, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *Journal of the American Medical Association.* 2003;289(14):1799-1804.

157. Ferrannini E, Camastra S. Relationship between impaired glucose tolerance, non-insulin-dependent diabetes mellitus and obesity. *European Journal of Clinical Investigation*. 1998; 28:3-6.

158. Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB. Years of life lost due to obesity. *Journal of the American Medical Association.* 2003;289(2):187-193.

159. Fryar CD, Carroll MD, Ogden CL. Prevalence of overweight, obesity, and extreme obesity among adults: United States, trends 1960–1962 through 2009–2010. Hyattsville MD. *National Center Health Statistics*.2012.

160. Garfinkel L. Overweight and cancer. *Annals of Internal Medicine*. 1985;103(6):1034-1036.

161. Guo F, Garvey WT. Trends in cardiovascular health metrics in obese adults: National Health and Nutrition Examination Survey (NHANES), 1988–2014. *Journal of the American Heart Association*. 2016;5(7).

162. Hartz AJ, Rupley Jr DC, Kalkhoff RD, Rimm AA. Relationship of obesity to diabetes: influence of obesity level and body fat distribution. *Preventive Medicine*. 1983;12(2):351-357.

163. Huang Z, Hankinson S, Colditz G, et al. Dual effects of weight and weight gain on breast cancer risk. *Journal of the American Medical Association.* 1997;278(17):1407-1411

164. Jallut D, Golay A, Munger R, et al. Impaired glucose tolerance and diabetes in obesity: a 6-year follow-up study of glucose metabolism. *Metabolism*. 1990;39(10):1068-1075.

165. Kang YJ, Wang HW, Cheon SY, Lee HJ, Hwang KM, Yoon HS. Associations of obesity and dyslipidemia with intake of sodium, fat, and sugar among Koreans: a qualitative systematic review. *Clinical Nutrition Research*. 2016;5(4):290-304.

166. Kumar S. Cardiovascular disease and its determinants: Public health issue. *Journal of Clinical Medicine*. 2017;2(1).

167. Kwee LC, Ilkayeva O, Muehlbauer MJ, et al. Metabolites and diabetes remission after weight loss. *Nutrition Diabetes*. 2021;11(1):1-13.

168. Lew EA, Garfinkel L. Variations in mortality by weight among 750,000 men and women. *Journal of Chronic Diseases*. 1979;32(8):563-576.

169. López-Suárez A. Burden of cancer attributable to obesity, type 2 diabetes and associated risk factors. *Metabolism*. 2019; 92:136-146.

170. McCann J. Obesity, cancer links prompt new recommendations. *Journal of the National Cancer Institue*. 2001;93(12):901-902.

171. McGuire MT, Wing RR, Klem ML, Lang W, Hill JO. What predicts weight regain in a group of successful weight losers? *Journal of Consulting and Clinical Psychology*. 1999;67(2):177.

172. Movahed M, Lee J, Lim W, Hashemzadeh M, Hashemzadeh M. Strong independent association between obesity and essential hypertension. *Clinical Obesity*. 2016;6(3):189-192.

173. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *Journal of the American Medical Association*. 1999;282(16):1523-1529.

174. Ogden C, Carroll M. Prevalence of obesity among children and adolescents: United States, trends 1963-1965 through 2007-2008. National Center for Health Statistics. 2010;303(3):242-249

175. Ogden CL, Fryar CD, Martin CB, et al. Trends in obesity prevalence by race and hispanic origin—1999-2000 to 2017-2018. *Journal of the American Medical Association*. 2020;324(12):1208-1210.

176. Poirier P, Eckel RH. Obesity and cardiovascular disease. *Current Atherosclerosis Reports*. 2002;4(6):448-453.

177. Power C, Pereira SMP, Law C, Ki M. Obesity and risk factors for cardiovascular disease and type 2 diabetes: investigating the role of physical activity and sedentary behaviour in mid-life in the 1958 British cohort. *Atherosclerosis*. 2014;233(2):363-369.

178. Pronk NP, Wing RR. Physical activity and long-term maintenance of weight loss. *Obesity Research*. 1994;2(6):587-599.

179. Rahmouni K, Correia ML, Haynes WG, Mark AL. Obesity-associated hypertension: new insights into mechanisms. *Hypertension*. 2005;45(1):9-14.

180. Rao SS, Disraeli P, McGregor T. Impaired glucose tolerance and impaired fasting glucose. *American Family Physician*. 2004;69(8):1961-1968.

181. Ravisankar P, Udupa K, Prakash ES. Correlation between body mass index and blood pressure indices, handgrip strength and handgrip endurance in underweight, normal weight and overweight adolescents. *Indian Journal of Physiology and Pharmacology*. 2005;49(4):455.

182. Schulte H, Cullen P, Assmann G. Obesity, mortality and cardiovascular disease in the Münster Heart Study (PROCAM). *Atherosclerosis*. 1999;144(1):199-209.

183. Segula D. Complications of obesity in adults: a short review of the literature. *Journal of Medical Association of Malawi*. 2014;26(1):20-24.

184. Viale PH. The American Cancer Society's facts & figures: 2020 edition. *Journal of the Advanced Practitioner in Oncology*. 2020;11(2):135.

185. Violán C, Bejarano-Rivera N, Foguet-Boreu Q, et al. The burden of cardiovascular morbidity in a European Mediterranean population with multimorbidity: a cross-sectional study. *BMC Family Practice*. 2016;17(1):1-12.

186. Wadden TA, Butryn ML, Byrne KJ. Efficacy of lifestyle modification for long-term weight control. *Obesity Research*. 2004;12(12):151-162.

187. Wadden TA, Butryn ML, Wilson C. Lifestyle modification for the management of obesity. *Gastroenterology*. 2007;132(6):2226-2238.

188. Wadden TA, Tronieri JS, Butryn ML. Lifestyle modification approaches for the treatment of obesity in adults. *American Psychologist*. 2020;75(2):235.

189. Wadden TA, Webb VL, Moran CH, Bailer BA. Lifestyle modification for obesity: new developments in diet, physical activity, and behavior therapy. *Circulation*. 2012;125(9):1157-1170.

190. Wall HK, Ritchey MD, Gillespie C, Omura JD, Jamal A, George MG. Vital signs: prevalence of key cardiovascular disease risk factors for Million Hearts 2022—United States, 2011–2016. *Morbidity and Mortality Weekly Report*. 2018;67(35):983.

191. Webber J. The comorbidities of obesity. *Practical Diabetes International Journal*. 2001;18(8):293-296.