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## Weight Loss with Diet or Diet Plus Physical Activity on Cardiac MRI and CVD Risk Factors: Heart Health Study Randomized Trial

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### Abstract

**Objective:** The primary aim was to examine the change in left ventricular mass (LVM) in adults with overweight or obesity in response to a behavioral weight loss intervention, with variable physical activity (PA) prescriptions.

**Methods:** 383 adults were randomized to a 12-month intervention of diet modification (DIET), DIET plus 150 min/wk of PA (DIET+MODPA), or DIET plus prescription of 250 min/wk of PA (DIET+HIGHPA). LVM was measured with cardiac magnetic resonance imaging (CMR).

**Results:** 12-month weight loss was  $-10.2\%$  (95% CI:  $-11.7, -8.8$ ) in DIET,  $-11.0\%$  (95% CI:  $-12.4, -9.5$ ) in DIET+MODPA, and  $-10.3\%$  (95% CI:  $-11.8, -8.9$ ) in DIET+HIGHPA. LVM decreased at 12 months in DIET [ $-2.9$  grams (95% CI:  $-5.2, -0.7$ );  $P=0.0114$ ] with no change observed in DIET+MODPA [ $-0.8$  grams (95% CI:  $-3.0, 1.5$ );  $P=0.4979$ ] or DIET+HIGHPA [ $-1.1$  grams (95% CI:  $-3.3, 1.1$ );  $P=0.3299$ ].

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**Conclusions:** Weight loss through dietary modification resulted in reduced LVM, whereas when combined with at least 150 minutes per week of prescribed moderate-to-vigorous PA LVM is preserved. These may both be favorable adaptations to weight loss and physical activity in adults with overweight or obesity that warrant further investigation to understand the clinical implications of these changes on cardiovascular disease risk.

### Keywords

obesity; physical activity; cardiovascular disease; weight loss

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## INTRODUCTION

Overweight (body mass index [BMI]  $\geq 25$  kg/m<sup>2</sup>) or obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) are associated with chronic diseases, with a major concern being the association with cardiovascular disease.(1, 2) Approximately 70% of adults in the United States are overweight with 40% of adults obese.(3) Weight loss improves in cardiovascular disease (CVD) risk factors,(1) and weight loss of at least 10% is associated with reduced CVD.(4)

Left ventricular mass (LVM) of the heart is a clinically important prognostic indicator of CVD,(5, 6) and BMI is associated with greater LVM measured with echocardiography.(7) Studies using cardiac magnetic resonance imaging (CMR) have also shown larger LVM at higher levels of BMI,(8) and we have shown that LVM measured by CMR is positively associated with weight and BMI in adults with overweight or obesity.(9)

The larger LVM associated with excess weight may lead to maladaptive hypertrophy and potentially heart failure,(10) this may be a pathway by which overweight or obesity contribute to CVD. While weight loss has been shown to reduce CVD risk factors and potentially the onset of CVD.(4) However, it is unclear if the method of weight loss has differential effects on LVM measured by CMR.

Physical activity (PA), when added to modest dietary restriction, can enhance weight loss and may be predictive of improved weight loss maintenance.(11) PA also contributes to improvements in cardiorespiratory fitness (CRF) in the presence of weight loss,(12, 13) and CRF may influence health even with excess weight.(14, 15, 16) We reported that CRF is associated with LVM in adults with overweight or obesity, possibly suggesting a favorable adaptive response.(9) This is consistent with the known effects of PA on an adaptive response that results in increased LVM while retaining or enhancing cardiac function.(17, 18) However, it is unclear if the dose of PA combined with moderate dietary restriction to achieve weight loss results in differential effects on LVM compared to weight loss achieved with moderate dietary restriction alone.

This study examined the change in LVM in response to a weight loss intervention that compared modest dietary restriction (DIET), DIET plus a moderate dose of PA (DIET+MODPA), and DIET plus a high dose of PA (DIET+HIGHPA). Changes in end-systolic (ESV) and end-diastolic volume (EDV) and ejection fraction (EF), weight, body composition, CRF, and other CVD risk factors were also examined.

## METHODS

### Design

This was a university-based (Pittsburgh) clinical trial with randomization to 1 of 3 interventions, with all groups receiving a 12-month behavioral weight loss intervention ([ClinicalTrials.gov NCT01500356](https://clinicaltrials.gov/ct2/show/study/NCT01500356)). The groups were: 1) DIET received a prescribed energy reduced diet with no PA, 2) DIET+MODPA received a prescribed energy reduced diet plus PA to progress to 150 minutes per week, 3) DIET+HIGHPA received a prescribed energy reduced diet plus PA to progress to 250 minutes per week. The randomization scheme was stratified by sex and race (white or nonwhite) in randomly selected block sizes. The randomization scheme was developed by the statistician and implemented by the principal investigator. The primary outcome was change in LVM from baseline to 12 months.

### Participants

Recruitment occurred between December 2011 and June 2015. Participants (N=383) were recruited through methods that included targeted mailing of post cards, email advertisements, research registries, and other referrals. Eligibility and exclusion criteria have been reported previously.<sup>(9)</sup> Eligibility included being 18 to 55 years and within a BMI range of 25 to <40 kg/m<sup>2</sup>. Ineligibility criteria included: 1) self-reporting 60 minutes per week of structured moderate-to-vigorous intensity PA (MVPA), 2) weight loss of 5% within the prior 6 months or a history of bariatric surgery, 3) history of cardiometabolic disease, diabetes mellitus, or cancer, 4) taking medication that could affect heart rate or blood pressure, 5) taking medication that could influence weight, 6) treatment for psychological conditions that included medication or counseling, 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, 10) or had a contraindication that would prohibit MRI scanning. Participants provided written informed consent and procedures were approved by the University of Pittsburgh's Institutional Review Board. Participants provided clearance from their personal physician prior to study participation.

### Intervention

**Intervention Contact**—The interventions received the same prescribed contact across the 12-month intervention. Weekly intervention sessions were scheduled during months 1-6. Each intervention session was scheduled to last approximately 30-45 minutes in duration, with these including discussion of theory-based strategies to promote adherence to the weight loss behaviors.<sup>(19, 20, 21, 22)</sup> If an intervention session was missed, attempts were made to engage the participant in an in-person or telephonic make-up session. During months 7-12, the in-person sessions were decreased to approximately two sessions per month along with two brief individual telephonic sessions per month.

**Dietary Intervention**—All of the interventions received the same prescribed diet.<sup>(23, 24)</sup> Calorie intake was prescribed at 1,200 kcal/d, 1,500 kcal/d, and 1,800 kcal/d for participants who weighed <90.7 kg, 90.7 kg to <113.4 kg, and 113.4 kg, respectively. Dietary fat intake was prescribed at 20% to 30% of total calorie intake, with specific

amounts of other nutrients (e.g., carbohydrates, protein, sodium, added sugars, etc.) not prescribed. Participants were instructed to record food intake in a diary that was reviewed by intervention staff with feedback provided. If weight loss was >6% during each 4-week period, or if BMI was reduced to  $< 22 \text{ kg/m}^2$ , calorie intake was adjusted to slow the rate of weight loss.

**Physical Activity**—DIET was instructed to maintain their PA across the 12-month intervention. DIET+MODPA and DIET+HIGHPA were prescribed PA that started at 100 min/wk and progress by 25 min/wk in 4-week intervals until achieving a prescribed dose of 150 min/wk for DIET+MODPA or 250 min/wk for DIET+HIGHPA. All activity was non-supervised, and participants were instructed to engage in PA similar to brisk walking, or other modes that were consistent with MVPA, for periods of 10 minutes to achieve the prescribe amount of PA. DIET+MODPA and DIET+HIGHPA were instructed to record PA in a diary that was reviewed by intervention staff with feedback provided. Participants engaging in PA that was not consistent with their prescription were counseled by the intervention staff.

## Outcome Measures

**CMR Measures:** CMR was performed at baseline and 12 months to examine changes in LVM, which was the primary outcome. CMR also assessed ESV, EDV, and EF. CMR staff were blinded to randomized assignment. As previously reported,(9) subjects were scanned on a 1.5 Tesla Siemens Magnetom Espree scanner (Erlangen, Germany) with a 32-channel phased array cardiovascular coil. Standard long axis cines were acquired in the 2, 3, and 4 chamber orientations. Measurements without geometric assumptions from manual end-diastolic and end-systolic endocardial and epicardial traces of short axis stacks of cines acquired with 6 mm slice thickness using commercially available software were taken for LVM. There was no inter-slice gap to improve spatial resolution in the long axis direction and accurately measure left ventricular myocardium at the base of the heart. Papillary muscles were excluded from LVM measures. Typical parameters were: FOV 380 x 340 cm, matrix 256 x 144, 1.5 x 2.4 mm pixels, FA 50 degrees, temporal resolution 30-45 msec, 30 frames per cardiac cycle, TR/TE=2.9/1.2 msec, pixel bandwidth=930 Hz, parallel imaging factor 2 or 3 (GRAPPA).

**Descriptive Characteristics:** Demographic characteristics (gender, race, ethnicity, education) were collected via questionnaire at baseline.

**Weight, Height, BMI, and Body Surface Area (BSA):** Weight was assessed at baseline, 6, and 12 months with the subject clothed in a lightweight hospital gown and shoes removed. Weight was assessed using a calibrated digital scale to the nearest 0.1 kg with duplicate measures differing by 0.5 kg. Height was assessed at baseline with shoes removed using a wall-mounted stadiometer to the nearest 0.1 cm with duplicate measures differing by 0.5 cm. Weight and height were used to compute BMI ( $\text{kg/m}^2$ ). BSA was computed as  $\text{BSA} = 0.0235 \times \text{Height in cm}^{0.42246} \times \text{Weight in kg}^{0.51456}$ . Weight change (kg) and percent weight change were computed at 6 and 12 months compared to baseline.

**Body Composition:** Body composition was measured as baseline, 6, and 12 months from a total body scan obtained from a dual-energy x-ray absorptiometer (DXA, GE Lunar iDXA, Madison, WI).(9)

**Cardiorespiratory Fitness:** CRF was assessed at baseline, 6, and 12 months with a submaximal graded treadmill exercise test (9, 23). Indirect calorimetry was used to assess oxygen consumption ( $L\cdot\text{min}^{-1}$  and  $\text{ml}\cdot\text{kg}\cdot\text{min}^{-1}$ ). The test was terminated when the participant achieved 85% of their age-predicted maximal heart rate.(23)

**Resting Blood Pressure:** Resting blood pressure was assessed at baseline, 6, and 12 months. Duplicate measures were obtained following a 5-minute seated rest period with systolic blood pressure (SBP) measures differing by 10 mmHg and diastolic blood pressure (DBP) measures differing by 6 mmHg, with a third measurement taken if these criteria were not achieved.

**Blood Samples:** Blood samples were collected using venipuncture at baseline, 6, and 12 months. Participants were instructed to fast for a period of 12 hours prior to sample collection. Samples were stored at  $-80^{\circ}\text{C}$  until the time of analysis by a CLIA certified laboratory. Samples were analyzed for total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) high-density lipoprotein cholesterol (HDL-C), glucose, insulin, and c-reactive protein (CRP).

**Physical Activity:** PA was assessed at baseline, 6 months, and 12 months using both a self-reported questionnaire(25) and a wearable device as previously described.(23, 26) The questionnaire queried on walking, flights of stairs climbed, and other sport, recreational, and fitness activities over the past week. For the wearable device, subjects wore it for a one-week period at each assessment period. Data were considered valid if the participant wore the device for 10 or more hours per day on 4 or more days during the observation period. Data were used to identify minutes and metabolic equivalent task (MET)-minutes per week of MVPA ( $\geq 3.0$  METs) and light-intensity PA (1.5 to  $<3.0$  METs). Percent sedentary time (awake time  $<1.5$  METs) was calculated as sedentary time divided by the activity monitor wear time.

**Dietary Intake:** Dietary intake was assessed used the Diet History Questionnaire, with DietCalc software (version 1.5.0) used for analysis. Subjects reported their typical dietary patterns over the prior month.

**Safety Monitoring:** An external data and safety monitoring board (DSMB) was appointed to assist with oversight of safety monitoring. Additionally, the investigators monitored a variety of safety measures (e.g., resting blood pressure, abnormal exercise test, etc.) and were referred to their primary care physician when appropriate. At each assessment period participants were queried regarding adverse events using a standardized questionnaire, and we observed no serious adverse events related to participation in this study.

## Statistical Analysis

The primary outcome was LVM, and this study was designed to detect an effect size of 0.45 for the change in LVM from baseline to the end of the 12-month weight loss intervention. Applying the Bonferroni-adjustment (2-tailed significance level of 0.0167) to control for three pairwise comparisons, it was estimated that 104 participants per group were required to provide 80% power to detect an effect size of 0.45. To account for up to a 20% attrition rate, the projected sample size was increased from 312 to 390 subjects.

Analyses were performed using SAS version 9.4 (SAS Institute, Cary NC). Baseline characteristics of study participants were presented both overall and by randomization groups, with frequency (percentage) for categorical variables and mean  $\pm$  standard deviation for continuous variables.

All randomized participants were included in intent-to-treat analyses. A linear regression model was fit to examine the effects of three interventions on the primary outcome, change in LVM from baseline to 12-months. Covariate adjustment in the model included randomization stratification factors of race and sex as well as baseline LVM. Adjusted least square mean (LSMEAN) for each intervention was obtained from the model and pairwise group comparison between the LSMEANs was tested at a significance level of 0.0167.

Changes from baseline in weight, BMI, body composition, CRF, fasting lipids, glucose, insulin, CRP, resting blood pressure, and PA measures were assessed at 6- and 12-month. These changes were analyzed by separate mixed effects models with two time points adjusting for race, sex, and baseline level of each outcome. Effects of interventions, time, and interventions by time interaction were tested at 0.05 significance level. Adjusted LSMEANs for each intervention at 6- or 12-month were obtained from the model. Since we considered these as exploratory analyses, each pairwise group comparison between the LSMEANs at 6- or 12-month was tested at a significance level of 0.0167. Missing data were assumed to be missing at random.

## RESULTS

This study randomized 383 participants (DIET=127, DIET+MODPA=129, DIET+HIGHPA=127) with reasons for exclusion shown in Figure 1. Descriptive characteristics are shown in Table 1. At 12 months, weight data were available for 84.1% (322/383) of randomized participants (86.6% [110/127] in DIET, 80.6% [104/129] in DIET+MODPA, 81.9% [105/127] in DIET+HIGHPA) and CMR data were available for 82.8% (317/383) of randomized participants (85.8% [109/127] in DIET, 80.6% [104/129] in DIET+MODPA, 81.9% [104/127] in DIET+HIGHPA).

### CMR Outcomes

CMR outcomes are shown in Table 2 and Figure 2. The primary outcome was LVM, and there was a significant reduction observed at 12 months in DIET [ $-2.9$  grams (95% CI:  $-5.2, -0.7$ );  $P=0.0114$ ] with no change observed in DIET+MODPA [ $-0.8$  grams (95% CI:  $-3.0, 1.5$ );  $P=0.4979$ ] or DIET+HIGHPA [ $-1.1$  grams (95% CI:  $-3.3, 1.1$ );  $P=0.3299$ ]. LVM relative to BSA increased in all groups [DIET= $1.2$  grams/BSA (95%



CI: 0.2, 2.3),  $P=0.0220$ ; DIET+MODPA=2.7 grams/BSA (95% CI: 1.6, 3.7);  $P<0.0001$ ; DIET+HIGHPA=2.0 grams/BSA (95% CI: 1.0, 3.1);  $P=0.0002$ ]. All groups had significant increases in ESV and EDV, with no change in EF. Prespecified pairwise comparisons showed that there was no difference between the interventions for the change in LVM, ESV, EDV, or EF (Table 2, Figure 2).

### Weight and Body Composition

Weight and body composition are shown in Table 3. Weight decreased significantly ( $P<0.0001$ ) across the 12-month intervention with no significant difference among interventions. Weight loss at 6 month was  $-9.3\%$  (95% CI:  $-10.3, -8.2$ ) in DIET,  $-10.3\%$  (95% CI:  $-11.4, -9.2$ ) in DIET+MODPA, and  $-10.3\%$  (95% CI:  $-11.3, -9.2$ ) in DIET+HIGHPA, and weight loss as 12 months was  $-10.2\%$  (95% CI:  $-11.7, -8.8$ ) in DIET,  $-11.0\%$  (95% CI:  $-12.4, -9.5$ ) in DIET+MODPA, and  $-10.3\%$  (95% CI:  $-11.8, -8.9$ ) in DIET+HIGHPA, with the weight loss at 6 and 12 months being significantly different (Time Effect  $P=0.0175$ ). A similar pattern was observed for absolute change in weight, BMI, fat mass, and percent body fat. A modest reduction in lean mass was also observed in each group ( $P<0.0001$ ), with no difference among interventions, and the change at 6 and 12 months did not differ.

### Cardiorespiratory Fitness

CRF is shown in Table 3. There was a significant increase in relative oxygen consumption (ml/kg/min) ( $P<0.0001$ ), with a difference in the pattern of change among the three interventions (Group X Time:  $P=0.0081$ ). A similar pattern was observed when CRF was assessed based on termination time on the graded exercise test. The change in absolute oxygen consumption (L/min) from baseline to 12 months significantly decreased in DIET ( $P=0.0106$ ) with no change in either DIET+MODPA ( $P=0.6158$ ) or DIET+HIGHPA ( $P=0.8883$ ).

### CVD Risk Factors

CVD risk factors are shown in Table 4. Total cholesterol decreased significantly in all groups at 6 months, but at 12 months was only significant for DIET ( $P=0.0004$ ) and DIET+HIGHPA ( $P=0.0010$ ). The decrease in LDL-C was significant at 6 ( $P's<0.0001$ ) and 12 months ( $P's 0.0059$ ) for DIET and DIET+HIGHPA. HDL-C decreased significantly at 6 months for DIET and no significant change for DIET+MODPA or DIET+HIGHPA, with all groups showing a significant increase at 12 months ( $P 0.0001$ ). Triglycerides decreases significantly ( $P<0.0001$ ) in all groups at both 6 and 12 months. Fasting glucose decreased significantly for all groups at 6 months, but at 12 months the decrease was only significant for DIET ( $P=0.0026$ ) and DIET+HIGHPA ( $P=0.0010$ ). Fasting insulin ( $P's<0.0001$ ) and CRP ( $P's 0.0107$ ) decreased significantly in all groups at both 6 and 12 months. SBP significantly decreased at both 6 and 12 months in all groups (all  $P's <0.0001$ ), with a similar pattern observed for change in DBP.

## Dietary Intake

Total calorie intake significantly decreased at both 6 and 12 months in all groups (all  $P$ 's  $<0.0001$ ), with a similar pattern observed for the change in percent of calories consumed as dietary fat (all  $P$ 's  $<0.0001$ ) (Table 5). The percent of calories consumed as carbohydrates increased at both 6 and 12 months in all groups (all  $P$ 's  $0.0035$ ), with a similar pattern for the increase in the percent of calories consumed as protein (all  $P$ 's  $0.0046$ ). The change in total calorie intake and macronutrient composition did not differ between groups.

## Physical Activity

PA is shown in Table 6. Minutes of self-reported PA increased in DIET+MODPA and DIET+HIGHPA at both 6 and 12 months ( $P$ 's $<0.0001$ ), with the change not being statistically significant at either 6 or 12 months for DIET. Based on pairwise comparisons, the change in self-reported PA was significantly different between groups when compared at both 6 months ( $P$ 's  $<0.0001$ ) and 12 months ( $P$ 's  $0.0156$ ). A similar pattern was observed for energy expenditure of self-reported PA; however, the change in self-reported PA did not differ between DIET+MODPA and DIET+HIGHPA at 12 months.

Objectively measured total minutes of MVPA significantly increased in DIET+MODPA and DIET+HIGHPA from baseline to 6 months ( $P$ 's  $0.0001$ ) and in all groups at 12 months ( $P$ 's  $0.0032$ ). Additional post-hoc comparisons showed that all groups differed from each other for the change at 6 months ( $P$ 's  $0.0085$ ) with the change in MVPA being greater in both DIET+MODPA ( $P=0.0081$ ) and DIET+HIGHPA ( $P=0.0064$ ) compared to DIET at 12 months. A similar pattern was observed for the change in total minutes of MVPA.

Objectively measured MET-min/week of MVPA in 10-minute sessions significantly increased in DIET+MODPA and DIET+HIGHPA from baseline to 6 months ( $P$ 's $<0.0001$ ) and in all groups at 12 months ( $P$ 's  $0.0041$ ). Additional post-hoc comparisons showed that all groups differed from each other for the change at 6 months ( $P$ 's  $0.0093$ ) with the change in being greater in both DIET+MODPA ( $P=0.0165$ ) and DIET+HIGHPA ( $P=0.0144$ ) compared to DIET at 12 months. A similar pattern was observed for the change in min/wk of MVPA in 10-minute sessions at 6 months, but the groups did not differ at 12 months.

Objectively measured MET-min/wk of light-intensity PA significantly increased for both DIET+MODPA and DIET+HIGHPA at 6 months ( $P$ 's $<0.0001$ ) and in all groups at 12 months ( $P$ 's  $0.0020$ ), with no difference between groups for the change at either 6 or 12 months. Similar findings were observed for min/wk of light-intensity PA. Sedentary behavior, based on percent of monitor wear time, significantly decreased in all groups at 6 months ( $P$ 's  $0.0123$ ) and 12 months ( $P$ 's $<0.0001$ ); however, only DIET+HIGHPA differed from DIET at 6 months ( $P=0.0039$ ) and DIET+MODPA differed from DIET at 12 months ( $P=0.0069$ ).

## DISCUSSION

This study was designed to examine changes in LVM with weight loss induced by moderate dietary restriction alone or in combination with a moderate or high amount of prescribed PA. Weight loss induced through dietary modification alone resulted in a significant reduction



in LVM, whereas dietary modification combined with moderate-to-high amounts of PA resulted in non-significant reductions in LVM. By comparison, an observational study reported that weight loss was associated with reduction in LVM, however, that study did not report on whether weight loss was achieved with diet or the combination of diet and PA.(27) Weight loss induced by bariatric surgery has also been shown to reduce LVM. (28) The reduction in LVM observed in this study with weight loss in the absence of increased PA, which may be a favorable adaptive response that reduces LVM hypertrophy and cardiovascular risk,(27) appears to be consistent with the prior studies of weight loss. (29) Unique to this study is the finding that weight loss combined with PA may preserve LVM, which may also be a favorable adaptive response that reflects normal or enhanced cardiac function.(17, 18) However, the prespecified pairwise comparisons suggest that the observed changes from baseline may not differ between the interventions. Moreover, the clinical implications of reducing, preserving, or increasing LVM during periods of weight loss are not able to be determined from this study and warrant further investigation.

One could hypothesize potential benefits and clinical implications of reducing LVM with weight loss or potentially preserving LVM with weight loss combined with PA. The Look AHEAD Study found that an intensive lifestyle intervention focused on weight loss did not decrease composite measures of CVD compared to a diabetes support and education condition;(30) however, post-hoc analysis has shown that participants with a weight loss of at least 10% at one-year or an increase in CRF of at least 2 metabolic equivalents (METS) did have a reduction in cardiovascular outcomes.(4) Additional post-hoc analyses showed that an increased in PA was associated with reduced risk of cardiovascular outcomes.(31) While the mechanisms by which weight loss, CRF, and PA reduced the risk of CVD outcomes in Look AHEAD have not been determined, the results of the current study showed that weight loss of at least 10% in the absence of increased PA may result in an adaptive reduction in LVM, whereas PA when added to weight loss may result in an adaptive preservation of LVM. These may provide potential mechanistic pathways for the cardiovascular benefits of weight loss and PA within the context of obesity treatment that warrant further investigation. Future studies should also consider inclusion of extracellular volume (ECV) measures, which may provide valuable information on myocardial “quality” (i.e., extent of excess interstitial expansion, usually from myocardial fibrosis) beyond quantity (LVM).(32)

Weight loss is associated with improvements in numerous cardiometabolic risk factors.(1) The interventions in this study improved resting blood pressure, fasting lipids, fasting glucose, fasting insulin, and inflammation. PA, when added to weight loss, did not add to the improvements in these CVD risk factors. This may suggest that weight loss of the magnitude achieved in this study should be a focus of interventions to improve cardiometabolic health in adults with overweight or obesity. However, it is possible that when weight loss of a lesser magnitude is achieved, PA may have a greater influence on these cardiometabolic risk factors.

Strengths include a randomized design with retention of >80% of participants. The intervention successfully achieving mean weight loss of approximately 10% of baseline weight in all interventions by 6 months with this magnitude of mean weight loss maintained

for an additional 6 months. There was randomization to different amounts of PA, and the intervention was successful at achieving different amounts of PA across the three groups. Moreover, this study included best practice assessment of LVM and other cardiometabolic profiles.

There are limitations to consider. Participants were age 18 to 55 years, primarily women who were white/Caucasian, and relatively healthy with no known medical conditions that would limit participation in this study (e.g., CVD, diabetes, etc.). It is unclear if similar results would be observed in populations with different characteristics or medical conditions that were excluded in this study. Moreover, objective measures of dietary intake and compliance were not included in this study. The lack of statistical significance between groups for the change in the primary outcome of LVM may be reflection of the sample size of this study, which should be considered for further studies of weight loss and its effects on LVM.

## CONCLUSIONS

Weight loss achieved through dietary modification resulted in reduced LVM, whereas with the addition of PA LVM appears to be preserved, and both may be favorable adaptive responses that reduce cardiovascular risk. Findings suggest that weight loss should be considered as a potential treatment to reduce LVM and its association with cardiovascular health risk. Findings also support that PA within the context of a behavioral weight loss intervention may assist in preserving or enhancing cardiac structure in adults with overweight or obesity. This may be a favorable adaptive response, but this cannot be confirmed with this study. Further investigation is needed to understand the complexity of lifestyle on LVM and the clinical implications of the potential opposing, and potential beneficial, effects of weight loss and PA on cardiac structure in adults with overweight or obesity.

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Data sharing for this study may be available after publication of the main outcomes and only for requests that meet the approved process contained within the informed consent and other institutional policies. These data will not be provided in a public use data set but rather may require approval through a material transfer agreement, and only deidentified data may be made available. Investigators interested in data from this study should contact Dr Jakicic (John.Jakicic@AdventHealth.com), who is the principal investigator, for data sharing policies and procedures after publication.

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Dr. Jakicic has received grant funding from the National Institutes of Health, is on the Scientific Advisory Board for Wondr Health, was formerly on the Scientific Advisory Board for WW International, Inc. and the Advisory Board for Spark360, serves on data and safety monitoring boards for U10HL131552 and P01AG052352, has received remuneration for professional presentations, and serves in as a volunteer in a professional leadership role to the American College of Sports Medicine. Dr. Rogers has received funding from the National Institutes of Health, is a consultant for Wondr Health, has received remuneration for professional presentations, and serves in as a volunteer

in a professional leadership role to the American College of Sports Medicine. Dr. Gibbs has received funding from the National Institutes of Health and the American Heart Association, and serves on data and safety monitoring board for HSRP20153604. Dr. Schelbert serves on the Scientific Advisory Board for Hay Therapeutics. Dr. Lang, Ms. Yuan, and Dr. Fridman have no disclosures.

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**What is already known about this subject?**

- Left ventricular mass (LVM) of the heart is a clinically important prognostic indicator of cardiovascular disease.
- Excess body weight is associated with a maladaptive larger LVM, which may contribute to hypertrophy and potential negative clinical outcomes such as heart failure, in adults with overweight or obesity.
- Exercise can contribute to an adaptive response resulting in larger LVM accompanied by normal or enhanced cardiac function.

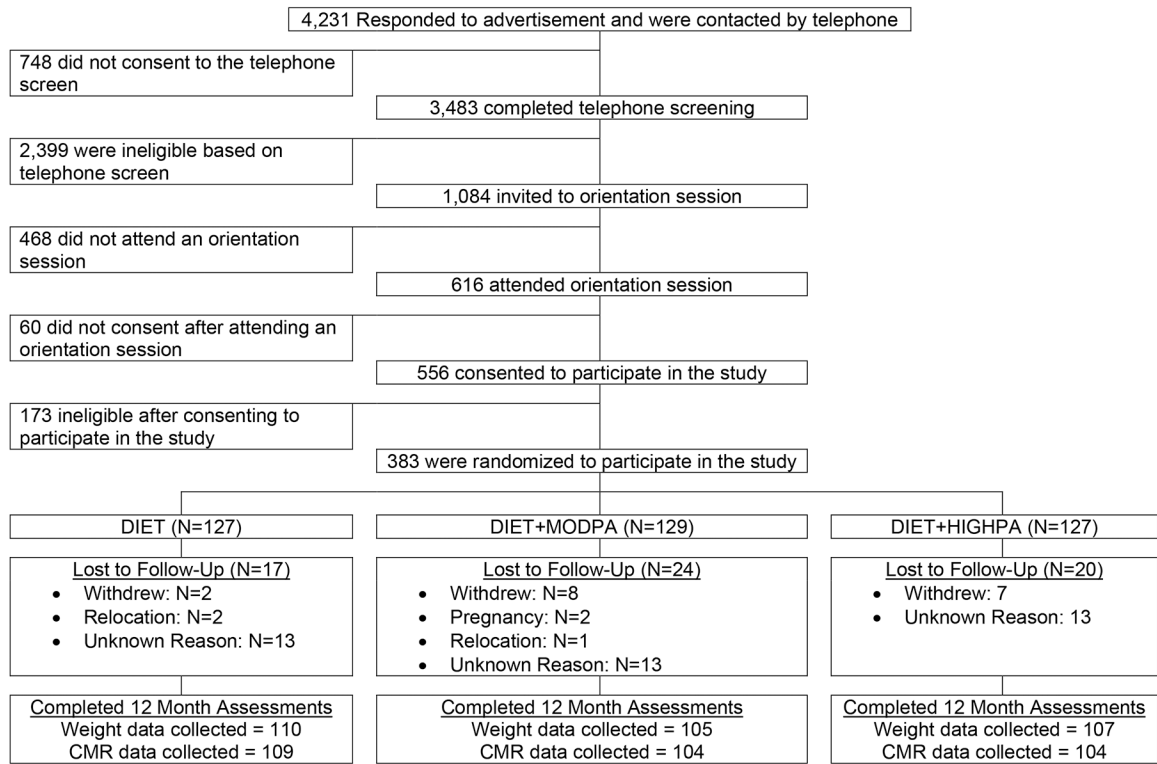
**What are the new findings in your manuscript?**

- Weight loss achieved through dietary modification results in reduced LVM in adults with overweight or obesity.
- Weight loss achieved through dietary modification combined with physical activity, prescribed at 150 minutes per week, preserved LVM in adults with overweight or obesity.

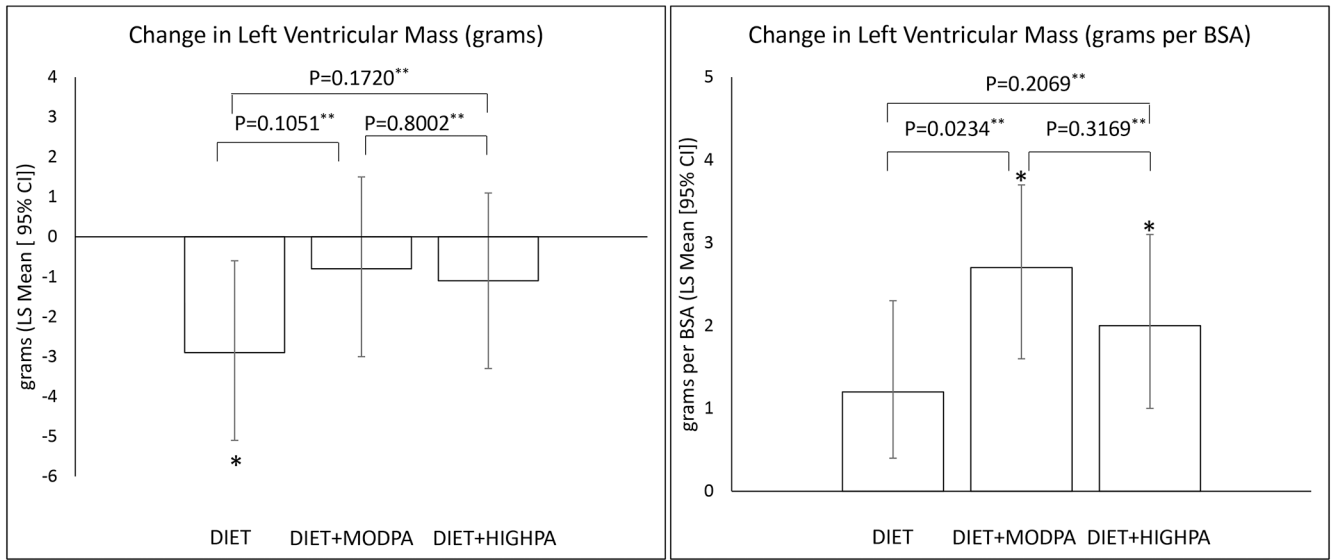


**How might your results change the direction of research or the focus of clinical practice?**

- Diet induced weight loss reduces LVM in adults with overweight or obesity, which may be a favorable adaptive response to reduce cardiovascular risk.
- Physical activity within a behavioral weight loss intervention may preserve cardiac structure in adults with overweight or obesity, and this may be a favorable adaptive response that reflects a normal or enhanced cardiac function.
- Investigation is needed to understand the complex and potential opposing effects of lifestyle on LVM.



**Figure 1.**  
Consort diagram.



**Figure 2.**  
 Change in left ventricular mass  
 \*indicates significant change from baseline at p 0.0167, \*\*indicates p-value for pairwise comparison, BSA = body surface area

**Table 1.**

Baseline characteristics of participants by intervention condition.

Variable	Total (N=383)	Randomized Group		
		DIET (N=127)	DIET+MODPA (N=129)	DIET+HIGHPA (N=127)
Age, years *	45.6±8.0	44.3±8.0	46.8±7.6	45.6±8.1
Gender **				
Male	N=79 (20.6%)	N=26 (20.5%)	N=27 (21.0%)	N=26 (20.5%)
Female	N=304 (79.4%)	N=101 (79.5%)	N=102 (79.1%)	N=101 (79.5%)
Race **				
White	N=273 (71.3%)	N=91 (71.7%)	N=93 (72.1%)	N=89 (70.1%)
Non-white	N=110 (28.7%)	N=36 (28.4%)	N=36 (28.0%)	N=38 (29.9%)
Hispanic/Latino **				
Yes	N=13 (3.4%)	N=5 (3.9%)	N=3 (2.3%)	N=5 (3.9%)
No	N=370 (96.6%)	N=122 (96.1%)	N=126 (97.7%)	N=122 (96.1%)
Weight, kg *	90.9±13.7	91.8±14.5	89.9±13.5	91.0±13.1
Body mass index, kg/m <sup>2</sup> *	32.4±3.8	32.6±3.5	32.3±3.8	32.2±4.0
Education **				
High school graduate or Graduate Equivalency Degree	N=123 (32.1%)	N=32 (25.2%)	N=46 (35.7%)	N=45 (35.4%)
College graduate or higher	N=256 (66.8%)	N=93 (73.3%)	N=82 (63.6%)	N=81 (63.8%)
Relationship Status **				
Married	N=225 (58.8%)	N=73 (57.5%)	N=82 (63.6%)	N=70 (55.1%)
Separated/Divorced	N=54 (14.1%)	N=21 (16.5%)	N=16 (12.4%)	N=17 (13.4%)
Widowed	N=2 (0.5%)	N=1 (0.8%)	N=0 (0.0%)	N=1 (0.8%)
Single/Not Married	N=102 (26.6%)	N=32 (25.2%)	N=31 (24.0%)	N=39 (30.7%)
Household income **				
Less than \$25,000	N=68 (17.9%)	N=23 (18.3%)	N=27 (21.3%)	N=18 (14.3%)
\$25,000 and more	N=300 (79.2%)	N=102 (81.0%)	N=96 (75.6%)	N=102 (81.0%)
Participant did not report income	N=11 (2.9%)	N=1 (0.8%)	N=4 (3.2%)	N=6 (4.8%)

\* indicates data presented as Mean ± Standard Deviation

\*\* indicates data presented as N (%)

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**Table 2.**

Change in cardiac magnetic resonance imaging measures by intervention condition.

	Least-Squares Mean (95% CI) *		P value *	P values for pairwise comparisons ***		
	Baseline	Change from baseline to 12 months		DIET vs. DIET+MODPA	DIET vs. DIET+HIGHHPA	DIET+MODPA vs. DIET+HIGHHPA
<b>Left Ventricular Mass (grams)</b>						
DIET	N = 383	N = 317	0.2169	0.1051	0.1720	0.8002
	90.9 (87.2, 94.6)	-2.9 (-5.2, -0.7) P = 0.0114				
DIET+MODPA	88.2 (84.2, 92.1)	-0.8 (-3.0, 1.5) P = 0.4979				
DIET+HIGHHPA	87.7 (84.4, 91.1)	-1.1 (-3.3, 1.1) P = 0.3299				
<b>Left Ventricular Mass (grams per BSA)</b>						
DIET	N = 383	N = 317	0.0752	0.0234	0.2069	0.3169
	43.2 (42.0, 44.5)	1.2 (0.2, 2.3) P = 0.0220				
DIET+MODPA	42.5 (41.0, 44.0)	2.7 (1.6, 3.7) P <0.0001				
DIET+HIGHHPA	42.0 (40.7, 43.2)	2.0 (1.0, 3.1) P = 0.0002				
<b>Resting End-Systolic Volume</b>						
DIET	N = 383	N = 317	0.5958	0.7457	0.3173	0.5053
	54.2 (51.8, 56.6)	3.6 (1.5, 5.7) P = 0.0010				
DIET+MODPA	54.3 (51.7, 56.9)	3.2 (1.0, 5.3) P = 0.0042				
DIET+HIGHHPA	55.4 (53.0, 57.8)	2.3 (0.1, 4.5) P = 0.0441				
<b>Resting End-Diastolic Volume</b>						
DIET	N = 383	N = 317	0.9994	0.9879	0.9845	0.9726
	151.1 (145.9, 156.3)	6.3 (3.4, 9.3) P <0.0001				
DIET+MODPA	145.8 (140.6, 151.0)	6.3 (3.4, 9.3) P <0.0001				
DIET+HIGHHPA	146.7 (142.5, 150.8)	6.4 (3.4, 9.4) P <0.0001				



	Least-Squares Mean (95% CI) *		P value *	P values for pairwise comparisons ***		
	Baseline	Change from baseline to 12 months		DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
<b>Resting Ejection Fraction</b>	N = 383	N = 317	0.7725	0.5629	0.5129	0.9378
DIET	64.4 (63.6, 65.2)	-0.3 (-1.2, 0.7) P = 0.5758 **				
DIET+MODPA	63.3 (62.5, 64.1)	-0.6 (-1.6, 0.3) P = 0.2104 **				
DIET+HIGHPA	63.0 (62.3, 63.8)	-0.7 (-1.6, 0.3) P = 0.1827 **				

\* P-value comparing the change between groups. The model includes adjustment for sex, race, and baseline value.

\*\* P-value for change from baseline for each specific group, with the critical p-value set at 0.0167 to adjust for multiple comparisons.

\*\*\* P-value for comparison of groups for change from baseline, with the critical p-value set at 0.0167 to adjust for multiple comparisons.



	Least-Squares Mean (95% CI)*			P value			P value for Pairwise Comparisons of Change at 6 Months****			P value for Pairwise Comparisons of Change at 12 Months****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
DIET+HIGHPA	32.2 (31.5, 32.9)	-3.3 (-3.6,*** -3.0)	-3.3 (-3.8,*** -2.8)									
<b>Lean mass (kg)</b>	N = 383	N = 339	N = 316	0.5348	0.0076	0.4961	0.1164	0.1467	0.9056	0.5206	0.7303	0.7688
DIET	39.3 (38.4, 40.2)	-7.0 (-7.8,*** -6.2)	-7.8 (-8.9,*** -6.6)									
DIET+MODPA	38.6 (37.6, 39.6)	-7.9 (-8.7,*** -7.1)	-8.3 (-9.5,*** -7.2)									
DIET+HIGHPA	39.6 (38.5, 40.8)	-7.8 (-8.6,*** -7.0)	-8.1 (-9.2,*** -6.9)									
<b>Lean mass (kg)</b>	N = 383	N = 339	N = 316	0.5501	0.8615	0.6134	0.7688	0.8999	0.6063	0.3502	0.7478	0.2134
DIET	49.3 (48.1, 50.5)	-1.4 (-1.7,*** -1.1)	-1.4 (-1.7,*** -1.1)									
DIET+MODPA	48.2 (47.2, 49.2)	-1.5 (-1.8,*** -1.2)	-1.6 (-2.0,*** -1.3)									
DIET+HIGHPA	48.3 (47.3, 49.3)	-1.4 (-1.7,*** -1.1)	-1.3 (-1.7,*** -1.0)									
<b>Percent body fat (%)</b>	N = 383	N = 339	N = 316	0.5868	0.0004	0.3299	0.1384	0.0934	0.8450	0.6492	0.7967	0.8458
DIET	43.1 (42.5, 43.7)	-4.2 (-4.8,*** -3.7)	-5.1 (-5.9,*** -4.2)									
DIET+MODPA	42.6 (41.8, 43.4)	-4.8 (-5.4,*** -4.3)	-5.3 (-6.2,*** -4.5)									

	Least-Squares Mean (95% CI)*			P value			P value for Pairwise Comparisons of Change at 6 Months****			P value for Pairwise Comparisons of Change at 12 Months****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
DIET+HIGHPA	43.5 (42.7, 44.2)	-4.9 (-5.5, -4.4)	-5.2 (-6.1, -4.4)									
<b>Cardiorespiratory Fitness (ml/kg/min)</b>	N = 381	N = 331	N = 309	0.0081	0.4946	0.0612	0.0888	0.0008	0.0943	0.0120	0.0476	0.5958
DIET	23.1 (22.5, 23.6)	2.0 (1.4, 2.5)	2.1 (1.4, 2.9)									
DIET+MODPA	22.3 (21.7, 22.9)	2.7 (2.1, 3.2)	3.3 (2.6, 3.7)									
DIET+HIGHPA	22.6 (22.0, 23.1)	3.4 (2.8, 3.9)	3.0 (2.3, 3.7)									
<b>Cardiorespiratory Fitness (L/min)</b>	N = 381	N = 331	N = 309	0.0435	0.1680	0.1228	0.4208	0.0141	0.0983	0.0330	0.0597	0.7983
DIET	2.1 (2.1, 2.2)	-0.03 (-0.08, 0.01)	-0.06 (-0.11, -0.01)									
DIET+MODPA	2.0 (1.9, 2.1)	-0.01 (-0.05, 0.04)	0.01 (-0.04, 0.06)									
DIET+HIGHPA	2.0 (2.0, 2.1)	0.05 (0.00, 0.09)	0.00 (-0.04, 0.05)									
<b>Cardiorespiratory Fitness (termination time, minutes)</b>	N = 383	N = 337	N = 312	0.0285	0.1598	0.5206	0.1630	0.0092	0.2306	0.0638	0.0631	0.09957
DIET	7.8 (7.5, 8.2)	1.6 (1.2, 2.1)	1.5 (1.0, 1.9)									
DIET+MODPA	7.5 (7.1, 7.9)	2.1 (1.6, 2.5)	2.1 (1.6, 2.5)									

	Least-Squares Mean (95% CI)*			P value		P value for Pairwise Comparisons of Change at 6 Months****			P value for Pairwise Comparisons of Change at 12 Months****			
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
DIET+HIGHPA	7.9 (7.5, 8.2)	2.4 (2.0, 2.8)***	2.1 (1.6, 2.5)***									

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\*Model adjusted for sex and race and baseline value.

\*\*P-value for comparison of change at 6 months to change at 12 months.

\*\*\*Indicates change from baseline is statistically significant at p-value 0.0167 to adjust for multiple comparisons.

\*\*\*\*P-value for comparison of groups at specific time points, with the critical p-value set at 0.0167 to adjust for multiple comparisons.

**Table 4.**

Fasting lipids, glucose, insulin, CRP, and resting blood pressure by intervention condition.

	Least-Squares Mean (95% CI) *			P value			P value for Pairwise Comparisons of Change at 6 Months ****			P value for Pairwise Comparisons of Change at 12 Months ****		
	Baseline N = 382	Change from Baseline to 6 months N = 335	Change from Baseline to 12 months N = 314	Group	Time **	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHHPA	DIET+MODPA vs. DIET+HIGHHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHHPA	DIET+MODPA vs. DIET+HIGHHPA
<b>Total Cholesterol (mg/dl)</b>												
DIET	197.2 (191.4, 203.0)	-13.5 (-17.9, -9.1) ****	-8.3 (-12.9, -3.7) ****	0.1091	0.0002	0.8536	0.0573	0.9489	0.0695	0.1576	0.8990	0.2026
DIET+MODPA	199.9 (194.5, 205.4)	-7.4 (-11.9, -2.9) ****	-3.6 (-8.3, 1.0)									
DIET+HIGHHPA	198.3 (191.8, 204.9)	-13.3 (-17.8, -8.7) ****	-7.9 (-12.5, -3.2) ****									
<b>LDL Cholesterol (mg/dl)</b>												
DIET	119.2 (114.0, 124.3)	-7.7 (-11.4, -3.9) ****	-5.7 (-9.8, -1.7) ****	0.1189	0.1437	0.8126	0.0827	0.7384	0.0410	0.2467	0.8706	0.1903
DIET+MODPA	122.2 (117.6, 126.7)	-3.0 (-6.8, 0.8)	-2.3 (-6.4, 1.8)									
DIET+HIGHHPA	120.3 (115.2, 125.4)	-8.6 (-12.4, -4.8) ****	-6.2 (-10.3, -2.1) ****									
<b>HDL Cholesterol (mg/dl)</b>												
DIET	53.6 (51.3, 56.0)	-1.5 (-2.6, -0.4) ****	2.6 (1.3, 3.9) ****	0.0267	<0.0001	0.9672	0.0520	0.0206	0.7039	0.0680	0.0573	0.9351



	Least-Squares Mean (95% CI) *			P value			P value for Pairwise Comparisons of Change at 6 Months ****			P value for Pairwise Comparisons of Change at 12 Months ****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time **	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
DIET+MODPA	52.9 (50.9, 54.9)	0.1 (-1.0, 1.3)	4.3 (3.0, 5.6) ***									
DIET+HIGHPA	53.2 (51.2, 55.2)	0.4 (-0.7, 1.6)	4.4 (3.0, 5.7) ***									
<b>Triglycerides (mg/dl)</b>	N = 382	N = 335	N = 314	0.7939	0.0052	0.9041	0.8752	0.6261	0.5233	0.8707	0.5767	0.6949
DIET	122.4 (109.4, 135.5)	-22.2 (-30.6, -13.9) ***	-27.6 (-33.7, -21.5) ***									
DIET+MODPA	124.9 (112.5, 137.3)	-21.3 (-29.7, -12.8) ***	-28.3 (-34.5, -22.1) ***									
DIET+HIGHPA	124.0 (112.6, 135.4)	-25.2 (-33.7, -16.6) ***	-30.1 (-36.3, -23.8) ***									
<b>Fasting Glucose (mg/dl)</b>	N = 382	N = 335	N = 314	0.7244	0.4840	0.3270	0.3110	0.1878	0.7586	0.6555	0.8124	0.4971
DIET	94.0 (92.0, 96.0)	-3.1 (-4.5, -1.7) ***	-2.7 (-4.5, -1.0) ***									
DIET+MODPA	94.3 (92.0, 96.6)	-2.1 (-3.5, -0.7) ***	-2.2 (-3.9, -0.4) ***									
DIET+HIGHPA	96.5 (94.1, 99.0)	-1.8 (-3.2, -0.4) ***	-3.0 (-4.8, -1.2) ***									
<b>Fasting Insulin (mIU/mL)</b>	N = 382	N = 335	N = 314	0.8412	0.7882	0.4091	0.4575	0.5594	0.8771	0.8919	0.5164	0.4346
DIET	17.5 (16.1, 18.8)	-3.1 (-4.2, -2.0) ***	-3.7 (-4.6, -2.8) ***									

	Least-Squares Mean (95% CI) *			P value			P value for Pairwise Comparisons of Change at 6 Months ****				P value for Pairwise Comparisons of Change at 12 Months ****				
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time **	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
DIET+MODPA	15.3 (14.0, 16.6)	-3.7 (-4.9, -2.6)	-3.8 (-4.7, -2.8)												
DIET+HIGHPA	16.3 (14.3, 18.3)	-3.6 (-4.8, -2.5)	-3.2 (-4.2, -2.3)												
<b>CRP (mg/L)</b>	N = 382	N = 335	N = 314	0.1888	0.8705	0.4596	0.6215	0.2192	0.4643	0.1208	0.1160	0.9802			
DIET	4.3 (3.4, 5.3)	-1.5 (-2.0, -1.0)	-1.8 (-2.5, -1.1)												
DIET+MODPA	4.1 (3.4, 4.8)	-1.3 (-1.8, -0.8)	-1.0 (-1.7, -0.2)												
DIET+HIGHPA	4.5 (3.7, 5.3)	-1.0 (-1.5, -0.6)	-1.0 (-1.7, -0.2)												
<b>Resting Systolic Blood Pressure (mmHg)</b>	N = 383	N = 340	N = 321	0.9809	0.0452	0.8414	0.8694	0.8397	0.7166	0.8631	0.7590	0.8940			
DIET	120.2 (118.2, 122.2)	-5.1 (-6.7, -3.4)	-4.3 (-6.0, -2.6)												
DIET+MODPA	120.1 (118.1, 122.1)	-4.9 (-6.6, -3.2)	-4.1 (-5.8, -2.3)												
DIET+HIGHPA	120.2 (118.0, 122.3)	-5.3 (-7.0, -3.6)	-3.9 (-5.7, -2.1)												
<b>Resting Diastolic Blood Pressure (mmHg)</b>	N = 383	N = 340	N = 321	0.1720	0.1483	0.5463	0.1347	0.7042	0.0635	0.6681	0.3075	0.1523			

	Least-Squares Mean (95% CI) *			P value			P value for Pairwise Comparisons of Change at 6 Months ****			P value for Pairwise Comparisons of Change at 12 Months ****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time **	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
DIET	72.0 (70.5, 73.5)	-3.2 (-4.3,*** -2.1)	-2.3 (-3.4,*** -1.1)									
DIET+MODPA	72.3 (70.8, 73.8)	-2.0 (-3.1,*** -0.8)	-1.9 (-3.1,*** -0.7)									
DIET+HIGHPA	72.5 (70.8, 74.1)	-3.5 (-4.7,*** -2.4)	-3.1 (-4.3,*** -1.9)									

\*Model adjusted for sex and race and baseline value.

\*\*P-value for comparison of change at 6 months to change at 12 months.

\*\*\*Indicates change from baseline is statistically significant at p-value 0.0167 to adjust for multiple comparisons.

\*\*\*\*P-value for comparison of groups at specific time points, with the critical p-value set at 0.0167 to adjust for multiple comparisons.

**Table 5.**

Dietary Intake by Intervention Condition.

	Least-Squares Mean (95% CI) *			P value			P value for Pairwise Comparisons of Change at 6 Months ****			P value for Pairwise Comparisons of Change at 12 Months ****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
<b>Intake: Total calories (kcal/day)</b>	N = 382	N = 332	N = 302	0.1633	0.7737	0.3997	0.1288	0.3917	0.5075	0.1201	0.7232	0.0595
DIET	1867.4 (1696.1, 2038.7)	-544.6 (-631.5, -457.7) ****	-526.7 (-610.7, -442.7) ****									
DIET+MODPA	1804.9 (1651.9, 1957.9)	-448.5 (-537.2, -359.7) ****	-431.2 (-517.8, -344.7) ****									
DIET+HIGHPA	1765.0 (1621.4, 1908.6)	-490.7 (-578.8, -402.5) ****	-548.3 (-633.9, -462.8) ****									
<b>Intake: % calories carbohydrates</b>	N = 382	N = 332	N = 302	0.9781	0.3009	0.3001	0.6576	0.4949	0.8139	0.5221	0.3206	0.7301
DIET	48.2 (46.6, 49.8)	3.9 (2.4, 5.4) ****	2.3 (0.8, 3.9) ****									
DIET+MODPA	47.7 (46.0, 49.4)	3.4 (1.9, 5.0) ****	3.1 (1.5, 4.7) ****									
DIET+HIGHPA	46.7 (45.1, 48.3)	3.2 (1.6, 4.7) ****	3.5 (1.9, 5.1) ****									
<b>Intake: % calories protein</b>	N = 382	N = 332	N = 302	0.3885	0.1684	0.4449	0.1590	0.0992	0.8143	0.5732	0.9264	0.6409
DIET	15.5 (14.9, 16.1)	0.9 (0.38, 1.4) ****	0.9 (0.3, 1.5) ****									
DIET+MODPA	15.8 (15.2, 16.4)	1.5 (0.9, 2.0) ****	1.1 (0.5, 1.7) ****									

	Least-Squares Mean (95% CI)*			P value			P value for Pairwise Comparisons of Change at 6 Months****			P value for Pairwise Comparisons of Change at 12 Months****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHHPA	DIET+MODPA vs. DIET+HIGHHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHHPA	DIET+MODPA vs. DIET+HIGHHPA
DIET+HIGHHPA	15.8 (15.2, 16.3)	1.6 (1.0, 2.1)***	0.9 (0.3, 1.5)***									
<b>Intake: % Calories fat</b>	N = 382	N = 332	N = 302	0.7443	0.0019	0.4207	0.3661	0.9141	0.4290	0.6751	0.3526	0.6165
DIET	36.2 (35.0, 37.4)	-5.3 (-6.5, -4.1)***	-3.3 (-4.7, -2.0)***									
DIET+MODPA	36.9 (35.5, 38.3)	-4.5 (-5.8, -3.3)***	-3.7 (-5.1, -2.4)***									
DIET+HIGHHPA	37.3 (36.0, 38.5)	-5.2 (-6.4, -4.0)***	-4.2 (-5.6, -2.9)***									

\*Model adjusted for sex and race and baseline value.

\*\*P-value for comparison of change at 6 months to change at 12 months.

\*\*\*Indicates change from baseline is statistically significant at p-value 0.0167 to adjust for multiple comparisons.

\*\*\*\*P-value for comparison of groups at specific time points, with the critical p-value set at 0.0167 to adjust for multiple comparisons.

**Table 6.**

Physical Activity by Intervention Condition.

	Least-Squares Mean (95% CI) *			P value		P value for Pairwise Comparisons of Change at 6 Months ****				P value for Pairwise Comparisons of Change at 12 Months ****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time **	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
<b>Self-Reported Physical Activity # (kcal/wk)</b>	N = 383	N = 338	N = 317	<0.0001	0.9476	0.0395	<0.0001	<0.0001	0.0001	<0.0001	<0.0001	0.2423
DIET	525.8 (453.7, 597.9)	122.3 (0.6, 244.1)	89.3 (-60.4, 238.9)									
DIET+MODPA	595.6 (493.3, 697.8)	580.2 (456.1, 704.4) ****	743.7 (590.8, 896.6) ****									
DIET+HIGHPA	638.3 (532.8, 743.8)	993.4 (869.3, 1117.5) ****	872.1 (720.3, 1024.0) ****									
<b>Self-Reported Physical Activity \$ (kcal/wk)</b>	N = 383	N = 338	N = 317	<0.0001	0.7290	0.0780	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0657
DIET	310.9 (241.8, 379.9)	121.6 (3.9, 239.3)	69.9 (-71.6, 211.5)									
DIET+MODPA	371.1 (276.6, 465.6)	562.6 (442.5, 682.7) ****	685.6 (540.8, 830.3) ****									
DIET+HIGHPA	404.6 (307.0, 502.2)	994.7 (874.7, 1114.6) ****	877.2 (733.5, 1020.8) ****									
<b>Self-Reported Physical Activity (min/wk) \$</b>	N = 383	N = 338	N = 317	<0.0001	0.3911	0.2904	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0156

	Least-Squares Mean (95% CI)*			P value			P value for Pairwise Comparisons of Change					
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA at 6 Months	DIET vs. DIET+HIGHPA at 6 Months	DIET vs. DIET+MODPA at 12 Months	DIET vs. DIET+HIGHPA at 12 Months	DIET vs. DIET+MODPA at 12 Months	DIET vs. DIET+HIGHPA at 12 Months
DIET	59.4 (46.3, 72.4)	23.0 (3.3, 42.6)	12.4 (-11.0, 35.8)									
DIET+MODPA	69.3 (52.1, 86.4)	105.3 (85.2, 125.4)***	114.8 (90.9, 138.7)***									
DIET+HIGHPA	75.7 (58.3, 93.0)	174.0 (154.0, 194.1)***	156.4 (132.7, 180.2)***									
<b>Total MVPAs<sup>†</sup> min/wk<sup>†</sup></b>	N = 375	N = 320	N = 301	<0.0001	0.0108	0.1192	0.0085	<0.0001	0.0081	0.0084	0.0064	0.9557
DIET	1292.3 (1051.5, 1533.0)	142.6 (-71.2, 356.4)	407.1 (137.1, 677.1)***									
DIET+MODPA	1392.4 (1127.6, 1657.1)	555.4 (335.7, 775.1)***	936.7 (654.3, 1219.0)***									
DIET+HIGHPA	1321.8 (1045.8, 1597.8)	969.7 (754.8, 1184.7)***	947.8 (669.7, 1226.0)***									
<b>Total MVPAs<sup>†</sup> (min/wk)<sup>†</sup></b>	N = 375	N = 320	N = 301	<0.0001	0.0086	0.1302	0.0364	<0.0001	0.0157	0.0066	0.0090	0.8595
DIET	346.2 (288.1, 404.3)	25.8 (-22.7, 74.3)	82.2 (23.0, 141.4)***									
DIET+MODPA	366.6 (301.0, 432.3)	100.1 (50.2, 149.9)***	188.0 (126.1, 249.9)***									
DIET+HIGHPA	350.4 (279.5, 421.3)	197.1 (148.3, 245.8)***	195.8 (134.8, 256.8)***									
<b>Total MVPAs<sup>†</sup> in &gt;40 minute</b>	N = 375	N = 320	N = 301	<0.0001	0.5106	0.0126	0.0093	<0.0001	0.0165	0.0006	0.0144	0.9758

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	Least-Squares Mean (95% CI)*			P value			P value for Pairwise Comparisons of Change at 6 Months****			P value for Pairwise Comparisons of Change at 12 Months****		
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
sessions (MET-min/wk) <sup>^</sup>												
DIET	926.8 (744.6, 1109.0)	128.8 (-59.1, 316.6)	317.2 (101.4, 532.9)***									
DIET+MODPA	1042.9 (834.8, 1250.9)	487.2 (294.1, 680.4)***	700.3 (474.0, 926.5)***									
DIET+HIGHPA	957.1 (749.3, 1165.0)	963.2 (774.4, 1152.2)***	705.2 (482.4, 928.0)***									
Total MET-PA in >10 minute sessions (min/wk) <sup>^</sup>	N = 375	N = 320	N = 301	<0.0001	0.4892	0.0108	0.0486	<0.0001	0.0003	0.0282	0.0282	0.9516
DIET	244.3 (200.9, 287.6)	21.0 (-20.6, 62.6)	57.9 (10.9, 105.0)***									
DIET+MODPA	265.5 (215.6, 315.4)	81.1 (38.3, 123.9)***	134.3 (85.0, 183.6)***									
DIET+HIGHPA	246.4 (193.2, 299.5)	193.4 (151.6, 235.2)***	136.4 (87.9, 185.0)***									
LPA (MET-min/wk) <sup>^</sup>	N = 375	N = 320	N = 301	0.0844	0.3343	0.2771	0.1149	0.1214	0.9662	0.0216	0.5744	0.0858
DIET	2773.3 (2530.3, 3016.3)	202.3 (-4.4, 409.1)	288.2 (106.6, 469.7)***									
DIET+MODPA	2829.4 (2618.8, 3040.1)	440.3 (228.0, 652.6)***	596.0 (406.51, 785.4)***									
DIET+HIGHPA	2556.5 (2362.7, 2750.3)	433.9 (225.9, 641.8)***	362.6 (175.9, 549.4)***									



	Least-Squares Mean (95% CI)*			P value			P value for Pairwise Comparisons of Change				P value for Pairwise Comparisons of Change				
	Baseline	Change from Baseline to 6 months	Change from Baseline to 12 months	Group	Time**	Group x Time	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA	DIET vs. DIET+MODPA	DIET vs. DIET+HIGHPA	DIET+MODPA vs. DIET+HIGHPA
LPA (min/wk) <sup>^</sup>	N = 375	N = 320	N = 301	0.1031	0.3454	0.3397	0.1221	0.1539	0.8934	0.0289	0.6075	0.0982	0.0289	0.6075	0.0982
DIET	1381.4 (1262.8, 1500.1)	158.3 (49.4, 267.2)***	201.9 (105.7, 298.1)***												
DIET+MODPA	1429.9 (1320.3, 1539.6)	281.2 (169.4, 393.1)***	357.0 (256.6, 457.3)***												
DIET+HIGHPA	1283.6 (1185.8, 1381.3)	270.5 (161.0, 380.1)***	238.0 (139.1, 336.9)***												
Sedentary (% of monitor wear time) <sup>^</sup>	N = 375	N = 320	N = 301	0.0096	0.0768	0.1004	0.0478	0.0039	0.3776	0.0069	0.1699	0.1825	0.0069	0.1699	0.1825
DIET	71.4 (68.8, 74.0)	-2.7 (-4.9, -0.6)***	-4.3 (-6.4, -2.2)***												
DIET+MODPA	70.6 (68.1, 73.2)	-5.8 (-8.0, -3.6)***	-8.6 (-10.8, -6.3)***												
DIET+HIGHPA	72.8 (70.3, 75.3)	-7.2 (-9.3, -5.1)***	-6.4 (-8.6, -4.2)***												
Sedentary (hr/day) <sup>^</sup>	N = 375	N = 320	N = 301	0.0748	0.1243	0.0975	0.0525	0.0357	0.8896	0.0587	0.9935	0.0654	0.0587	0.9935	0.0654
DIET	10.4 (9.9, 10.8)	-0.4 (-0.7, -0.1)	-0.7 (-1.1, -0.4)***												
DIET+MODPA	10.3 (9.8, 10.7)	-0.9 (-1.2, -0.5)***	-1.2 (-1.62, -0.9)***												
DIET+HIGHPA	10.5 (10.1, 10.9)	-0.9 (-1.3, -0.6)***	-0.8 (-1.1, -0.4)***												

MET: metabolic equivalent; LPA: light-intensity physical activity (1.5 to <3.0 METs); MVPA: moderate-to-vigorous physical activity (> 3.0 METs).

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\* Model adjusted for sex and race and baseline value.

\*\* P-value for comparison of change at 6 months to change at 12 months.

\*\*\* Indicates change from baseline is statistically significant at p-value 0.0167 to adjust for multiple comparisons.

\*\*\*\* P-value for comparison of groups at specific time points, with the critical p-value set at 0.0167 to adjust for multiple comparisons.

# Indicates self-report and that the variable includes flights of stairs climbed when computing kcal/week.

\$ Indicates self-report and that the variable excludes flights of stairs climbed when computing kcal/week or min/week.

^ Indicates objectively measured.