Physical Activity Level and Insulin Resistance in 6,500 NHANES Adults: The Role of Abdominal Obesity

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Physical Activity Level and Insulin Resistance in 6,500 NHANES Adults:
The Role of Abdominal Obesity

James R. Fowler

A thesis submitted to the faculty of Brigham Young University in partial fulfillment of the requirements for the degree of Master of Science

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ABSTRACT

Physical Activity Level and Insulin Resistance in 6,500 NHANES Adults: The Role of Abdominal Obesity

James R. Fowler
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Master of Science

OBJECTIVE: This cross-sectional study investigated insulin resistance (IR) variation across physical activity (PA) levels in U.S. adults.

METHODS: MET-minutes were utilized to quantify PA using 2 methods: 4 categories were based on relative MET-minutes, and 5 were based on U.S. PA guidelines. IR was indexed using the homeostatic model assessment (HOMA). Effect modification was tested by dividing waist circumferences into sex-specific quartiles, and then evaluating the relationship between PA and HOMA-IR within each quartile separately.

RESULTS: Relative PA was associated with HOMA-IR after controlling for demographic and lifestyle covariates ($F = 11.5$, $P < 0.0001$ and $F = 6.0$, $P = 0.0012$, respectively). Adjusting for demographic and lifestyle covariates also revealed relationships between guideline-based PA and HOMA-IR ($F = 8.0$, $P < 0.0001$ and $F = 4.9$, $P = 0.0017$, respectively). Controlling for waist circumference with the other covariates nullified the relationship between PA and HOMA-IR. Effect modification testing showed that when the sample was delimited to adults with extra-large waists (Quartile 4), relative ($F = 5.6$, $P = 0.0019$), and guideline-based PA ($F = 3.7$, $P = 0.0098$) and HOMA-IR were related. PA and HOMA-IR were not related within the other quartiles.

CONCLUSION: High levels of PA may play a meaningful role in glucose and insulin metabolism in those with abdominal obesity, but not in adults with smaller waists.

Keywords: waist circumference, obesity, fitness, fat, diabetes
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INTRODUCTION

Type 2 diabetes is a serious disease. It is associated with increases in an array of comorbidities, including hypertension, depression, coronary heart disease, and obesity.¹ In 2016, 21 million U.S. adults had diagnosed type 2 diabetes, mostly caused by insulin resistance (IR).² The 2017 National Diabetes Statistics Report estimated that another 84.1 million U.S. adults had prediabetes in 2015, based on fasting glucose or hemoglobin A1c (HbA1c) levels indicative of insulin resistance.³ Combined estimates of those with diagnosed, undiagnosed or prediabetes show that these conditions affect an alarming 43.3% of U.S. adults.³

The disease progression of type 2 diabetes is typically described as the inability of the body to react to the intake of a glycemic load with the correct level of insulin to enable glucose uptake.⁴,⁵ In most cases, failure of the body to respond with the right amount of insulin occurs because the individual is resistant to insulin.⁴,⁵ The natural development usually begins with insulin resistance and progresses until the individual becomes a full-fledged diabetic.

Several factors increase the likelihood of becoming insulin resistant, including obesity, especially abdominal obesity, and physical inactivity.⁶,⁷,⁸ Obesity is associated with increased adipose tissue inflammation and changes in circulating concentrations of adipokines, which contribute to insulin resistance in fat, liver, and skeletal muscle tissue.⁶ The positive relationship between obesity, insulin resistance, and type 2 diabetes is even more troubling as recent trends show that the prevalence of obesity and severe obesity in U.S. adults has grown from 33.7% in 2007 to 2008 to 39.6% in 2015 to 2016. These upward trends further demonstrate the importance of finding effective strategies for the treatment and prevention of insulin resistance and type 2 diabetes.⁹
One strategy, which seems to decrease insulin resistance and reduce the risk of type 2 diabetes, is regular physical activity. This decrease apparently occurs after chronic exercise training, even when the training does not elicit weight loss or a change in body composition. According to some research, when measured objectively, the amount of time engaged in physical activity is associated with increased insulin sensitivity, even in the absence of changes in bodyweight.

While it is recognized that physical activity plays a role in reducing the risk of diabetes and increasing insulin sensitivity, abdominal obesity also appears to influence these relationships meaningfully. However, conclusions regarding the nature of the influence of physical activity and abdominal obesity on insulin sensitivity vary. Some evidence suggests that exercise does not improve insulin sensitivity without concurrent weight loss. Other research indicates that improved insulin sensitivity is influenced by decreases in abdominal fat resulting from exercise training interventions. Furthermore, some investigations have found that exercise alone improves insulin sensitivity independent of changes in body composition. Despite the varying conclusions, evidence shows that lean individuals and those with little abdominal fat present less insulin resistance and diabetes compared to obese individuals. These conflicting findings call for further investigation.

With the incidence of obesity steadily increasing and the many negative health consequences that accompany insulin resistance and type 2 diabetes, more research is needed to develop efficacious prevention and treatment strategies. While many studies have found an inverse relationship between physical activity and insulin resistance, the potential mitigating role abdominal obesity plays in this relationship is not clear. Analyzing data from the National Health and Nutrition Examination Survey (NHANES) could help foster a better understanding of the
interplay between physical activity, abdominal obesity, and insulin resistance within the U.S.

The present study had multiple objectives. The first was to identify the relationship between total physical activity and insulin resistance, indexed by using the homeostatic model assessment of insulin resistance (HOMA-IR), in a large, nationally representative sample of nondiabetic adults. Another purpose was to examine the extent to which age, race, sex, smoking, and BMI (body mass index) collectively influence the relationship between total physical activity and insulin sensitivity. The final aim was to examine the extent to which abdominal obesity, indexed by waist circumference, affects the association between physical activity and insulin resistance.

METHODS
Design

A cross-sectional study design was employed using data acquired from NHANES. NHANES has been a major program of the National Center for Health Statistics (NCHS) since the early 1960s. Findings from the hundreds of variables collected by NHANES are used to determine the prevalence of major diseases and risk factors for diseases with the aim of health promotion and disease prevention. NHANES surveys a nationally representative sample of several thousand, noninstitutionalized civilians in the country each year. Collected information is published online as data files and used in a variety of epidemiological studies and is helpful in creating public health policy and programs. Data from four 2-year cycles (NHANES 1999 to 2000, 2001 to 2002, 2003 to 2004, and 2005 to 2006) were used in this study. After the 2005 to 2006 cycle, NHANES changed the methods used to measure physical activity, hence, additional years could not be included in the present study.
Subjects

NHANES subjects in the present study ranged from 20 to 84 years of age and had data on participation in 48 leisure-time physical activities, fasting blood glucose and insulin levels, race, sex, BMI, smoking status, and waist circumference. A total of 6,500 participants were included in the sample.

Race. The demographic Race was divided by NHANES into Non-Hispanic White, Non-Hispanic Black, Mexican American, Other Race (including Multi-Racial), and Other Hispanic categories. Race was used as a covariate in the investigation.

Height. A stadiometer was used to assess maximum vertical size. With the head free of obstructions, subjects were positioned with head, shoulder blades, buttocks, and heels touching a vertical backboard. Subjects were instructed to look straight ahead, with limbs straight and feet flat on the floor. While the subject took a deep breath and stood as tall as possible, the headboard was lowered, and height was measured. Height measurements were included in the study for the purpose of calculating BMI.

Weight. Overweight and obesity increase risk of insulin resistance and type 2 diabetes. Consequently, body weight data were included in the present study to permit calculation of BMI, which was used as a covariate. Participant weight was measured using a Toledo digital scale. Measurements were taken with subjects wearing minimal clothing, including underwear, disposable paper gowns, and foam slippers.

Body Mass Index (BMI). BMI was used as a covariate in the study. Reductions in BMI are associated with decreased HOMA-IR. BMI allows body weights to be compared independent of height. BMI was calculated by dividing the subject’s weight in kilograms by the square of height in meters. BMI (kg/m²) was classified as follows: underweight (BMI: <
Total Physical Activity. Participants reported the number of days spent participating in each of 48 distinct leisure-time activities (e.g., aerobics, bicycling, running, hunting, soccer, swimming, tennis, yoga, yard work, walking, etc) over the past 30 days, as well as the typical amount of time spent performing each activity per session, in the NHANES physical activity questionnaire (PAQ). Intensity level for each of the 48 activities listed in the PAQ was self-reported. Intensity levels were defined as either moderate (activities that cause only light sweating or a slight to moderate increase in breathing or heart rate) or vigorous (activities that cause heavy sweating or large increases in breathing or heart rate). Frequency of participation and time per bout were used to calculate total time spent in each physical activity. Metabolic equivalents (MET-minutes) were then used to index physical activity quantities for each participant. MET-minutes represent the ratio between metabolic rates while engaging in physical activity and at rest. MET-minutes were calculated by determining the MET value of the activity and multiplying by the duration the activity was performed. MET values assigned by NHANES for the specific activities are listed on the NHANES website. Several studies support the validity of the NHANES self-reported physical activity measure, indexed using MET-minutes, since the variable has been shown to be associated with accelerated aging, risk of mortality, and obesity.

Two methods were used to categorize participant physical activity (PA) based on calculated MET-minutes. The relative method was based on the distribution of MET-minutes within the large NHANES sample. Participants who reported no PA over the past 30 days were classified as Sedentary, comprising 34% of the weighted sample. The remaining participants who
reported some physical activity in the past 30 days were divided into Low (22.5%), Moderate (22.1%), or High (21.4%) categories as evenly as possible without placing participants with the same calculated MET-minute values in different PA categories.

The guideline-based method categorized participants into 5 PA categories according to the 2018 U.S. Physical Activity Guidelines for Americans.³⁰ Again, 34% of the sample was categorized as Sedentary as they reported no PA. Those categorized as Low (21.7%) reported some PA but less than 500 MET-minutes per week. Participants with Moderate physical activity (13.7%) reported ≥ 500 and < 1000 MET-minutes per week. PA levels ≥ 1000 and < 1500 MET-minutes per week were categorized as High (9.3%). Participants with Very High PA levels (21.3%) reported more than 15000 MET-minutes per week. As the with the relative categories, the guideline-based categories were divided as evenly as possible without placing participants with the same calculated MET-minute values in different PA categories.

Waist Circumference. Waist circumference was used as a covariate in the study. Waist circumference is strongly associated with insulin resistance.³¹ One NHANES study of over 3,500 subjects demonstrated that waist circumference is a significantly better predictor of HOMA-IR, fasting glucose, and HbA1c, than BMI.³² Waist circumference is an effective and economical way to index abdominal obesity.

Waist circumference measurements were taken with a steel measuring tape extended parallel to the floor, across the iliac crests, and snug without compressing the skin. A wall mirror was used to ensure correct horizontal alignment of the measuring tape and the recorder verified that the measurer positioned the tape parallel to the floor and that the tape was snug. Each waist circumference measurement was recorded to the nearest 0.1 cm.²¹
Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). Homeostasis model assessment of insulin resistance is the most common method used to calculate insulin resistance. Increased HOMA-IR has been shown to strongly predict the development of type 2 diabetes, statistically independent of impaired glucose tolerance status, obesity, and body fat distribution. Additionally, higher HOMA-IR has also been shown to be independently associated with the risk of developing prediabetes.

HOMA-IR uses the following formula to index insulin resistance: fasting plasma insulin (µU/ml) x fasting plasma glucose (mg/dL)/405. NHANES provided data on participant fasting insulin and fasting glucose measures as well as detailed assessment procedures.

Plasma Fasting Glucose. The NHANES IV data collection protocol was followed for the gathering of fasting blood specimens for glucose analysis. The enzyme hexokinase methodology was used during the three 2-year cycles from 1999 to 2004 to catalyze the reaction necessary to elicit an increase in NADH (nicotinamide adenine dinucleotide) concentration indicative of glucose concentration. The 2005 to 2006 laboratory methodology changed slightly from the previous cycle methods in that it determined glucose concentration by a hexokinase method that used a sample blank correction. To resolve the differences in methodology between cycles, NHANES created a regression equation to convert 2005 to 2006 glucose data to values comparable to 1999 to 2004.


Plasma Fasting Insulin. The NHANES IV data gathering protocol was followed for the collection of fasting blood specimens for insulin analysis. The 1999 to 2000 and 2001 to 2002 cycles used an insulin double-antibody batch method radioimmunoassay (RIA) to measure insulin levels. The 2003 to 2004 NHANES cycle used the Tosoh AIA-PACK
two-site immunoenzymometric assay to assess fasting insulin levels. In the 2005 to 2006 NHANES cycle, the two-site enzyme immunoassay method, Merocodia Insulin ELISA, was used. Due to the changes in the insulin measurement procedures after the 1999 to 2002 cycles, NHANES created a regression equation with the 2003 to 2004 cycle as the reference:

$$\text{Insulin}_{2003-2004} = (1.0027 \times \text{insulin}_{1999-2002}) - 2.2934 \quad (n = 245, r = 0.981).$$

To adjust the 2005 to 2006 insulin data to equate to the 2003 to 2004 data cycle, the following equation was used:

$$\text{Insulin}_{2003-2004} = 1.0526 \times \text{Insulin}_{2005-2006} - 1.5674 \quad (n = 189, r = 0.9870).$$

Smoking. The NHANES smoking file provided data on current cigarette use, history of use, number of cigarettes smoked daily, and other smoking related details for participants. The cumulative tobacco exposure of NHANES participants was measured in pack years. Packs are comprised of 20 cigarettes each. The number of cigarettes smoked per day was multiplied by the number of total years smoked and then divided by 20. Pack years were used as a covariate in this study.

Statistical Analyses

NHANES selects participants using a 4-stage sampling strategy. Therefore, results are generalizable to all noninstitutionalized civilians residing in the United States. In order to generate findings that represent the U.S. population, individual sample weights were applied as part of the analysis process, as recommended by NHANES.

Descriptive data were provided by reporting means ± standard errors (SE) for continuous variables and percentages ± SE for categorical variables. Because fasting blood draws were only performed by NHANES on a subsample of those who gave blood, special sample weights were used, as prescribed by NHANES. SurveyMeans was employed with sample weights to calculate...
means that reflect values for the United States. Similarly, SurveyFreq was utilized to produce prevalence data that reflect values that can be generalized to the United States.

In the present investigation, HOMA-IR was the outcome variable. Individuals who had elevated fasting blood glucose levels signifying diabetes were not included in the analyses. Likewise, participants who took medications to control their blood sugar or to influence their insulin sensitivity were not included. The HOMA-IR distribution was found to deviate significantly from a normal distribution, therefore values were log-transformed.

Total MET-minutes of leisure-time physical activity served as the exposure variable. The relationship between total physical activity and HOMA-IR was determined using linear regression and the SurveyReg procedure. To examine the extent to which the potential confounding variables (ie, age, race, sex, year of assessment, smoking, BMI, and waist circumference) influenced the physical activity and HOMA-IR association, partial correlation was employed.

Effect modification of waist circumference was tested by dividing waist circumferences into sex-specific quartiles, and then evaluating the relationship between total physical activity and HOMA-IR within each sex-specific quartile separately. Partial correlation was also employed in the effect modification test to examine the influence of the potential confounding variables on the relationship between physical activity and HOMA-IR.

Statistical significance was determined using the common 0.05 cut-point, and all P-values were two-sided. SAS version 9.4 (SAS Institute, Inc., Cary, NC) was the computer application employed to generate the statistical outcomes.
RESULTS

Sample weights provided by NHANES were incorporated into each analysis so that all findings are generalizable to the noninstitutionalized adult population of the United States. The frequencies and weighted percentages for each of the categorical exposure variables and covariates are displayed in Table 1. Participants ranged in age from 20 to 84 with a mean (± SE) age of 44.2 ± 0.4 years. Average (± SE) BMI and waist circumference were 27.8 ± 0.1 kg/m² and 95.5 ± 0.3 cm, respectively. Mean (± SE) physical activity (PA) MET-minutes of the sample was 952.1 ± 29.2 minutes per week. Average (± SE) fasting glucose, fasting insulin, and HOMA-IR were 95.1 ± 0.3 mg/dL, 9.3 ± 0.2 mg/dL, and 2.2 ± 0.04, respectively.

According to Table 2, weekly relative physical activity was significantly and inversely related to HOMA-IR after adjusting for age, sex, race, and year of assessment (F = 11.5, P < 0.0001). After further adjusting for BMI and cigarette smoking, participants in the High-R and Moderate-R categories had significantly lower HOMA-IR than adults in the Low-R and Sedentary-R groups (F = 6.0, P = 0.0012). However, when waist circumference values were controlled simultaneously with the other covariates, there was no relationship between relative physical activity and HOMA-IR (F = 1.6, P = 0.1937).

In Table 3, mean HOMA-IR differed significantly across guideline-based physical activity levels in U.S. men and women with the demographic covariates controlled statistically (F = 8.0, P < 0.0001). Specifically, adults in the Sedentary-G and Low-G PA groups differed significantly in HOMA-IR from those in the Moderate-G and High-G PA groups, with adults in the Very High-G category differing significantly from all the other physical activity levels. After adjusting for the demographic and lifestyle variables together, the relationship between HOMA-IR and weekly guideline-based physical activity level was weakened, but remained significant.
(F = 4.9, P = 0.0017). However, after adjusting for all the covariates concurrently, including waist circumference, the relationship was attenuated beyond statistical significance (F = 1.7, P = 0.1673).

To examine the potential modifying effect of waist circumference more comprehensively, the relationship between total MET-minutes of physical activity and insulin resistance was studied across 4 sex-specific quartiles based on waist circumference. The sex-specific quartiles were labeled small, medium, large, and extra-large, with precisely 25% of the sample in each quartile.

Waist circumference for the quartile labeled small averaged (± SE) 78.1 ± 0.2 cm for men and women combined. Small waist circumferences ranged from 50 cm to 89.25 cm for men and 50 cm to 80.8 cm for women. Men and women in the medium quartile had an average (± SE) waist circumference of 89.5 ± 0.1 cm, with men’s waists ranging from 89.25 to 97.6 cm and women’s waists ranging from 80.8 to 90.15 cm. The average (± SE) waist circumference for a person in the large waist quartile was 98.9 ± 0.1 cm, with men’s waist ranging from 97.6 to 107.25 cm and women’s waists ranging from 90.15 to 102.25 cm. Participant waist circumferences in the extra-large quartile averaged (± SE) 115.7 ± 0.4 cm, with men’s waists measuring > 107.25 cm and women’s > 102.25 cm, respectively.

Table 4 shows that there were no significant relationships between relative PA and HOMA-IR among those with small, medium, or large waists. However, when the sample of 6,500 was delimited to adults with extra-large waists only (Quartile 4), total MET-minutes of relative physical activity and HOMA-IR were related significantly. Specifically, with the demographic covariates controlled, mean HOMA-IR levels between the Sedentary-R and Low-R participants were not different; likewise, there was no difference between the mean HOMA-IR
levels of Moderate-R and High-R participants. However, mean HOMA-IR levels differed significantly between the Sedentary-R and Low-R participants compared to the Moderate-R and High-R participants across the relative physical activity categories (F = 8.8, P < 0.0001).

Moreover, after adjusting for the lifestyle covariates, in addition to the demographic variables, the relative PA and HOMA-IR relationship was strengthened between the Sedentary-R and Low-R participants, and the Moderate-R and High-R participants (F = 10.5, P < 0.0001). Including waist as a covariate with the other covariates weakened the relationship within the sample of individuals with extra-large waists, but it remained strong and significant (F = 5.6, P = 0.0019).

Specifically, the Sedentary-R category differed significantly from the Moderate-R and High-R groups.

In Table 5, all the models that focused on guideline-based physical activity and HOMA-IR were significant with the sample delimited to adults with extra-large waists. Specifically, applying the covariates of each model in succession, Sedentary-G and Low-G participants differed significantly from the Moderate-G, High-G, and Very High-G groups for each model respectively (F = 4.3, P = 0.0039, F = 5.3, P = 0.0011, and F = 3.7, P = 0.0098).

DISCUSSION

The primary objective of the present investigation was to examine the relationship between physical activity, indexed using total MET-minutes per week based on 48 leisure-time activities, and insulin resistance, indexed by HOMA-IR, in a large representative sample of the U.S. adult population. A secondary aim was to determine the extent to which age, race, sex, year of assessment, smoking, and BMI collectively influence the relationship between total physical activity and insulin sensitivity. Another key objective was to identify the role abdominal obesity plays in the association between physical activity and insulin resistance.
To assess the relationship between physical activity and insulin resistance, 2 methods of categorizing physical activity were employed. The Relative method was based on the distribution of MET-minutes within the large NHANES sample. The guideline-based method employed the 2018 Physical Activity Guidelines for Americans to form categories. According to Guideline criteria, 44.3% of U.S. adults met or exceeded the physical activity standards.

Interestingly, average HOMA-IR levels for adults in the High category for relative physical activity were nearly identical to those in the Very High category using the guideline-based method. Similarly, HOMA-IR means in the Moderate category based on the relative method were nearly identical to those in the Moderate and High categories using the guideline-based method. The use of 2 methods to categorize physical activity allows the findings of this study to be compared more easily to other investigations.

Results from the present investigation indicate that after controlling for age, sex, race, and year of assessment, mean HOMA-IR decreased significantly as levels of weekly physical activity increased. Though weakened, this relationship persisted after additionally controlling for BMI and cigarette smoking. However, the relationship between physical activity and HOMA-IR completely disappeared after adjusting for differences in waist circumference simultaneously with the other covariates. These findings suggest that waist circumference mediates the relationship between physical activity level and HOMA-IR. In other words, if all adults had the same waist circumference in the U.S., physical activity and insulin resistance would not be related. Evidently, insulin resistance decreases as physical activity levels increase in U.S. adults, mostly because active individuals tend to have smaller waists than those who are inactive.
In reference to Table 2, of the 4 categories of relative physical activity, the Sedentary and Low HOMA-IR means were strikingly similar for each covariate model. The same was true for the HOMA-IR means associated with the Moderate and High categories. Due to these similarities, it would be reasonable to combine the 4 categories in Table 2 into 2 physical activity categories: Sedentary with Low, and Moderate with High. Significant differences in HOMA-IR only became apparent in the demographics and demographics & lifestyle covariate models when participants achieved the Moderate physical activity threshold.

Due to the mediating influence waist circumference seems to have on the relationship between physical activity level and HOMA-IR, the association was examined within each sex-specific quartile of waist circumference. The effect modification findings were enlightening. There was no relationship between physical activity and HOMA-IR among adults with small (Quartile 1), medium (Quartile 2), or large (Quartile 3) waists, considered separately. However, among adults with extra-large waists (Quartile 4), the association between physical activity and HOMA-IR was strong. Again, differences in waist circumference seem to be a key factor underlying the association between physical activity and insulin resistance. Physical activity does not appear to play a role in HOMA-IR differences among adults with small, medium, or large waists. However, evidence from the present study suggests that activity level plays a major role in insulin resistance in U.S. adults with extra-large waists. In short, although physical activity is important for all adults, when it comes to adults with abdominal obesity, an abundance of physical activity seems to account for lower levels of insulin resistance.

A 2016 cross-sectional study by García-Hermoso et al examined the influence of abdominal obesity on the relationship between physical activity and insulin resistance in 1,163 adult men and women randomly selected from outpatient clinics in different regions of Spain.44
As with the present investigation, García-Hermoso found that controlling for waist circumference completely removed the association between moderate to vigorous physical activity and fasting plasma glucose, fasting plasma insulin, and HOMA-IR. Similarly, a 2006 study by O’Leary et al concluded that the loss of abdominal visceral fat through exercise alone correlated with decreased insulin resistance. These studies confirm the findings of the present study showing that reduced waist circumference and abdominal adiposity may play a critical role in mediating the relationship between physical activity and insulin resistance.

Notwithstanding the studies by García-Hermoso and O’Leary, there is no clear consensus about the mitigating role abdominal obesity plays in the relationship between physical activity and insulin resistance. A study by DiPietro et al found that moderate-intensity aerobic training improved glucose tolerance, independent of changes in abdominal adiposity. Moreover, in a 2007 study on exercise and insulin resistance in obese children, it was determined that exercise alone, independent of body composition changes, reduced insulin resistance. Interestingly, waist circumferences for these children decreased significantly over the exercise training period while DEXA-measured abdominal fat and lean mass remained the same.

An overwhelming majority of observational and population-based studies examining the effects of body fat on health have determined that central obesity is the most significant risk factor for insulin resistance and type 2 diabetes. The accumulation of excess visceral fat has destructive effects on glucose and insulin metabolism. Obese individuals show increased proliferation of macrophages and increased macrophage participation in inflammatory pathways compared with lean individuals. Visceral fat is a key endocrine organ engaged in the intricate interplay between obesity and systemic inflammation, due partially to its direct hepatic portal access and its ability to secrete greater amounts of proinflammatory adipokines than
subcutaneous fat. The literature widely acknowledges that the chronic inflammation associated with obesity induces pancreatic beta cell dysfunction and insulin resistance.

A study by Barzilai et al demonstrated that visceral fat is a potent modulator of insulin action by surgically removing selective intra-abdominal fat deposits in rats, which improved levels and rates of insulin infusion necessary to maintain plasma glucose levels. Furthermore, a study by Gabriely et al found that removing visceral fat in rats improved insulin action and delayed the onset of diabetes.

Evidently, not all lipectomies performed in human subjects have shown the link between insulin resistance and visceral fat. One study examining laparotomic gastric bypass with or without omentectomy showed no additional benefit to improved blood glucose levels or serum insulin from the omentectomy surgery. Another similar study found that omentectomy did not enhance the effect of Roux-en-Y gastric bypass surgery on insulin sensitivity, but was associated with preserved insulin secretion, lower circulating C-reactive protein (CRP) levels, and greater weight loss. In a more recent study, significant quantities of mesenteric visceral fat were successfully surgically excised from obese, insulin-resistant baboons, effectively reversing insulin resistance and promoting significant weight loss.

In the present study, adults with extra-large waists (Quartile 4) showed a strong association between higher levels of physical activity and lower HOMA-IR values, while effect modification showed no association between physical activity levels and insulin resistance in adults with small, medium, or large waists, considered separately. It may be that adults with extra-large waists who participate in regular physical activity are able to decrease the inflammation contributing to increased insulin resistance. Increasing evidence supports the idea that physical inactivity directly causes the inflammation and metabolic dysfunction associated
with obesity.\textsuperscript{55,56} Furthermore, physical activity is able to mediate inflammation and metabolic dysfunction without changes in body weight.\textsuperscript{55} Moreover, obese individuals typically have 2 to 3 times the plasma concentration of inflammatory markers such as Interleukin (IL)-6 and c-reactive protein of nonobese individuals.\textsuperscript{55}

Strengths of the present study include its large sample size of 6,500 U.S. adults from the ongoing NHANES study conducted by the Centers for Disease Control and Prevention. Participants were randomly selected within the United States. Therefore, the results can be generalized to all civilian, noninstitutionalized adults in the United States. Another strength is that 2 methods of categorizing PA were employed: relative PA, based on the distribution of MET-minute levels for the NHANES sample, and guideline-based PA, based on the 2018 U.S. Physical Activity Guidelines for Americans.\textsuperscript{30} In addition to waist circumference, a number of demographic and lifestyle covariates were controlled, including age, sex, race, year of assessment, BMI, and cigarette smoking. Lastly, evidence of effect modification was tested by examining the activity and HOMA-IR relationship within each sex-specific quartile of waist circumference.

Weaknesses inherent to this investigation include the cross-sectional design of the study, which prohibits the establishment of causal relationships. Additionally, it is possible that participants who self-reported high levels of physical activity are representative of adults who engage in lifestyles uniquely different from others. Statistical controls were applied to minimize the lifestyle differences, but this risk cannot be eliminated.

CONCLUSION

In a random sample of 6,500 U.S. adults, total MET-minutes of leisure-time physical activity accounted for significant differences in measured insulin resistance. However, the
inverse relationship was nullified when participant waist sizes were included in the model, suggesting that the physical activity and insulin resistance relationship is mediated by abdominal obesity. Moreover, effect modification showed that there was no association between physical activity level and insulin resistance in adults with small, medium, or large waists, considered separately. Nevertheless, the relationship was strong among U.S. adults with very large waists (4th quartile), suggesting that high levels of physical activity may play a meaningful role in glucose and insulin metabolism among those with abdominal obesity, but not in adults with smaller waists.
REFERENCES


15. DiPietro L, Dziura J, Yeckel CW, Neufer PD. Exercise and improved insulin sensitivity in
older women: evidence of the enduring benefits of higher intensity training. *J Appl Physiol.* 2006;100(1):142-149. doi:10.1152/japplphysiol.00474.2005


36. NHANES 1999-2000: plasma fasting glucose, serum c-peptide and; insulin data


49. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion


Table 1. Descriptive characteristics of the sample (n = 6500).

<table>
<thead>
<tr>
<th>Variable</th>
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<td>Non-Hispanic Black</td>
<td>1190</td>
<td>10.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Mexican American</td>
<td>1463</td>
<td>7.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Other Race</td>
<td>213</td>
<td>4.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Other Hispanic</td>
<td>263</td>
<td>4.7</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>3090</td>
<td>47.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Women</td>
<td>3410</td>
<td>52.2</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Waist Circumference</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>1447</td>
<td>25.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Medium</td>
<td>1555</td>
<td>25.0</td>
<td>0.7</td>
</tr>
<tr>
<td>Large</td>
<td>1775</td>
<td>25.0</td>
<td>0.7</td>
</tr>
<tr>
<td>Extra-large</td>
<td>1723</td>
<td>25.0</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Body Mass Index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>108</td>
<td>2.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Normal weight</td>
<td>2058</td>
<td>34.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Overweight</td>
<td>2331</td>
<td>34.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Obese</td>
<td>2003</td>
<td>29.4</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Physical Activity (relative)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary-R</td>
<td>2640</td>
<td>34.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Low-R</td>
<td>1354</td>
<td>22.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Moderate-R</td>
<td>1309</td>
<td>22.1</td>
<td>0.7</td>
</tr>
<tr>
<td>High-R</td>
<td>1197</td>
<td>21.4</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Physical Activity (guidelines)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary-G</td>
<td>2640</td>
<td>34.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Low-G</td>
<td>1326</td>
<td>21.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Moderate-G</td>
<td>809</td>
<td>13.7</td>
<td>0.5</td>
</tr>
<tr>
<td>High-G</td>
<td>529</td>
<td>9.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Very High-G</td>
<td>1196</td>
<td>21.3</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Note: Values in the column Weighted % reflect the distribution of participants after the NHANES sample weights were applied. The Physical Activity (relative) categories were based on the distribution of MET-minute levels for the present NHANES sample. Specifically, participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some physical activity in the past 30 days, were divided into sex-specific tertiles. The Physical Activity (guidelines) categories were based on the 2018 U.S. Physical Activity Guidelines. Specifically, Sedentary-G included those reporting no regular physical activity, Low-G included those performing some regular activity, but not reaching the minimum standards of the guidelines, and Moderate-G included those performing ≥ 500 and < 1000 MET-minutes of activity per week, High-G included those performing ≥ 1000 and < 1500 MET-minutes, and Very High-G included those performing ≥ 1500 MET-minutes of activity per week. Age and smoking (pack-years) were treated as continuous variables in the analyses.
Table 2. Differences in mean HOMA values by level of weekly relative physical activity in U.S. men and women, after adjusting for covariates.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Sedentary-R Mean ± SE</th>
<th>Low-R Mean ± SE</th>
<th>Moderate-R Mean ± SE</th>
<th>High-R Mean ± SE</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>2.6a ± 0.08</td>
<td>2.6a ± 0.09</td>
<td>2.2b ± 0.11</td>
<td>2.0c ± 0.08</td>
<td>11.5</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>2.2a ± 0.07</td>
<td>2.2a ± 0.08</td>
<td>1.9b ± 0.09</td>
<td>1.9b ± 0.07</td>
<td>6.0</td>
<td>0.0012</td>
</tr>
<tr>
<td>Demographics, Lifestyle, &amp; Waist Circ.</td>
<td>2.7 ± 0.09</td>
<td>2.6 ± 0.08</td>
<td>2.5 ± 0.10</td>
<td>2.5 ± 0.08</td>
<td>1.6</td>
<td>0.1937</td>
</tr>
</tbody>
</table>

a,b Means on the same row with the same superscript letter were not statistically different (P > 0.05). Because of nesting, there were only 59 degrees of freedom in the denominator of each model. The physical activity categories were based on relative MET-minute levels. Participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some physical activity in the past 30 days, were divided into sex-specific tertiles. Across the 4 categories of relative physical activity, weighted percentages were: 34% (n = 2640) reported no regular physical activity (Sedentary), 22.5% (n = 1354) reported Low levels, 22.1% (n = 1309) reported Moderate levels, and 21.4% (n = 1197) reported High levels of physical activity (MET-minutes). Because sample weights were applied to each participant, differences in the size of each category should be interpreted relative to percentages, not n. Means on the same row were adjusted for the covariates in the left column. Moderate and High mean differences in the Demographics model were statistically significant at the p = 0.0658 level. The demographic covariates were: age, sex, race, and year of assessment. The lifestyle covariates were: body mass index and cigarette smoking. Waist Circ. = waist circumference measured in cm.
Table 3. Differences in mean HOMA values by level of weekly guideline-based physical activity in U.S. men and women, after adjusting for covariates.

<table>
<thead>
<tr>
<th>Weekly Guideline-Based Physical Activity Level</th>
<th>Sedentary-G</th>
<th>Low-G</th>
<th>Moderate-G</th>
<th>High-G</th>
<th>Very High-G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covariate</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
</tr>
<tr>
<td>Demographics</td>
<td>2.6a ± 0.08</td>
<td>2.5a ± 0.09</td>
<td>2.3b ± 0.12</td>
<td>2.2b ± 0.16</td>
<td>2.0c ± 0.08</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>2.2a ± 0.07</td>
<td>2.1abc ± 0.09</td>
<td>2.0b,c ± 0.09</td>
<td>2.0b,c ± 0.14</td>
<td>1.8b ± 0.07</td>
</tr>
<tr>
<td>Demographics</td>
<td>2.7 ± 0.09</td>
<td>2.6 ± 0.09</td>
<td>2.6 ± 0.11</td>
<td>2.5 ± 0.14</td>
<td>2.5 ± 0.08</td>
</tr>
</tbody>
</table>

a,b,c Means on the same row with the same superscript letter were not statistically different (P > 0.05). Because of nesting, there were only 59 degrees of freedom in the denominator of each model. The physical activity categories were based on MET-minute guideline levels. Across the 5 guideline-based categories of physical activity, weighted percentages were: 34% (n = 2640) reported no physical activity (Sedentary-G), 21.7% (n = 1326) reported Low-G levels (> 0 and < 500 MET-minutes per week), 13.7% (n = 809) reported Moderate-G levels (≥ 500 and < 1000 MET-minutes per week), 9.3% (n = 529) reported High-G levels (≥ 1000 and < 1500 MET-minutes per week), and 21.3% (n = 1196) reported Very High-G levels of physical activity (≥ 1500 MET-minutes per week).

Sedentary-G and High-G mean differences in the Demographics model were statistically significant at the p = 0.0667 level. Moderate-G and Very High-G mean differences in the Demographics model were statistically significant at the p = 0.0802 level. Because sample weights were applied to each participant, differences in the number of subjects in each category should be interpreted using percentages, not N. Means on the same row were adjusted for the covariates in the left column. The demographic covariates were: age, sex, race, and year of assessment. The lifestyle covariates were: body mass index and cigarette smoking.

Waist Circ. = waist circumference measured in cm.
Table 4. Differences in mean HOMA values by level of weekly relative physical activity in U.S. men and women, after adjusting for covariates applied to waist circumference groups divided into sex-specific quartiles.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Sedentary-R Mean ± SE</th>
<th>Low-R Mean ± SE</th>
<th>Moderate-R Mean ± SE</th>
<th>High-R Mean ± SE</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>1.2 ± 0.05</td>
<td>1.2 ± 0.06</td>
<td>1.1 ± 0.06</td>
<td>1.2 ± 0.06</td>
<td>0.1</td>
<td>0.9634</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>1.2 ± 0.05</td>
<td>1.2 ± 0.06</td>
<td>1.1 ± 0.06</td>
<td>1.1 ± 0.06</td>
<td>0.3</td>
<td>0.8233</td>
</tr>
<tr>
<td>Demographics, Lifestyle, &amp; Waist Circ.</td>
<td>1.2 ± 0.05</td>
<td>1.2 ± 0.06</td>
<td>1.1 ± 0.06</td>
<td>1.2 ± 0.06</td>
<td>0.2</td>
<td>0.9123</td>
</tr>
<tr>
<td>Medium Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>0.4 ± 0.05</td>
<td>0.4 ± 0.05</td>
<td>0.4 ± 0.05</td>
<td>0.4 ± 0.05</td>
<td>0.6</td>
<td>0.6335</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>0.4 ± 0.06</td>
<td>0.5 ± 0.06</td>
<td>0.4 ± 0.07</td>
<td>0.4 ± 0.07</td>
<td>0.3</td>
<td>0.8091</td>
</tr>
<tr>
<td>Demographics, Lifestyle, &amp; Waist Circ.</td>
<td>1.8 ± 0.09</td>
<td>1.8 ± 0.09</td>
<td>1.8 ± 0.10</td>
<td>1.8 ± 0.11</td>
<td>0.3</td>
<td>0.8137</td>
</tr>
<tr>
<td>Large Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>2.9 ± 0.17</td>
<td>2.8 ± 0.20</td>
<td>3.0 ± 0.30</td>
<td>2.7 ± 0.20</td>
<td>1.2</td>
<td>0.3241</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>2.8 ± 0.16</td>
<td>2.6 ± 0.19</td>
<td>2.8 ± 0.29</td>
<td>2.5 ± 0.20</td>
<td>2.2</td>
<td>0.0938</td>
</tr>
<tr>
<td>Demographics, Lifestyle, &amp; Waist Circ.</td>
<td>2.8 ± 0.16</td>
<td>2.7 ± 0.19</td>
<td>2.9 ± 0.29</td>
<td>2.6 ± 0.20</td>
<td>1.8</td>
<td>0.1639</td>
</tr>
<tr>
<td>Extra-Large Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>4.1a ± 0.24</td>
<td>4.0a ± 0.20</td>
<td>3.1b ± 0.21</td>
<td>3.4b ± 0.25</td>
<td>8.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>2.7a ± 0.26</td>
<td>2.6a ± 0.26</td>
<td>1.7b ± 0.28</td>
<td>2.0b ± 0.32</td>
<td>10.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Demographics, Lifestyle, &amp; Waist Circ.</td>
<td>3.3a ± 0.26</td>
<td>3.2a,c ± 0.24</td>
<td>2.5b ± 0.23</td>
<td>2.7b,c ± 0.27</td>
<td>5.6</td>
<td>0.0019</td>
</tr>
</tbody>
</table>

Means on the same row with the same superscript letter were not statistically different (P > 0.05). Because of nesting, there were only 59 degrees of freedom in the denominator of each model. The physical activity categories were based on relative MET-minute levels. Participants reporting no regular physical activity were classified as Sedentary, and the remaining adults, each reporting some physical activity in the past 30 days, were divided into sex-specific tertiles. Across the 4 categories of relative physical activity, weighted percentages were: 34% (n = 2640) reported no regular physical activity (Sedentary), 22.5% (n = 1354) reported Low levels, 22.1% (n = 1309) reported Moderate levels, and 21.4% (n = 1197) reported High levels of physical activity (MET-minutes). Because sample weights were applied to each participant, differences in the size of each category should be interpreted relative to percentages, not n. Means on the same row were adjusted for the covariates in the left column. Low and High mean differences in the Demographics, Lifestyle, & Waist Circ. model were statistically significant at the p = 0.0761 level. The demographic covariates were: age, sex, race, and year of assessment. The lifestyle covariates were: body mass index and cigarette smoking. Waist Circ. = waist circumference measured in cm.
Table 5. Differences in mean HOMA values by level of weekly guideline-based physical activity in U.S. men and women, after adjusting for covariates applied to waist circumference groups divided into sex-specific quartiles.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Sedentary-G</th>
<th>Low-G</th>
<th>Moderate-G</th>
<th>High-G</th>
<th>Very High-G</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>1.2 ± 0.05</td>
<td>1.2 ± 0.06</td>
<td>1.1 ± 0.06</td>
<td>1.2 ± 0.07</td>
<td>1.2 ± 0.06</td>
<td>0.9</td>
<td>0.4589</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>1.2 ± 0.05</td>
<td>1.2 ± 0.06</td>
<td>1.1 ± 0.09</td>
<td>1.1 ± 0.08</td>
<td>1.1 ± 0.06</td>
<td>0.9</td>
<td>0.4738</td>
</tr>
<tr>
<td>Demographics, Waist Circ.</td>
<td>1.2 ± 0.05</td>
<td>1.2 ± 0.06</td>
<td>1.1 ± 0.07</td>
<td>1.2 ± 0.07</td>
<td>1.2 ± 0.06</td>
<td>0.9</td>
<td>0.4985</td>
</tr>
<tr>
<td>Medium Waist Only</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>1.8 ± 0.06</td>
<td>1.9 ± 0.08</td>
<td>1.9 ± 0.11</td>
<td>1.7 ± 0.08</td>
<td>1.8 ± 0.07</td>
<td>0.6</td>
<td>0.6776</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>1.8 ± 0.10</td>
<td>1.9 ± 0.10</td>
<td>1.9 ± 0.11</td>
<td>1.7 ± 0.11</td>
<td>1.8 ± 0.11</td>
<td>0.4</td>
<td>0.8382</td>
</tr>
<tr>
<td>Demographics, Waist Circ.</td>
<td>1.8 ± 0.09</td>
<td>1.8 ± 0.10</td>
<td>1.8 ± 0.11</td>
<td>1.7 ± 0.11</td>
<td>1.8 ± 0.11</td>
<td>0.4</td>
<td>0.8435</td>
</tr>
<tr>
<td>Large Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>2.9 ± 0.17</td>
<td>2.8 ± 0.21</td>
<td>2.9 ± 0.27</td>
<td>2.9 ± 0.42</td>
<td>2.7 ± 0.19</td>
<td>0.8</td>
<td>0.5234</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>2.8 ± 0.16</td>
<td>2.7 ± 0.20</td>
<td>2.8 ± 0.26</td>
<td>2.8 ± 0.42</td>
<td>2.6 ± 0.19</td>
<td>1.7</td>
<td>0.1606</td>
</tr>
<tr>
<td>Demographics, Waist Circ.</td>
<td>2.8 ± 0.16</td>
<td>2.7 ± 0.20</td>
<td>2.8 ± 0.26</td>
<td>2.8 ± 0.42</td>
<td>2.6 ± 0.20</td>
<td>1.3</td>
<td>0.2669</td>
</tr>
<tr>
<td>Extra Large Waist Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td>4.1a ± 0.24</td>
<td>3.9a ± 0.21</td>
<td>3.3b ± 0.27</td>
<td>3.3b ± 0.31</td>
<td>3.2b ± 0.26</td>
<td>4.3</td>
<td>0.0039</td>
</tr>
<tr>
<td>Demographics &amp; Lifestyle</td>
<td>2.7a ± 0.26</td>
<td>2.5a ± 0.27</td>
<td>1.9b ± 0.30</td>
<td>1.9b ± 0.38</td>
<td>1.8b ± 0.33</td>
<td>5.3</td>
<td>0.0011</td>
</tr>
<tr>
<td>Demographics, Waist Circ.</td>
<td>3.3a ± 0.26</td>
<td>3.1a ± 0.25</td>
<td>2.7b ± 0.24</td>
<td>2.5b ± 0.29</td>
<td>2.6b ± 0.28</td>
<td>3.7</td>
<td>0.0098</td>
</tr>
</tbody>
</table>

a,b Means on the same row with the same superscript letter were not statistically different (P > 0.05). Because of nesting, there were only 59 degrees of freedom in the denominator of each model. The physical activity categories were based on MET-minute guideline levels. Across the 5 guideline-based categories of physical activity, weighted percentages were: 34% (n = 2640) reported no physical activity (Sedentary-G), 21.7% (n = 1326) reported Low-G levels (> 0 and < 500 MET-minutes per week), 13.7% (n = 809) reported Moderate-G levels (≥ 500 and < 1000 MET-minutes per week), 9.3% (n = 529) reported High-G levels (≥ 1000 and < 1500 MET-minutes per week), and 21.3% (n = 1196) reported Very High-G levels of physical activity (≥ 1500 MET-minutes per week). Because sample weights were applied to each participant, differences in the number of subjects in each category should be interpreted using percentages, not n. Means on the same row were adjusted for the covariates in the left column. The demographic covariates were: age, sex, race, and year of assessment. The lifestyle covariates were: body mass index and cigarette smoking. Waist Circ. = waist circumference measured in cm.