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Leisure Time Physical Activity Among Non-Smoking, Normal Weight Adults: Assessing Prevalence of Central Adiposity, Insulin Resistance, and Systemic Inflammation

Maria M. Corallo
University of Connecticut-Public Health, corallo@mph.uchc.edu

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Maria Marisa Corallo

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Leisure Time Physical Activity among Non-Smoking, Normal Weight Adults: Assessing Prevalence of Central Adiposity, Insulin Resistance, and Systemic Inflammation

Presented by

Maria Marisa Corallo, B.S.

Major Advisor ______________________________
Helen Swede, Ph.D.

Associate Advisor ______________________________
Linda Pescatello, Ph.D.

Associate Advisor______________________________
Anthony Vella, Ph.D.

University of Connecticut
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TABLE OF CONTENTS

TABLES AND FIGURES

ABSTRACT

BACKGROUND: The prevalence of pre-diabetes and diabetes along with concomitant low-grade systemic inflammation continues to increase, particularly as a consequence of excess body weight. Physical activity (PA) has been examined as a preventive intervention against these conditions primarily through its role in weight reduction. It remains unknown, however, if individuals of normal weight who do not engage in regular physical activity are at increased risk for pre-diabetes.

METHODS: A cross-sectional analysis was conducted of n=6085 participants from the National Health and Nutrition Examination Survey (NHANES) annual surveillance surveys conducted from 2001-2006, who met the following criteria: 20-64 years, disease-free (self-report of no diabetes, asthma, arthritis, CHD, angina, stroke, emphysema, chronic bronchitis, and cancer), and non-smoker. Three self-reported measures of physical activity (PA) in the past 30 days, the independent variable, were assessed: (1) Intensity Level (moderate or vigorous); (2) Agreement with the American College of Sports Medicine (ACSM) guidelines for frequency, intensity, and time/duration (FIT) of PA (i.e., ≥ 5 days per week of moderate intensity PA for ≥ 30 min, or, ≥ 3 days per week of vigorous intensity PA for ≥ 20 min); and, (3) ACSM recommendations for MET-Mins Per Week (i.e., total work expenditure of specific activities engaged in by participants) of 500–1000 MET-Mins Per Week. Logistic Regressions (Crude and Age-Sex Adjusted) were performed between each of the three PA measures in relation to the following two dependent variables that reflect pre-diabetes status: 1) sex-specific elevated waist circumference (≥ 40 in for men and ≥ 35 in for women); and, (2) homeostatic model assessment for insulin resistance (HOMA-IR) using an established cutpoint of >2.2). Exploratory analyses were performed of immune system cells as markers of low-grade systemic inflammation in relation to the dependent variables. We assessed relationships separately among individuals who were of normal weight, overweight and obese to determine if the benefits of PA are reduced among the latter two groups due to, presumably, the burden of excess body weight.

RESULTS: Elevated waist circumference was inversely associated with vigorous intensity level PA, compared to referent group, among those with a normal weight (Crude OR 0.33, 95% CI 0.22-0.51) and overweight (Crude OR 0.50, 95% CI 0.41-0.62). No such association was observed for moderate intensity and elevated waist circumference. Adjusted odd ratios (ORs) persisted among only the normal weight group. Elevated waist circumference also was inversely associated (Crude ORs) with the highest level of MET-Mins Per Week (≥ 500) and those who met ACSM guidelines for FIT criteria among both the normal and overweight in crude analyses. These associations were maintained in adjusted analyses for the most part. Regarding immune function, those who reported a vigorous intensity or those who met ACSM weekly guidelines exhibited an inverse correlation with levels of white blood cell count, segmented neutrophil percent and segmented neutrophil number. A direct correlation, however, was observed with lymphocyte percent, monocyte percent, and basophil percent with MET-Min Per Week. While findings suggested an inverse relationship between PA and HOMA, few tests were statistically significant.

CONCLUSIONS: Among the normal weight, an elevated waist circumference was far less likely among those who engaged at the highest levels of PA. Similarly, for elevated HOMA, data suggested that higher levels of PA among those of normal weight were associated with a reduced chance of exhibiting insulin resistance, but findings did not reach statistical significance. Data suggests a positive relationship between White Blood Cells and having an Elevated Waist Circumference among females who were of normal weight but not so among their male counterparts. Findings regarding the benefits of PA in relation to insulin resistance, however, were not consistent possibly owing to low prevalence of this state in the study sample. Future research is recommended to confirm our findings with objective measures of PA, such as an accelerometer, and to clarify divergent results regarding immune system cells.

INTRODUCTION

1.1 Burden of Pre-diabetes and Diabetes

Among adults aged 20 years or older in the United States, 25.6 million or 11.3% have diabetes, with an additional 79 million people having the pre-cursor state of prediabetes[1]. In 2007, diabetes was listed as the underlying cause on 71,382 death certificates, and listed as a contributing factor on an additional 160,022 death certificates; contributing to a total of 231, 404 deaths in 2007[1]. Diabetes contributes to many complications including heart disease and stroke, high blood pressure, blindness, kidney disease, neuropathy, amputation, and certain cancers. Type 2 diabetes, which accounts for about 95% of diagnosed diabetes in adults, is incurable once the disease is achieved. Although individuals with prediabetes are at substantially increased risk of developing Type 2 Diabetes, the onset can be prevented or delayed by losing 5-7% of their body weight and expending at least 150 minutes per week of moderate intensity physical activity[2]. Pre-diabetes is defined as having blood glucose levels that are higher than normal, but not high enough to be diagnosed as diabetes (i.e. fasting glucose >100 mg/dl). It is estimated that 33% of U.S. adults have prediabetes, although awareness of this condition is low[2].

The metabolic syndrome (MetS), another pre-cursor state for diabetes, affects millions nationwide, with the prevalence increasing with age and body mass index (BMI)[3]. Epidemiological studies have reported an increased prevalence of the syndrome worldwide[4], posing significant health problems with the global epidemic of overweight and sedentary lifestyle[5]. About 34% of adults in the U.S. (> 20 years of age) meet the criteria for metabolic syndrome[3]. The metabolic syndrome is a constellation of risk factors that places individuals at an increased risk for not only Type 2 Diabetes but cardiovascular disease (CVD), polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma, sleep disturbances, and some forms of cancer[6]. The most commonly used clinical definition of the Metabolic Syndrome is derived from National Cholesterol Education Program's Adult Treatment Panel III (ATP III), which specifies that three of the following five criteria must be met: abdominal obesity (men > 40in, women >35in), elevated triglycerides (≥ 150mg/dL), low HDL cholesterol (men <40mg/dL, women <50mg/dL), hypertension (≥135/85mmHg), and high fasting glucose(≥100mg/dL)[3]. The core pathophysiology of MetS is abdominal adiposity and insulin resistance[7], the latter being considered a pre-diabetic state. The chief characteristic of insulin resistance is hyperglycemia, which reflects reduced uptake of insulin by cells resulting in a buildup of excess glucose in the bloodstream. In fact, the majority (78%) of people who have the MetS are insulin resistant[7].

1.2 Physical Activity and Pre-Diabetes

ATP III has recommended incorporating physical activity for weight loss and the reduction of insulin resistance[6]. The difficulty in determining the effect of exercise independent of weight loss has made exercise prescription unclear, although dose-dependent trends display increasing levels of physical activity lowering the incidence of the MetS and higher levels of physical activity protecting against the development of the MetS[7]. The incidence of the MetS is twice as high in adults reporting no moderate or vigorous intensity physical activity compared with those reporting engaging in at least 150 min/wk[7, 8]. LaMonte and colleagues have shown that the MetS incidence was lower in middle-aged women and men with higher cardiorespiratory fitness when followed in a prospective study for an average of 5.7 years[9].

Physical activity has been shown to reduce insulin sensitivity, dyslipidemia, and hypertension even among obese/overweight people who have not lost weight[7]. Exercise improves glucose homeostasis by enhancing glucose transport and insulin action in working skeletal muscle during muscle contraction by stimulating glucose uptake. In addition, after a single bout of aerobic exercise, sensitivity to insulin-mediated glucose uptake is greatly improved immediately after exercise[10, 11]. Repeated bouts of exercise that are accompanied by improvements in cardiorespiratory fitness (i.e., aerobic exercise training), do not appear to improve glucose uptake beyond the effect of the last bout of exercise independent of change in body weight[12]. Segal et al suggested for the continued benefit of exercise on insulin action, an individual would need to follow the American College of Sports Medicine (ACSM) and Centers of Disease Control and Prevention (CDC) recommendations to engage in 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic activity every week[13]. Evidence suggests that aerobic training may need to be accompanied by weight loss for an effective change in insulin sensitivity beyond the immediate post exercise effects[7].

1.3 American College of Sports Medicine Physical Activity Recommendations

Several studies have supported a dose–response relationship between regular physical activity and health outcomes[14, 15]. Epidemiologic studies have estimated that the volume of physical activity needed to lower rates of CVD and premature mortality related to cardiac health and diabetes is: moderate intensity physical activity for about 150 min/wk; OR; vigorous-intensity exercise performed for a total of 75 min/wk[16].

Another way to measure energy expenditure is by the metabolic equivalent (MET), which is the ratio of the rate of energy expended during one minute of activity at rest[16]. The recommended target volume in MET/min/wk is 500–1000 MET/min/wk[16].

1.4 Inflammation in Pre-Diabetes and Diabetes

Low grade inflammation is present in the pathogenesis of certain metabolic disorders such as insulin resistance, the metabolic syndrome, and adult-onset diabetes[17]. Inflammation is secondary to the activation of the acute phase response of the innate immune system which respond to tissue damage and infection[17]. Immune cells such as macrophages, lymphocytes, and eosinophils have been implicated as playing a role in this process[18-24]. Neutrophils, the first immune cells to respond to inflammation, promote a more chronic inflammatory state by secreting several proteases, specifically neutrophil elastase[18, 25].

White blood cells (include e.g., basophils, eosinophils, monocytes, neutrophils, and lymphocytes) help fight infections when the body encounters a foreign invader, producing a generalized, non-specific reaction known as inflammation[26]. Activation of the innate immune pathways has been implicated in the pathogenesis of insulin resistance; however, these pathways are also closely linked to changes in lipid deposition[27]. White Blood Cell (WBC) count is elevated in those with obesity and impaired glucose tolerance, such as pre-diabetes and diabetes[18]. Specifically, neutrophils in adipose tissue are associated with a marked increase in neutrophil elastase release, which may contribute to cellular insulin resistance; this is supported by the observation that inhibiting elastase improved insulin resistance[18]. Also, Talukdar and others suggest that neutrophils, particularly the associated neutrophil elastase release, promote the metabolic syndrome[18].

1.5 Physical Activity and Inflammation

High intensity aerobic training has been found to be effective in reducing low-grade inflammation in people with metabolic syndrome[28]. In a NHANES III study, more frequent physical activity (i.e, measured by engagement in 9 activities in last 30 days) was associated with lower prevalence of inflammation (e.g., C-reactive protein) among healthy US adults (exclusion of individuals with self-reported diabetes, asthma, arthritis, CHD, angina, stroke, emphysema, chronic bronchitis, and a personal history of cancer)[29]. Also aerobic and resistance training also have been reported to reduce circulating levels of inflammation[30].

First-degree relatives of patients with Type 2 Diabetes may exhibit a disproportionately elevated risk of insulin resistance, obesity, and Type 2 Diabetes as a result of physical inactivity, which in part, might be due to low-grade inflammation[31]. The key finding of Hojbjerre et al, 2011 is that nonobese, insulin-resistant individuals with a family predisposition for Type 2 Diabetes exhibited low-grade inflammation and, notably, as little as 10 days of physical inactivity negatively affected the condition and exhibited insulin sensitivity in response to bed rest[31].

1.6 Research Aims

Assessing the relationship between physical activity and insulin resistance among individuals of normal weight provides an opportunity to examine the health benefits independent of body fat reduction. Further, the prevalence of insulin resistance in normal weight individuals has not been well studied. The primary aim of this study is to determine, among the normal weight, if the prevalence of insulin resistance is greater among those who engage in less physical activity. Secondly, we will assess this relationship among individuals who are overweight and obese to determine if the benefits of physical activity are reduced due to, presumably, the burden of excess body weight. Our third aim is to assess waist circumference, and inflammation measured by
immune system cell function as the dependent variables in relation to physical activity.

2.0 METHODS

2.1 Study Population in NHANES

Data from the National Health and Nutrition Examination Survey (NHANES) annual data from 2001 to 2006 were analyzed. NHANES is a program of the Centers for Disease Control and Prevention (CDC) that collects the health and nutritional status of adults and children in the United States[32]. The survey examines a nationally representative sample, combining interviews and physical and laboratory examinations to determine the prevalence of major diseases and risk factors for diseases[32]. A complex statistical process using the most current Census information selects persons from a broad range of age groups and racial/ethnic backgrounds.

NHANES participants are a nationally representative sample of a civilian, noninstitutionalized US population, selected by using a multistage, stratified sampling design. A complete description of the NHANES sampling design and recruitment process has been published previously[33]. All participants were interviewed at home and subsets were invited to mobile examination centers for additional questionnaires, physical examinations and laboratory measures. The NHANES protocol was approved by the National Center for Health Statistics' Institutional Review Board (IRB) and all participants provided informed consents[32].

2.2 Eligibility Criteria

Individuals who participated in the National Health and Nutrition Examination Survey (NHANES) from 2001 to 2006 were determined to be eligible for this study if they were: 20 to 64 years of age and non-smokers (i.e., never or former). Body Mass Index (BMI) was calculated as kg/m^2. Individuals classified as underweight (BMI < 18.50) were excluded as were those missing BMI status. The following three categories of BMI were used to classify excess body weight: Normal (18.51-24.99), Overweight (25.00-29.99), and Obese (≥ 30.00.)[34].

Individuals were excluded with conditions that could affect inflammation levels as well as one's ability to engage in physical activity, as used in several prior similar studies[29]. These conditions (self-report) were: diabetes, asthma, arthritis, coronary heart disease, angina, stroke, emphysema, chronic bronchitis, and a personal history of cancer.

Smoking status was determined based on the question "Do you now smoke cigarettes" or "Have you previously smoking cigarettes". We excluded individuals with diabetes whose fasting glucose was greater than 100 mg/dL. From the initial sample population of 31,485 from the NHANES 2001- 2006 annual data, our study included

6,085 participants who met all the inclusion and exclusion criteria. Subgroups were selected to attend the mobile examination centers for more laboratory testing, which consisted of: insulin (n=2814), glucose (n=4119), cholesterol (n=5755), and white blood cell counts (n=5804).

2.3 Physical Activity Measures

Intensity Level

Intensity was defined as: vigorous, moderate and no vigorous or moderate activity. To determine intensity level, NHANES questioned participants “Over the past 30 days, did you do any vigorous activities for at least 10 minutes that caused heavy sweating, or large increases in breathing or heart rate?” Examples provided for vigorous activities in the survey included running, lap swimming, aerobics classes, or fast bicycling. Respondents were also asked “Over the past 30 days, did you do moderate activities for at least 10 minutes that caused only light sweating or a slight to moderate increase in breathing or heart rate?” Examples provided for moderate activities in the survey included brisk walking, bicycling for pleasure, golf, and dancing. Participants who answered ‘yes’ to either intensity were included in the ‘vigorous ’or ‘moderate’ physical activity group. Participants who responded in the affirmative to both questions were included in the ‘vigorous’ physical activity, whereas those who answered both questions in the negative were included in the ‘neither’ category for physical activity. This category was labeled ‘intensity level’ in analyses.

ACSM Frequency, Intensity, and Time Guidelines for Exercise (FIT)

American College of Sports Medicine (ACSM) provides recommendations for moderate and vigorous exercise[16]. The recommendations include performing at least 5 days per week of moderate intensity physical activity for 30 minutes or more, or at least 3 days per week of vigorous intensity physical activity for 20 minutes or more, or a combination of both[16]. Individuals were interviewed about specific individual moderate and vigorous leisure-time activities. For each reported leisure-time activity, participants were asked to report: intensity as moderate (see definition above) or vigorous (see definition above), number of times the activity was carried out during the past 30 days, and average number of minutes the activity was done.

Activities with a reported total time per day of 12 hours or more were excluded from analyses[32]. For example, if bowling was reported an average of 3 times a day for an average of 4 hours each time, the person was re-classified as having engaged in no activities.

ACSM weekly guidelines differ for aerobic and non-aerobic activities[16]. Hence, we placed non-aerobic activities in a separate level in the FIT variable. Non-aerobic activities included flexibility, resistance training activities, and other activities that could not be classified as cardiovascular. Please visit *Figure 2* for a breakdown of the individual physical activities into aerobic and non-aerobic groups.

ACSM MET-Minutes Per Week Recommendations

The total metabolic equivalent score (MET score) was calculated for each week based on the information from the individual activities, using the Ainsworth Compendium[35]. MET-Minutes is an index of energy expenditure that quantifies the total amount of physical activity (i.e., volume) performed in a standardized manner across individual activities[16]. Metabolic equivalent scores (METs) are a useful, convenient, and standardized way to describe the absolute intensity of a variety of physical activities. Light physical activity is defined as requiring ≤ 3 METs, moderate as 3–6 METs, and vigorous as ≥ to 6 METs[31]. MET score or MET-Minutes Per Week is calculated as the product of the number of METs associated with one or more physical activities and the number of minutes the activities was performed per week or per day. Example: jogging (at 7 METs) for 30 min on 3 d/wk would equal: 7 METs *30 min* 3d/week = 630 MET/min/wk[31].

The categories of MET-minutes per week for vigorous and moderate activities included no moderate or vigorous activity reported, ≤ 250 MET-mins/wk, 250-499 MET-mins/wk, and ≥ 500 MET-mins/wk. These categories were created to distinguish amount of MET-Minutes needed to induce outcome changes. As stated previously, the ACSM recommended target volume in MET/min/wk is 500–1000 MET/min/wk[16].

2.4 Outcomes

Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)

HOMA-IR is a mathematical equation to calculate insulin resistance using fasting glucose and insulin values as follows: [Glucose (mmol/L), X Iinsulin (uU/mL)] / divided by 22.5][37]. Values of 2.2 and greater signify insulin resistance[36].

Several techniques are available for measuring insulin resistance, including the hyperinsulinemic-euglycemic clamp technique, the intravenous glucose tolerance test, and the insulin suppression test. However, these techniques are complicated and not suitable for large-scale population studies or routine clinical work, therefore simpler clinical measurements have been proposed for assessing insulin resistance such as HOMA[37, 38].

Waist Circumference

An elevated waist circumference was defined as measuring greater than or equal to 40 inches for men and 35 inches for women[34]. Waist Circumference was determined by measuring the circumference of the abdomen (cm) at the natural waist, around the bellybutton, and was classified as 'elevated' for males at >102 cm and females at >88 cm.

Low-Grade Systemic Inflammation: Immune System Cells

Several cells of the immune system were assessed to approximate if inflammation levels varied in relation to the physical activity measures, as evidence of metabolic disturbance: white blood cell count, lymphocyte percentage and number, monocyte percentage and number, segmented neutrophils percentage and number, eosinophils percentage and number, and basophils percentage and number. Mean values for all markers will be obtained to determine relationship with physical activity level.

The technique used by NHANES to collect blood samples is detailed elsewhere[39]. Exclusion criteria for laboratory analyses were: hemophiliacs, participants who received chemotherapy within last 4 weeks, the presence of the following on both arms: rashes, gauze dressings, casts, edema, paralysis, tubes, open sores or wounds, withered arms or limbs missing, damaged, sclerosed or occluded veins, allergies to cleansing reagents, burned or scarred tissue, and shunt or IV[39].

2.5 Statistical Analyses

Pearson Chi-squared Test, and the Spearman and Pearson Coefficients of Correlation were calculated for descriptive analyses. Univariate and Age and Sex Adjusted Logistic regression analysis were performed. Analyses were stratified by BMI status (Normal, Overweight, Obese). Results for all tests were considered statistically significant if $p<0.05$ or if confidence intervals (95%) did not include the value of 1.0. SPSS ver. 20.0 was used to perform all statistical analyses.

3.0 RESULTS

3.1 Participant Characteristics according to BMI Group

Participant characteristics are reported in Table 1. Individuals who were of normal weight tended to be younger than the overweight and obese groups (Mean ages of 36.31, 40.38, and 41.15, respectively, $p<.001$). Compared to the obese group, the normal weight group contained a greater percentage of college graduates and females, and fewer non-Hispanic Blacks and Mexican Americans.

Individuals with normal weight were far more likely to exhibit a normal HOMA Index compared to the obese group (46.6% and 15.3%, respectively, $p<.001$). The number of people who were classified as having the metabolic syndrome increased with increasing BMI group, but there were a significant number of people with missing data of two or more of the components (41.5%, $p<.001$).

White blood cell count, numbers of lymphocyte, monocyte, segmented neutrophils, eosinophils, and basophils, display a positive linear trend with increasing BMI ($p<.001$). In contrast, percent of monocyte displayed a negative inverse trend with increasing BMI ($p<.001$). Percent of lymphocyte, segmented neutrophils, eosinophils, and basophils did not vary according to weight status.

3.2 Participant Characteristics according to PA Measures

Intensity Level

As seen in Table 2-A, compared to those who did not engage in either moderate or vigorous intensity physical activity in the past 30 days, individuals who reported engaging in vigorous intensity leisure time activities were more likely to be male (30.8% versus 46.0%, respectively, $p < .001$), and slightly younger (40.26 versus 37.69, respectively, $p<.001$). Those who reported engaging in vigorous intensity physical activities were less likely to exhibit the metabolic syndrome compared to those who engaged in moderate intensity activities or no such activities during the time period (28.55%, 32.7%, 38.8%, respectively, $p < .001$). Similarly, mean HOMA was greater among those who did not engage in any leisure time activities compared to those who engaged in moderate or vigorous intensity physical activities (3.66 and 2.64, respectively, $p <.001$).

White blood cell count, percent of lymphocyte, eosinophils, monocyte, and segmented neutrophils, and numbers of lymphocyte and segmented neutrophils all displayed lower values in the vigorous intensity group when compared to those who engaged in no moderate or vigorous intensity activities. However, in these cells the moderate intensity group displayed higher immune system cell values compared to the no activity group. In post hoc comparisons, only percent of lymphocyte and segmented neutrophils, and numbers of segmented neutrophils between the no physical activity group and moderate intensity physical activity group were statistically significant.

Frequency, Intensity, and Time (FIT)

As reported in Table 2-B, among individuals who engaged in moderate or vigorous intensity activities in the past 30 days, those who met the ACSM guidelines (i.e., ≥ 5 days per week of moderate intensity PA for ≥30 minutes; or ≥3 days per week of vigorous intensity physical activity for ≥20 minutes) were slightly younger (38.71 vs 40.39, respectively, p<.001), more likely to be male (17.9% vs 15.3%, respectively, p<.001), and had lower rates of the MetS (14.2% vs 39.4%, respectively, p<.001) when compared to the group who did not engage in such activities. Mean HOMA-IR was lower (2.59) among individuals who reached the ACSM recommended level of activity compared to those in the other three FIT groups: who engaged in some level of moderate or vigorous intensity activity during the time period, only non-aerobic activities, or those who did not engage in such activities (2.98, 3.13 and 3.74, respectively, p<0.001). Participants who met the ACSM guidelines exhibited lower levels of, WBC count, percent of monocyte and basophils, and numbers of segmented neutrophil and eosinophil compared to the other three PA groups (P <0.001). In contrast, monocyte number and basophils percent did not vary according to PA FIT group.

MET-Minutes per Week

As reported in Table 2-C, individuals who expended greater than 500 MET-Mins Per Week were slightly younger than those who engaged in no moderate or vigorous activities in the past 30 days (38.87 vs 40.39, respectively, p<.001), more likely to be male (49.9% vs 31.3%, respectively, p <.001), and exhibited reduced mean HOMA values (2.76 vs 3.74, respectively, p<.001) and metabolic syndrome (35.0 vs 39.4, respectively, p<.001). Significant differences in immune system cell function were only seen between individuals in groups who exceeded 500

MET-Mins Per Week when compared to the group who reported no physical activities for white blood cell count, percent of lymphocyte and segmented neutrophils, and number of lymphocyte, segmented neutrophils, and eosinophils . Conversely, percent of monocyte and basophils displayed increasing numbers with an increase in MET-Mins Per Week.

3.3 ORs for At-Risk Waist Circumference and Elevated HOMA in relation to PA

<u>Waist Circumference</u>

Intensity Level

For these analyses, the obese group was eliminated because the vast majority (e.g., 61.2%) of individuals in this group had an elevated waist size. As seen in Table 4, among those of normal weight and overweight, individuals who reported engaging in vigorous physical activity in the past 30 days displayed a significant decrease in elevated waist (Age and Sex-Adjusted OR=0.37, 95% CI=0.24-0.57; OR=0.65, 95% CI=0.52-0.83) compared to both the no activity group and moderate intensity group. As displayed, the benefits of physical activity were observed even among the normal weight, thus reducing the risk for pre-diabetes.

Frequency, Intensity, and Time (FIT)

In Table 4, both normal weight and overweight individuals displayed a decreased risk for elevated waist circumference if they engaged in either non-aerobic activities or aerobic activities that met or did not meet the ACSM guidelines. Those normal weight and overweight individuals who did meet the ACSM guidelines (i.e., ≥ 5 days per week of moderate intensity PA for ≥30 minutes; or ≥3 days per week of vigorous intensity physical activity for ≥20 minutes), displayed greater decreases in risk (Age and Sex-adjusted OR=0.60, 95%CI=0.37-0.98; OR=0.62, 95% CI=0.45-0.84) when compared to the group who did not meet the guidelines.

MET-Min per Week

In Table 4, individuals with normal weight or overweight displayed a reduced likelihood for having an elevated waist only at the highest level of PA volume. (i.e., >500 MET-Mins Per Week.), which was maintained in adjusted analyses (OR=0.52, 95% CI=0.36-0.77; OR=0.72, 95% CI=0.57-0.90, respectively.).

HOMA

Intensity Level

As seen in Table 4, among those with normal weight, individuals who reported engaging in vigorous physical activity in the past 30 days, were less likely to have an elevated HOMA value (>2.2) compared to those who did not engage in any such activities but did not reach statistical significance (Adjusted OR=0.70, 95% CI=0.45-1.09). The OR in relation to moderate intensity physical activities also was not suggestive of a preventive effect (OR 0.92, 95% CI = 0.58-1.46). Similar trends were observed among individuals who were overweight. In contrast, among those with obesity, engaging in either moderate or vigorous intensity physical activities was associated with a significantly reduced likelihood of elevated HOMA (Age and Sex-adjusted OR = 0.66, 95% CI = 0.45-0.96; Age and Sex-adjusted OR =0.59, 95% CI = 0.40-0.87), compared to obese individuals who did not engage in any such activities.

Frequency, Intensity, and Time (FIT)

Among individuals with normal weight in Table 4, those who met the ACSM guidelines (i.e., ≥ 5 days per week of moderate intensity PA for ≥30 minutes; or ≥3 days per week of vigorous intensity physical activity for ≥20 minutes) had a reduced risk for elevated HOMA (Age and Sex-adjusted OR=0.69, 95% CI=0.39-1.22) compared to the group who did not engage in any activity. Individuals, who engaged in physical activity but did not meet the ACSM guidelines, displayed a reduced risk for elevated HOMA. This reduced risk was to a lesser extent compared to the group who met the ACSM physical activity guidelines. Similar trends were observed for the overweight. In contrast, the obese engaging in any activity, either not meeting the ACSM guidelines or meeting the guidelines, displayed a significantly reduced likelihood of elevated HOMA (Age and Sex-Adjusted OR=0.61, 95% CI=0.43-0.86; OR=0.60, 95% CI=0.38-0.96).

MET-Min Per Week

In Table 4, the normal weight, overweight, and obese displayed decreased risks for elevated HOMA when compared to the group who did not engage in any such activity. Although all groups had a decreased risk in all MET-Mins Per Week categories, the obese group had the most significant decline in risk for all MET-Mins Per Week groups <250, 250-499, and >500 (Age and Sex-Adjusted OR=0.67, 95% CI=0.43-1.06; OR=0.59, 95% CI=0.34-1.03; OR=0.59, 95% CI=0.41-0.84).

3.4 Partial Correlation Coefficients of Immune Cells with Waist Circumference and MET-Mins per Week according to BMI Group

Waist Circumference

A positive correlation between waist circumference and white blood cell count was observed among the normal weight, overweight and obese (0.213, p<.001; 0.209, p<.001; 0.204, p<.001, respectively) controlling for age. This same pattern was observed in relation to percent segmented neutrophils (0.164, p<.001; 0.179, p<.001; 0.100, p=0.002, respectively). Percent lymphocyte, however, displayed an inverse correlation with waist circumference across the weight groups (-0.180, p=0.000; -0.202, p=0.000; -0.103, p=0.002, respectively).

MET-Mins Per Week

Among both normal and overweight individuals, white blood cell count displayed an inverse relationship (-0.119, p=0.001; -0.085, p=0.006), while percent monocyte (0.151, p<.001; 0.105, p=0.001) displayed a positive relationship. Individuals with normal weight also displayed a significant inverse relationship for percent segmented neutrophils (-0.117, p=0.001). The obese displayed no correlation to any of the immune system cells for MET-Mins Per Week.

3.5 Partial Correlation Coefficients of Immune System Cells with Waist Circumference: Stratified by BMI and Sex

Exploratory analyses identifying correlations of WBCs with waist circumference were further stratified by gender owing to reported physiological consequences with regard to sex and central adiposity[40]. Analyses were restricted to WBCs to avoid false-positive findings stemming from multiple tests. Among individuals of normal weight, a strong positive correlation was observed with waist circumference among females but not males in relation to waist circumference and WBC count (r_P =0.309, p=<.001; r_P =0.01, p=0.80, respectively.) Among the overweight and obese, significant positive correlations (r_P =0.16 to 0.22) were found for both males and females (See Table 6.)

4.0 DISCUSSION

Among the normal weight, having an elevated waist circumference was far less likely among those who engaged at the highest levels of PA (vigorous intensity level, met ACSM FIT guideline, and ≥ 500 MET-Min Per Week. This relationship also was observed among the overweight and obese but to a lesser extent. Findings regarding the benefits of PA in relation to insulin resistance, however, were not consistent possibly owing to low prevalence of this state in the study sample.

Waist Circumference. The strongest associations with PA were observed with elevated waist circumference. For example, individuals of normal and overweight engaging in vigorous physical activity showed a decreased risk in elevated waist circumference compared to both the no activity and moderate intensity group. Also, overweight individuals who engaged in any activity (whether or not they met the ACSM physical activity guidelines of ≥ 5 days per week of moderate intensity PA for ≥30 minutes; or ≥3 days per week of vigorous intensity physical activity for ≥20 minutes), and in both normal and overweight individuals who engaged in >500 MET-Mins Per Week displayed lower risk for elevated waist.

Our results suggest that, even among the normal weight individuals, physical activity can help prevent an elevated waist circumference, a major risk factor for disease. Our findings are consistent with a number of prior studies. Hamer and colleagues (2013) reported that regular physical activity, particularly vigorous intensity, was associated with a smaller waist circumference[41]. Stamatakis et al (2009) displayed that sedentary behavior, measured in television time per day, was associated with increased waist circumference independent of engagement in physical acivity[42].

Although our study has shown an increased benefit in engaging in vigorous physical activity, the risk of exercise increases including an increased risk of musculoskeletal injury and cardiovascular complications which include cardiac arrest or sudden death[43]. It is important to obtain medical clearance before engaging in any type of physical activity.

HOMA. Health benefits from PA associated with insulin resistance were suggestive but not definitive. For example, prevalence of HOMA was lower among all weight groups (normal, overweight, and obese) for both moderate intensity and vigorous intensity groups compared to participants who engaged in no physical activities. This association was statistically significant only among the obese, however.

Given that absolute prevalence of HOMA was low among the normal and overweight in our study, HOMA as an outcome appears to be a less sensitive reflection of the benefits regarding physical activity. Nonetheless, the general tendency for reduced insulin resistance in a possible dose-response manner in relation to increased physical activity is consistent with prior studies. Adams et al (2013) states that although moderate intensity exercise improves blood glucose levels, the total volume needed is difficult to achieve, making brief bouts of high intensity exercise favorable[43]. In a review by Adams et al, two weeks of high intensity exercise (either by cycle ergometer or sprinting) improved insulin sensitivity 1 to 3 days post-exercise in nondiabetics when compared to a sedentary group[44]. This suggests that health-related benefits still occur at a higher intensity level of physical activity comparable to moderate intensity. Janssen and Ross (2012) used accelerometer data from 2003-04 and 2005-06 cycles of NHANES which displayed lower rates of the metabolic syndrome with vigorous intensity exercise independent of physical activity dose measured in energy expenditure[45]. There is a growing body of literature that supports the additional benefits of vigorous exercise in all-cause mortality, cardiovascular risk, and diabetes when compared to moderate intensity physical activity[46-48].

Similarly, when assessing the FIT measure of PA (compliance to ACSM PA guidelines for aerobic exercise) in relation to elevated HOMA, only the obese displayed statistically significant values in all activity groups (i.e., met ACSM guidelines, did not meet ACSM guidelines, and engagement in non-aerobic activity) when compared to those who did not engage in any physical activities. This suggests that the obese might gain health benefits from any physical activity, even if attainment of existing ACSM physical activity recommendations does not occur. Similar results were seen for the obese reaching >500 MET-Mins Per Week. Nelson and others (2003) using objective accelerometer data, established an association between time engaged in daily physical activity (measured in minutes) and lower insulin resistance[49]. This study suggests amount of time engaged in daily physical activity is an important determinant for improving glucose metabolism[49].

Immune System Cells. Associations between this outcome and PA are suggestive but currently do not appear to be cohesive. Vigorous intensity was associated with decreased rates of white blood cell count as well as segmented neutrophils (percent and number) when compared to individuals who reported no activity. Although this suggests engagement in activity with greater intensity decreases low-grade inflammation, the moderate intensity group displayed higher immune system cell values compared to the non-activity group. *Ad hoc* comparisons revealed that percent and number of segmented neutrophils between the no activity group and the moderate intensity, as well as between the moderate versus vigorous intensity group to be significant.

Similarly, in categories of MET-Minutes Per Week, no positive linear trend was demonstrated for increasing MET-Minutes. Instead percent monocyte and basophils actually increased with a rise in MET-Minutes Per Week. In post hoc analyses, these relationships were statistically significant. Only those exceeding 500 MET-Minutes Per Week displayed lower immune cell values for WBC count, lymphocyte number, and segmented neutrophils (percent and number). Absence of a positive linear trend with increasing physical activity suggests either an artifact of data collection where participants incorrectly self-reported their activities, presence of intervariablity between individuals, or inconsistencies that are currently not well understood. Another possibility is that some cells in the circulating innate system are relatively immature and, might not respond to anti-inflammatory effects (i.e. physical activity) as might fully differentiated tissue-based cells[50]. Thus, specificity is needed in regarding an immune cell which might promote or actually decrease inflammation. This consideration can be addressed in future analyses with analysis of activation markers on immune cells or their capacity to release pro-inflammatory factors.

Regarding the ACSM weekly recommendations for FIT physical activities, individuals who met the guidelines exhibited decreased WBC count as well as percent monocyte and basophil, and number segmented neutrophil and eosinophil. Again however, percent monocyte and basophils increased when individuals met ACSM guidelines, suggesting self-report bias or interindividual variability. The displayed decreases in white blood cell values in response to exercise in this study, has been suggested by other studies. Neutrophil counts are enhanced following exercise, and exert anti-inflammatory effects such as the production of soluble TNF receptors or sTNFs, which bind circulating TNF-alpha which is a pro-inflammatory cytokine[51-54].

Lower white blood cells also may be attributed to the indirect decreases in adipose tissue as physical activity increases. Veronelli showed WBC count elevated in the obese, and changed only as a function of BMI change[55-57].

Among those with normal weight, we observed that as waist circumference increased with WBC and percent segmented neutrophils, while percent lymphocyte decreased. A strong correlation coefficient between waist circumference and WBC count was observed among normal-weight females. In contrast, normal weight males exhibited no correlation between waist circumference and WBC count. Among individuals of normal weight, as MET-Mins Per Week increased with percent monocyte, while WBC and percent segmented neutrophils decreased. In the overweight, as waist circumference increased, WBC count increased (significant in both sexes in stratified model), percent segmented neutrophils increased, while percent lymphocyte decreased. This trend was also seen in the obese group. Also among the overweight as MET-Mins Per Week increased, WBC count decreased while percent monocyte increased. The obese displayed no correlations to immune cells and MET-Mins Per Week. This could suggest that increased BMI decreases physical activity's anti-inflammatory effect, and is dependent on weight change.

Strengths and Limitations. A key strength of our study is the use of a disease-free and non-smoking population, eliminating many sources of confounding that might not be adequately controlled in multivariate analyses. Also, having data from laboratory tests provides objective measures of insulin resistance. Waist measurements taken by trained personnel also enhance validity of our analyses. Limitations include self-reported physical activity, increasing the possibility inaccurate information. However, data were collected by well-trained study personnel administered the physical activity questionnaires in order to reduce errors of self-report. Further, our large sample size could offset some level of error in reporting. Other limitations include assuming modality of exercise into classifications of aerobic and non-aerobic physical activity, and being truly able to calculate volume of PA.

Summary. Our study suggests that a greater level of intensity is associated with the most favorable health status (lowered waist circumference and increased insulin sensitivity) among adults, supporting the need to emphasize intensity when prescribing exercise. Benefits of physical activity were observed even among the normal weight, particularly regarding prevention of elevated waist circumference which is an emerging risk factor for diabetes. To verify our findings, future studies should obtain objective physical activity measures to more accurately categorize physical activity history such as use of accelerometer or measuring cardiorespiratory output or VO2 Max. It is also of interest to monitor specific measures of low-grade inflammation that might be associated with physical inactivity, and to further inspect divergent results across cell types. One example would be to collectively assess the levels of pro-inflammatory cytokines such as TNF-alpha with the percent and number of monocytes.

Table 1 Participant Characteristics: NHANES 2001-2006 Stratified by BMI Group

	Normal 18.5-24.9 n=1774	Overweight 25.0-29.9 n=2230	Obese >30 n=2081	P Value[1,2]
Age[3]	36.32 (12.40)	40.38 (12.44)	41.15 (12.62)	<.001
Sex				
Male	679 (25.2)	1173 (43.6)	840 (31.2)	
Female	1095 (32.3)	1057 (31.2)	1241 (36.6)	<.001
Smoking[4]				
Never	1365 (30.3)	1604 (35.5)	1543 (34.2)	
Former	408 (26.0)	625 (39.8)	536 (34.2)	.001
Education[4]				
Less than High School	328 (22.6)	576 (39.7)	548 (37.7)	
High School Grad/GED	361 (27.3)	482 (36.4)	481 (36.3)	
Some College	510 (28.3)	641 (35.6)	650 (36.1)	
College Grad or above	575 (38.2)	530 (35.2)	401 (26.6)	<.001
Race/Ethnicity[4]				
Non-Hispanic White	872 (33.2)	916 (34.8)	841 (32.0)	
Non-Hispanic Black	295 (23.0)	443 (34.6)	543 (42.4)	
Mexican American	399 (24.3)	665 (40.6)	575 (35.1)	
Other Race	208 (38.8)	206 (38.4)	122 (22.8)	<.001
HOMA[3]	1.62 (1.31)	2.79 (2.87)	4.97 (5.46)	
<2.2[4]	671 (46.6)	549 (38.1)	221 (15.3)	
>2.2	138 (10.1)	500 (36.5)	733 (53.5)	<.001
Met Syndrome[4, 5]				
Yes	18 (4.1)	136 (31.1)	283 (64.8)	
No	1432 (47.3)	1141 (37.7)	453 (15.0)	
Indeterminate[6]	319 (18.0)	932 (41.9)	1271 (61.2)	<.001
Components(Elevated)[3]				
Abdominal Obesity	170 (5.4)	1046 (33.4)	1915 (61.2)	<.001
Triglycerides	126 (13.3)	393 (41.6)	426 (45.1)	<.001
HDL Cholesterol	95 (16.0)	213 (35.9)	286 (48.1)	<.001
Blood Pressure	151 (17.0)	331 (37.3)	405 (45.7)	<.001
Fasting Glucose	140 (15.2)	363 (39.5)	416 (45.3)	<.001
Immune System Cells[3]				
White blood cell count (SI)	6.80	7.08	7.61	<.001
Lymphocyte %	30.26	30.52	30.46	.635
Lymphocyte #	1.98	2.07	2.26	<.001
Monocyte %	7.73	7.84	7.44	<.001
Monocyte #	0.51	0.54	0.55	<.001
Segmented neutrophils %	58.82	58.37	58.88	.188
Segmented neutrophils #	4.09	4.23	4.56	<.001
Eosinophils %	2.58	2.66	2.58	.374
Eosinophils #	.17	.18	.19	.001
Basophils %	.64	.65	.66	.276
Basophils #	.03	.04	.04	<.001

1 Pearson Chi-Square Test for categorical variables
2 One-Way ANOVA for continuous variables
3 Mean (SD)
4 n (%)
5 Categorization: Three of the following five criteria must be met: abdominal obesity (men > 40in, women >35in), elevated triglycerides (≥ 150mg/dL), low HDL cholesterol (men <40mg/dL, women <50mg/dL), hypertension (≥135/85mmHg), and high fasting glucose(≥100mg/dL) (3).
6 2 or more components were missing

Table 2 Health Status of NHANES Participants (2001-06) according to PA Status

A. Intensity Level

	LEISURE-TIME PA AT MODERATE OR VIGOROUS LEVEL IN PAST 30 d PAST 30 d			
	None[7] n=2061	**Moderate n=1689**	**Vigorous n=2252**	**P-Value[1,2]**
HOMA[3,5]	3.66 (4.99)	3.26 (3.86)	2.64 (2.37)	
<2.2[4]	448 (31.5)	386 (27.1)	588 (41.4)	
>2.2	519 (38.6)	378 (28.1)	446 (33.2)	< .001
MetS[4]				
Normal	928 (31.0)	739 (24.7)	1330 (44.4)	< .001
Metabolic Syndrome	166 (38.8)	140 (32.7)	122 (28.6)	< .001
Indeterminate[8]	915 (36.9)	783 (31.6)	781 (31.5)	< .001
Waist Circumference[4]				
Normal	1184 (38.5)	995 (32.3)	898 (29.2)	
Elevated	810 (29.0)	662 (23.7)	1320 (47.3)	<.001
Immune System Cells[3,5]				
White blood cell count (SI)	7.33 (2.19)	7.48 (2.62)	6.82 (1.91)	< .001
Lymphocyte %	30.46 (8.61)	29.59 (8.77)	31.04 (8.167)	< .001
Lymphocyte #	2.15 (.88)	2.14 (1.40)	2.05 (.64)	.003
Monocyte %	7.54 (2.09)	7.45 (2.12)	2.13 (.05)	< .001
Monocyte #	.54 (.18)	.53 (.18)	.53 (.17)	.188
Segmented neutrophils %	58.74 (9.83)	59.84 (9.93)	57.70 (9.25)	< .001
Segmented neutrophils #	4.39 (1.78)	4.56 (1.94)	4.02 (1.56)	< .001
Eosinophils %	2.66 (2.22)	2.49 (1.94)	2.67 (1.99)	.011
Eosinophils #	.19 (.18)	.18 (.16)	.18 (.15)	.028
Basophils %	.63 (.44)	.65 (.44)	.67 (.48)	.039
Basophils #	.04 (.05)	.04 (.06)	.03 (.05)	.007

1 Pearson Chi-Square Test for categorical variables
2 One-Way ANOVA for continuous variables
3 Mean (SD)
4 n (%)
5 Significant differences (p < .05) between groups found for: **HOMA** = None vs Vig, and Mod vs Vig; MET-Min per week None vs Mod, None vs Vig, and Mod vs Vig; **White blood cell count =** None vs Vig and Mod vs Vig; **Lymphocyte %** = None vs Mod and Mod vs Vig; **Lymphocyte #** = None vs Vig and Mod vs Vig; **Monocyte %** = None vs Vig and Mod vs Vig; **Segmented neutrophils %** = all groups; **Segmented neutrophils #** = all groups; **Eosinophils %** = None vs Mod and Mod vs Vig; **Eosinophils #** = None vs Vig; **Basophils %** = None vs Vig; Basophils # Mod vs Vig.
6 Index of energy expenditure calculated as the product of the number of METs associated with one or more physical activities and the numbers of minutes the activities were performed per week or per day.
7 Those who responded as ‘no’ to having engaged in either ‘vigorous’ or ‘moderate’ physical activity.
8 2 or more components were missing

B. Frequency, Intensity, and Time (FIT)

	LEISURE-TIME PA AT MODERATE OR VIGOROUS LEVEL IN PAST 30 d				
	None[8] n=2124	**Non-Aerobic Only n=231**	**Did not Meet ACSM Guideline[5] n=2729**	**Met ACSM Guideline[5] n=1001**	**P-Value[1,2]**
HOMA[3,7]	3.74 (5.08)	3.13 (3.91)	2.98 (3.19)	2.59 (2.50)	< .001
<2.2[4]	457 (31.7)	62 (4.3)	671 (46.6)	251 (17.4)	
>2.2	543 (39.6)	61 (4.4)	581 (42.4)	186 (13.6)	
MetS[2]					
Normal	949 (31.4%)	126 (4.2%)	1412 (46.7%)	539 (17.8%)	
Metabolic Syndrome	172 (39.4%)	23 (5.3%)	180 (41.2%)	62 (14.2%)	
Indeterminate[9]	949 (37.6%)	78 (3.1%)	1102 (43.7%)	393 (15.6%)	< .001
Waist Circumference[2]					
Normal	822 (29.2)	120 (4.3)	1339 (47.6)	530 (18.9)	
Elevated	1225 (39.1%)	107 (3.4%)	1346 (43.0%)	453 (14.5%)	< .001
Immune System Cells[3,7]					
White blood cell count (SI)	7.33 (2.19)	7.01 (2.41)	7.18 (2.34)	6.91 (1.98)	< .001
Lymphocyte %	30.45 (8.61)	29.49 (8.77)	30.30 (8.81)	30.93 (8.53)	.085
Lymphocyte #	2.15 (.87)	2.03 (1.33)	2.10 (1.12)	2.06 (.64)	.073
Monocyte %	7.54 (2.09)	7.74 (2.24)	7.67 (2.11)	7.92 (2.19)	< .001
Monocyte #	.54 (.18)	.52 (.18)	.53 (.17)	.53 (.17)	.437
Segmented neutrophils %	58.77 (9.84)	59.40 (9.60)	58.81 (9.55)	57.94 (9.77)	.058
Segmented neutrophils #	4.40 (1.78)	4.22 (1.68)	4.30 (1.79)	4.10 (1.66)	< .001
Eosinophils %	2.65 (2.21)	2.76 (2.00)	2.58 (2.04)	2.57 (1.76)	.430
Eosinophils #	.19 (.18)	.19 (.16)	.18 (.16)	.17 (.13)	.018
Basophils %	.63 (.44)	.66 (.43)	.65 (.45)	.69 (.49)	.017
Basophils #	.04 (.05)	.04 (.05)	.04 (.05)	.04 (.05)	.762

1 Pearson Chi-Square Test for categorical variables
2 One-Way ANOVA for continuous variables
3 Mean (SD)
4 n (%)
5 ACSM recommendations: ≥ 5 days per week of moderate intensity physical activity for ≥30 min, or, ≥ 3 days per week of vigorous intensity physical activity for ≥ 20 min(16)
6 Index of energy expenditure calculated as the product of the number of METs associated with one or more physical activities and the numbers of minutes the activities were performed per week or per day.
7 Significant differences (p < .05) between groups found for: **HOMA** = None vs Did not meet ACSM; and; None vs Met ACSM; **White blood cell count =** None vs Met ACSM and Did not meet ACSM vs Met ACSM; **Monocyte %** = None vs Met ACSM; **Segmented neutrophils # =** None vs Met ACSM and Did not meet ACSM vs Met ACSM; **Eosinophils #** = None vs met ACSM; **Basophils = %** None vs met ACSM.
8 Those who responded as 'no' to having engaged in either 'vigorous' or 'moderate' physical activity.
9 2 or more components were missing

C. Metabolic Equivalent Volume (MET-Minutes per Week)

	LEISURE-TIME PA AT MODERATE OR VIGOROUS LEVEL IN PAST 30 d				
	None[7]	< 250[5]	250-499	500+	P-Value[1,2]
HOMA[3,6]	3.74 (5.08)	3.37 (4.07)	2.85 (3.09)	2.76 (2.70)	< .001
<2.2[4]	457 (31.7)	190 (13.2)	142 (9.9)	652 (45.2)	
>2.2	543 (39.6)	189 (13.8)	114 (8.3)	525 (38.3)	<.001
MetS[4]					
Normal	949 (31.4)	370 (12.2)	280 (19.3)	1427 (47.2)	
Metabolic Syndrome	172 (39.4)	63 (14.4)	49 (11.2)	153 (35.0)	< .001
Indeterminate[8]	949 (37.6)	363 (14.4)	228 (9.0)	982 (38.9)	
Waist Circumference[3]					
Normal	822 (29.2)	338 (12.0)	247 (8.8)	1404 (49.9)	
Elevated	1125 (39.1%)	459 (14.7%)	306 (9.8%)	1141 (36.4%)	< .001
Immune System Cells[3,6]					
White blood cell count (SI)	7.33 (2.19)	7.49 (2.31)	7.20 (2.19)	6.96 (2.25)	< .001
Lymphocyte %	30.45 (8.61)	29.43 (8.49)	30.29 (8.27)	30.75 (8.48)	.002
Lymphocyte #	2.15 (.87)	2.10 (.62)	2.10 (.62)	2.08 (1.20)	.158
Monocyte %	7.53 (2.09)	7.36 (2.12)	7.63 (2.02)	7.88 (2.16)	< .001
Monocyte #	0.54 (.18)	0.53 (.18)	0.53 (.17)	0.53 (.17)	.532
Segmented neutrophils %	58.77 (9.84)	60.01 (9.80)	58.85 (9.42)	58.15 (9.56)	< .001
Segmented neutrophils #	4.40 (1.78)	4.60 (1.98)	4.34 (1.85)	4.12 (1.64)	< .001
Eosinophils %	2.65 (2.21)	2.56 (2.13)	2.61 (2.25)	2.60 (1.85)	.710
Eosinophils #	0.19 (.18)	0.19 (.18)	0.18 (.19)	0.18 (.14)	.036
Basophils %	0.63 (.44)	0.63 (.41)	0.65 (.47)	0.67 (.47)	.020
Basophils #	0.04 (.05)	0.04 (.05)	0.04 (.06)	0.04 (.05)	.918

1 Pearson Chi-Square Test for categorical variables
2 One-Way ANOVA for continuous variables
3 Mean (SD)
4 n (%)
5 Index of energy expenditure calculated as the product of the number of METs associated with one or more physical activities and the numbers of minutes the activities were performed per week or per day. Recommended target volume in MET/min/wk is 500–1000 MET/min/wk as recommended by the ACSM (16)
6 Significant differences (p < .05) between groups found for: **HOMA** = None vs 250 to <499, None vs 500, and <250 vs >500; **White blood cell count** = None vs >500, and <250 vs >500; **Lymphocyte %** = None vs <250, and <250 vs >500; **Monocyte %** = None vs >500 and <250 vs >500; **Segmented neutrophils % =** None vs <250, and <250 vs >500; **Segmented neutrophils # =** None vs <250, None vs > 500, <250 vs >500, 250 to <500 vs >500; **Eosinophils # =** None vs >500; **Basophils %** None vs >500.
7 Those who responded as 'no' to having engaged in either 'vigorous' or 'moderate' physical activity.
8 2 or more components were missing

Table 3 ORs and 95% CIs for Insulin Resistance (HOMA > 2.2) in relation to PA and stratified by BMI Group

		Crude OR (95% CI)	Age and Sex Adjusted OR (95% CI)
Intensity Level			
Normal	None[1]	1.00	1.00
	Moderate	0.92 (.58-1.46)	0.94 (.59-1.50)
	Vigorous	0.72 (.47-1.12)	0.70 (.45-1.09)
Overweight	None	1.00	1.00
	Moderate	0.95 (.70-1.30)	0.95 (.69-1.31)
	Vigorous	0.80 (.60-1.07)	0.76 (.57-1.02)
Obese	None	1.00	1.00
	Moderate	0.67 (.46-.98)	0.66 (.45-.96)
	Vigorous	0.66 (.46-.96)	0.59 (.40-.87)
FIT[2]			
Normal weight	None	1.00	1.00
	Non-Aerobic Only	0.42 (.12-1.43)	0.39 (.11-1.34)
	Did not meet ACSM	0.88 (.56-1.33)	0.87 (.58-1.32)
	Met ACSM	0.70 (.40-1.24)	0.69 (.39-1.22)
Overweight	None	1.00	1.00
	Non-Aerobic Only	1.01 (.55-1.88)	0.92 (.49-1.72)
	Did not meet ACSM	0.86 (.66-1.13)	0.84 (.64-1.11)
	Met ACSM	0.68 (.47-.99)	0.65 (.45-.95)
Obese	None	1.00	1.00
	Non-Aerobic Only	0.81 (.38-1.71)	0.65 (.30-1.38)
	Did not meet ACSM	0.65 (.46-.91)	0.61 (.43-.86)
	Met ACSM	0.63 (.40-1.01)	0.60 (.38-.96)
MET-Min Per Week[3]			
Normal	None	1.00	1.00
	<250	0.74 (.40-1.40)	0.74 (.40-1.40)
	250 to 499	0.82 (.42-1.60)	0.82 (.42-1.60)
	>500	0.82 (.54-1.24)	0.80 (.53-1.22)
Overweight	None	1.00	1.00
	<250	0.94 (.63-1.40)	0.96 (.64-1.43)
	250 to 499	0.84 (.54-1.31)	0.84 (.53-1.31)
	>500	0.79 (.60-1.04)	0.75 (.56-.99)
Obese	None	1.00	1.00
	<250	0.67 (.43-1.06)	0.67 (.43-1.06)
	250 to 499	0.58 (.33-1.01)	0.59 (.34-1.03)
	>500	0.66 (.47-.94)	0.59 (.41-.84)

[1] Those who responded as ‘no’ to having engaged in either ‘vigorous’ or ‘moderate’ physical activity.
[2] ACSM recommendations: ≥ 5 days per week of moderate intensity physical activity for ≥ 30 min, or, ≥ 3 days per week of vigorous intensity physical activity for ≥ 20 min. (16)
[3] Index of energy expenditure calculated as the product of the number of METs associated with one or more physical activities and the numbers of minutes the activities were performed per week or per day. Recommended target volume in MET/min/wk is 500–1000 MET/min/wk as recommended by the ACSM (16)

Table 4 ORs and 95% CIs for Sex-Specific At-Risk Waist Circumference in relation to PA

		Crude OR (95% CI)	Age and Sex-Adjusted OR (95% CI)
Intensity Level			
Normal	None[1]	1.00	1.00
	Moderate	1.22 (.84-1.76)	1.13 (.77-1.66)
	Vigorous	0.33 (.22-.51)	0.37 (.24-.57)
Overweight	None	1.00	1.00
	Moderate	1.14 (.92-1.42)	1.53 (1.21-1.94)
	Vigorous	0.50 (.41-.62)	1.59 (1.23-2.06)
FIT[2]			
Normal weight	None	1.00	1.00
	Non-Aerobic Only	0.32 (.10-1.05)	1.67 (1.02-2.74)
	Did not meet ACSM	0.67 (0.47-0.95)	0.82 (.23-2.91)
	Met ACSM	0.58 (0.36-0.94)	1.12 (.70-1.81)
Overweight	No mod/vig	1.00	1.00
	Non-Aerobic Only	0.52 (.32-.82)	0.49 (.14-1.68)
	Did not meet ACSM	0.77 (0.64-0.93)	0.67 (.46-.97)
	Met ACSM	0.58 (0.45-0.75)	0.60 (.37-.98)
MET-Min Per Week[3]			
Normal Weight	None	1.00	1.00
	<250	0.86 (.53-1.41)	0.85 (.51-1.42)
	250 to 499	1.01 (.60-1.70)	0.99 (.58-1.70)
	>500	.50 (.34-.72)	0.52 (.36-.77)
Overweight	None	1.00	1.00
	<250	0.94 (.71-1.23)	0.88 (.64-1.22)
	250 to 499	1.09 (.80-1.48)	1.05 (.73-1.51)
	>500	0.58 (.48-.71)	0.72 (.57-.90)

[1] Those who responded in 'no' having engaged in either 'vigorous' or 'moderate' physical activity.
[2] ACSM recommendations: ≥ 5 days per week of moderate intensity physical activity for ≥ 30 min, or, ≥ 3 days per week of vigorous intensity physical activity for ≥ 20 min. (16)
[3] Index of energy expenditure calculated as the product of the number of METs associated with one or more physical activities and the numbers of minutes the activities were performed per week or per day. Recommended target volume in MET/min/wk is 500–1000 MET/min/wk as recommended by the ACSM. (16)

Table 5 Age-Adjusted Correlation Coefficients[1] of Immune System Cells with HOMA, Waist Circumference and MET-Minutes per Week according to BMI Group

	HOMA	Waist Circumference	MET-Mins Per Week
Normal			
White Blood Cell Count	0.07 (.05)	**0.21 (< .01)**	**-0.12 (<.01)**
Monocyte %	-0.06 (.11)	-0.01 (.77)	**0.15 (<.01)**
Segmented Neutrophils %	0.02 (.54)	**0.16 (<.01)**	**0.12 (<.01)**
Eosinophils %	-0.01 (.76)	-0.02 (.58)	0.05 (.17)
Basophils %	-0.10 (.01)	-0.03 (.38)	0.03 (.40)
Lymphocyte %	-0.00 (.92)	**-0.18 (<.01)**	0.09 (.02)
Overweight			
White Blood Cell Count	0.09 (.00)	**0.21 (<.01)**	-0.09 (.01)
Monocyte %	-0.07 (.02)	0.01 (.85)	**0.11 (<.01)**
Segmented Neutrophils %	0.03 (.38)	**0.18 (<.01)**	-0.04 (.19)
Eosinophils %	-0.05 (.13)	-.01 (.72)	-0.04 (.21)
Basophils %	-0.03 (.42)	-0.04 (.17)	0.01 (.77)
Lymphocyte %	0.00 (.99)	**-0.20 (<.01)**	0.03 (.37)
Obese			
White Blood Cell Count	**0.13 (.00)**	**0.20 (<.01)**	-0.06 (.06)
Monocyte %	-0.06 (.05)	-0.02 (.61)	0.06 (.07)
Segmented Neutrophils %	0.03 (.44)	0.10 (<.01)	-0.03 (.34)
Eosinophils %	-0.01 (.86)	-0.03 (.43)	-0.02 (.66)
Basophils %	-0.01 (.71)	-0.00 (.93)	0.06 (.10)
Lymphocyte %	-0.01 (.74)	**-0.10 (<.01)**	0.02 (.54)

[1] Pearson Partial Correlation Coefficient (P-Value)

Table 6 Age-Adjusted Correlation Coefficients[1] Stratified by BMI and Sex

	White Blood Cell Count with Waist Circumference
Normal	
Male	0.01 (0.80)[1]
Female	**0.31 (<.001)**
Overweight	
Male	**0.16 (<.001)**
Female	**0.22 (<.001)**
Obese	
Male	**0.19 (<.001)**
Female	**0.17 (<.001)**

[1] Pearson Partial Correlation Coefficient (P-Value)

Scatterplots for White Blood Cell Counts (SI) and Waist Circumference Stratified by BMI Group and Sex

Figure 1A:

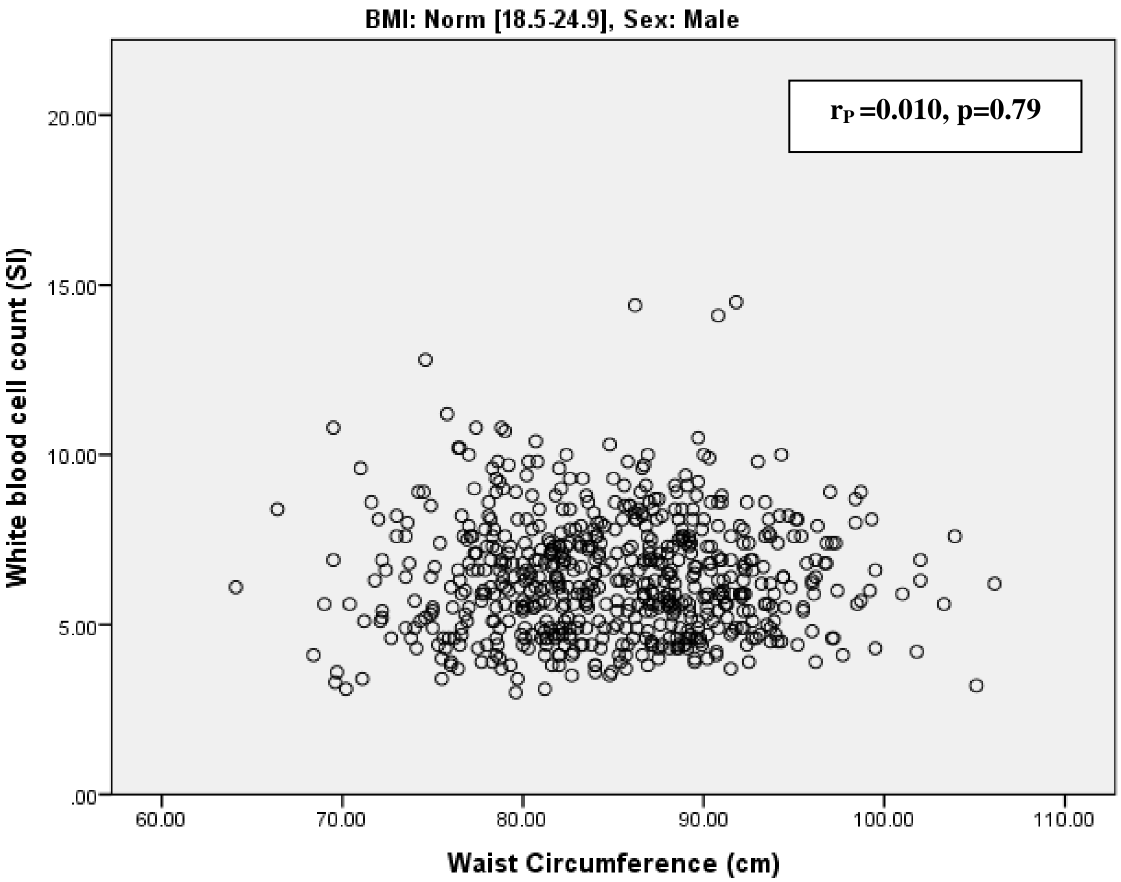


Figure 1B:

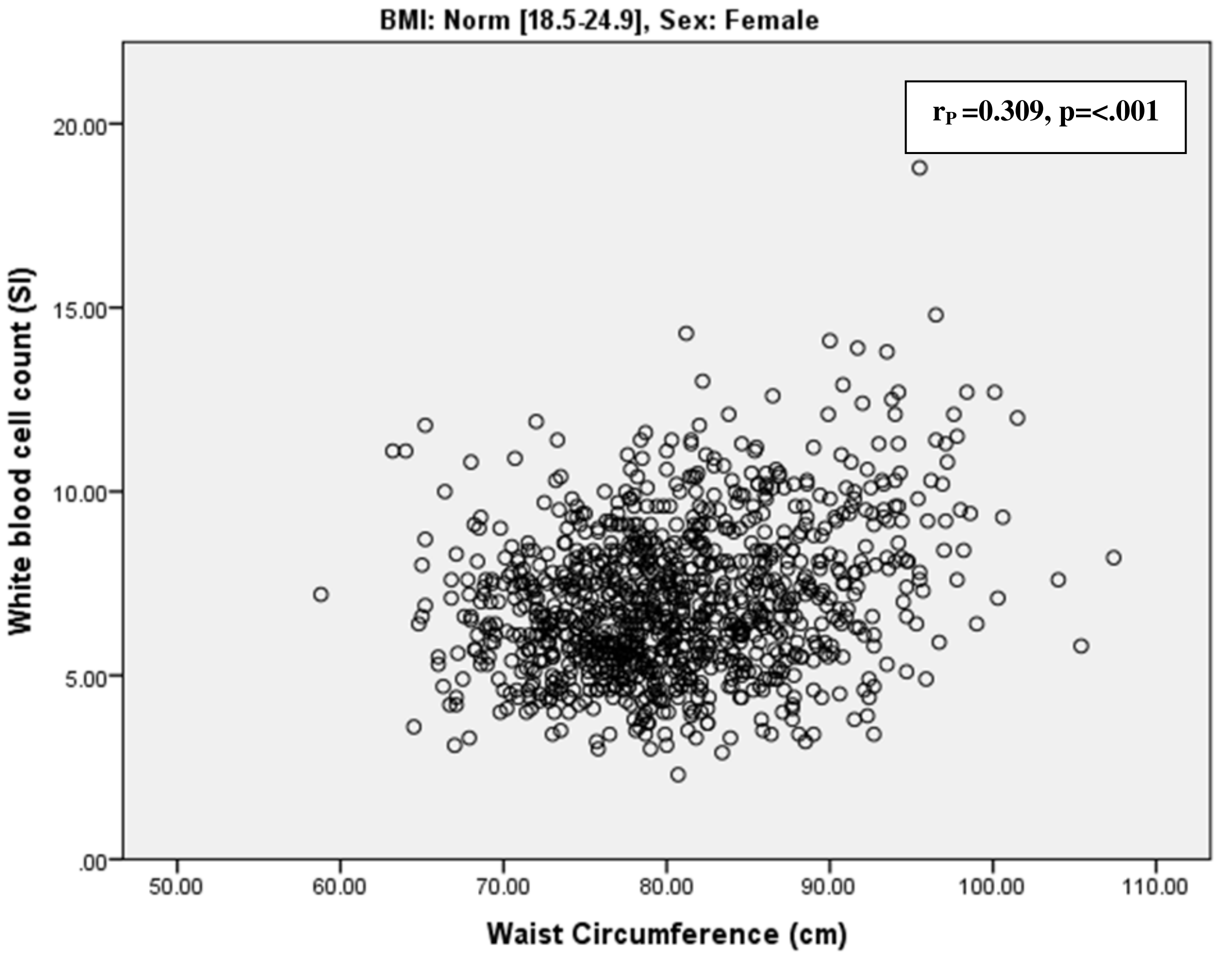

BMI: Norm [18.5-24.9], Sex: Female
rP =0.309, p=<.001
White blood cell count (SI)
20.00
15.00
10.00
5.00
.00
50.00
60.00
70.00
80.00
90.00
100.00
110.00
Waist Circumference (cm)

Figure 1C:

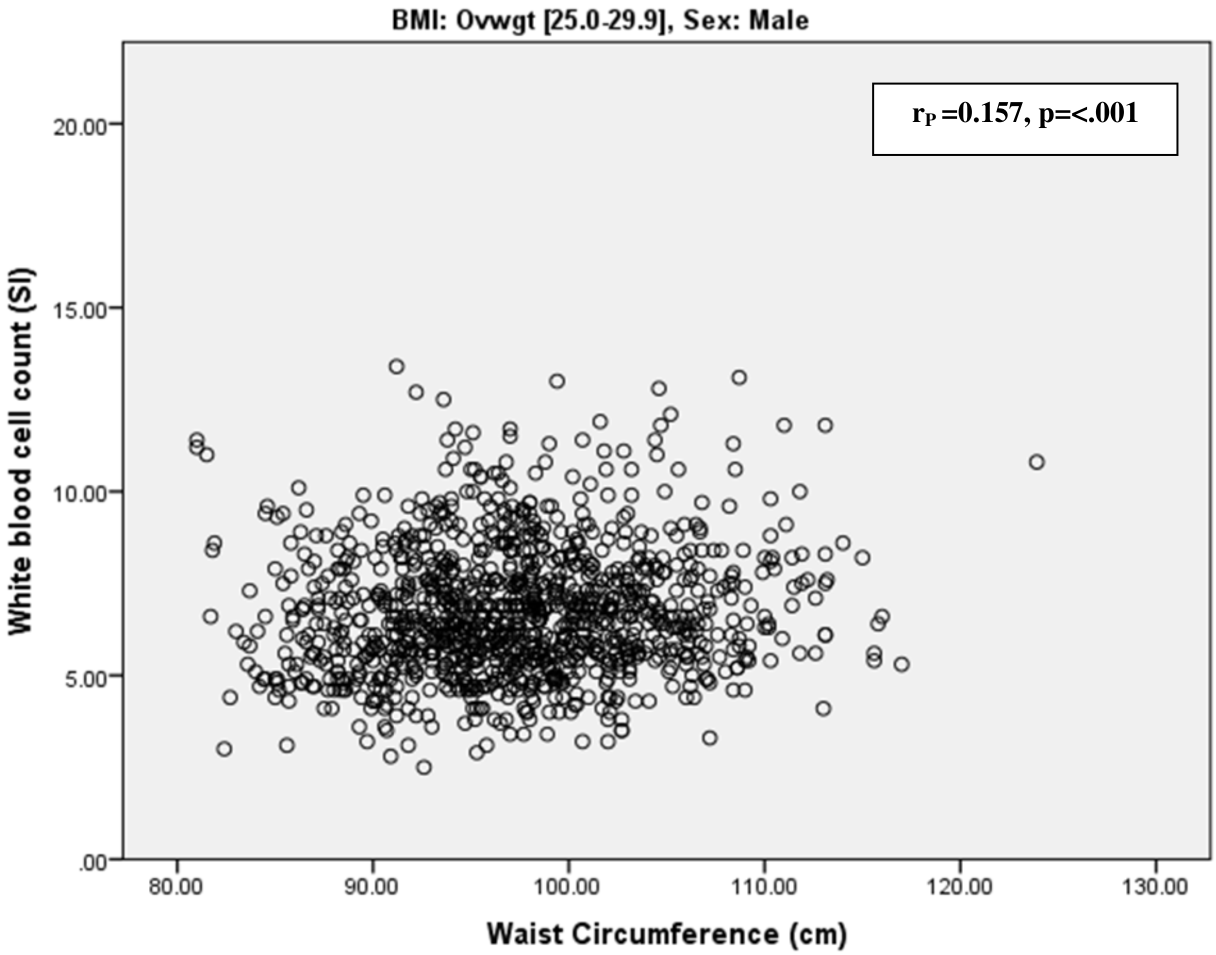

BMI: Ovwgt [25.0-29.9], Sex: Male
rP =0.157, p=<.001
20.00
15.00
10.00
5.00
.00
White blood cell count (SI)
80.00
90.00
100.00
110.00
120.00
130.00
Waist Circumference (cm)

Figure 1D:

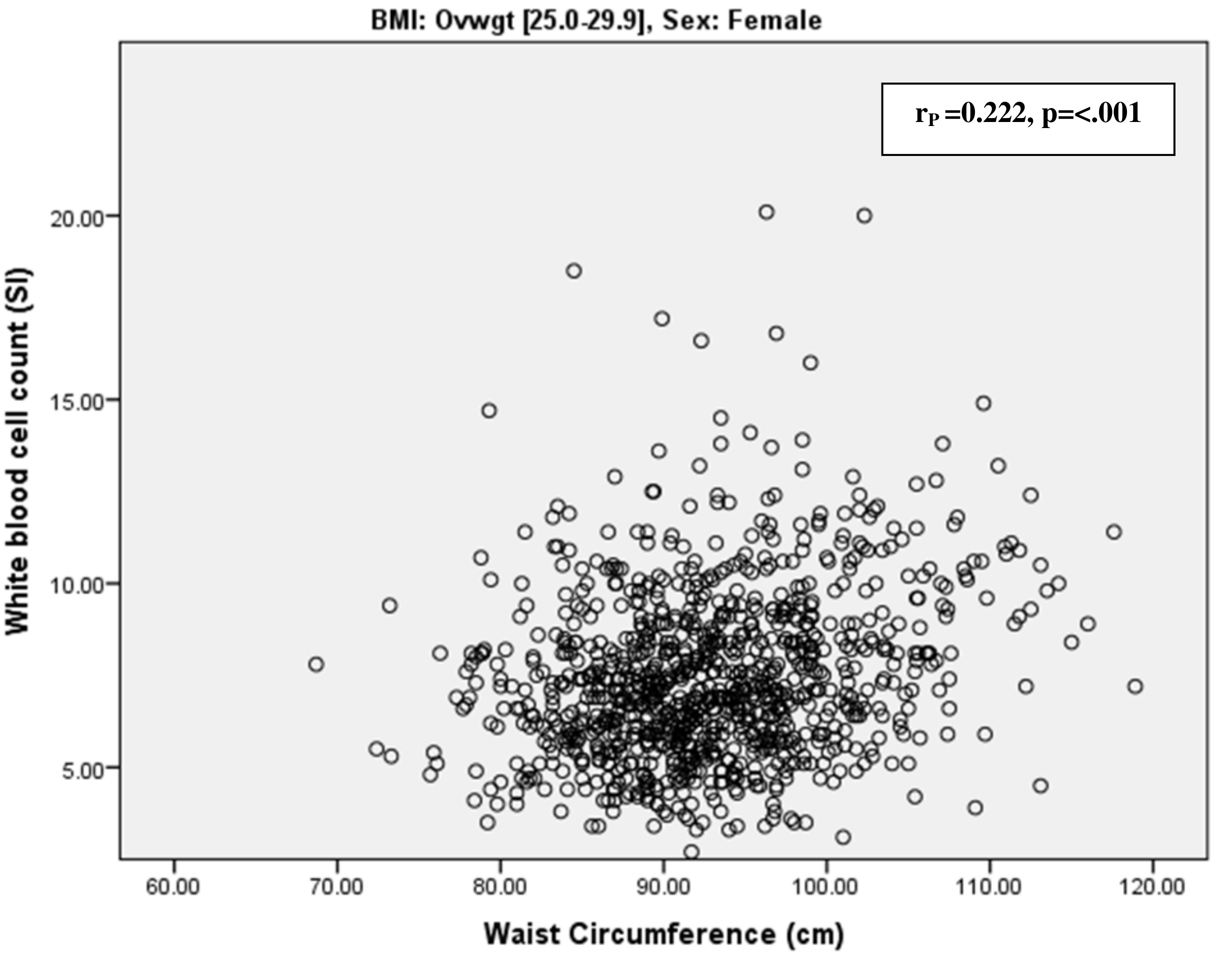

BMI: Ovwgt [25.0-29.9], Sex: Female
r_P =0.222, p=<.001
20.00
15.00
10.00
5.00
White blood cell count (SI)
60.00
70.00
80.00
90.00
100.00
110.00
120.00
Waist Circumference (cm)

Figure 1E:

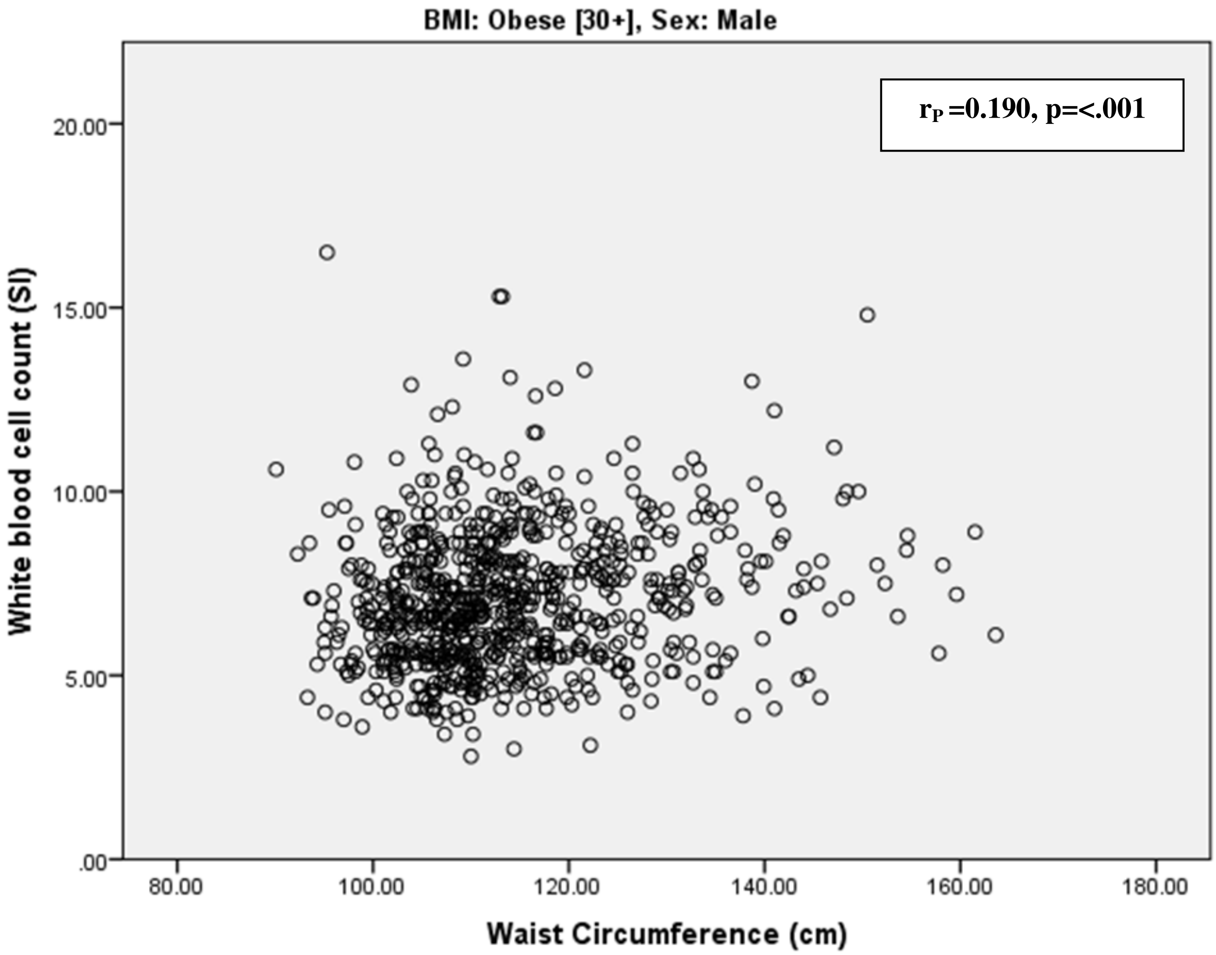
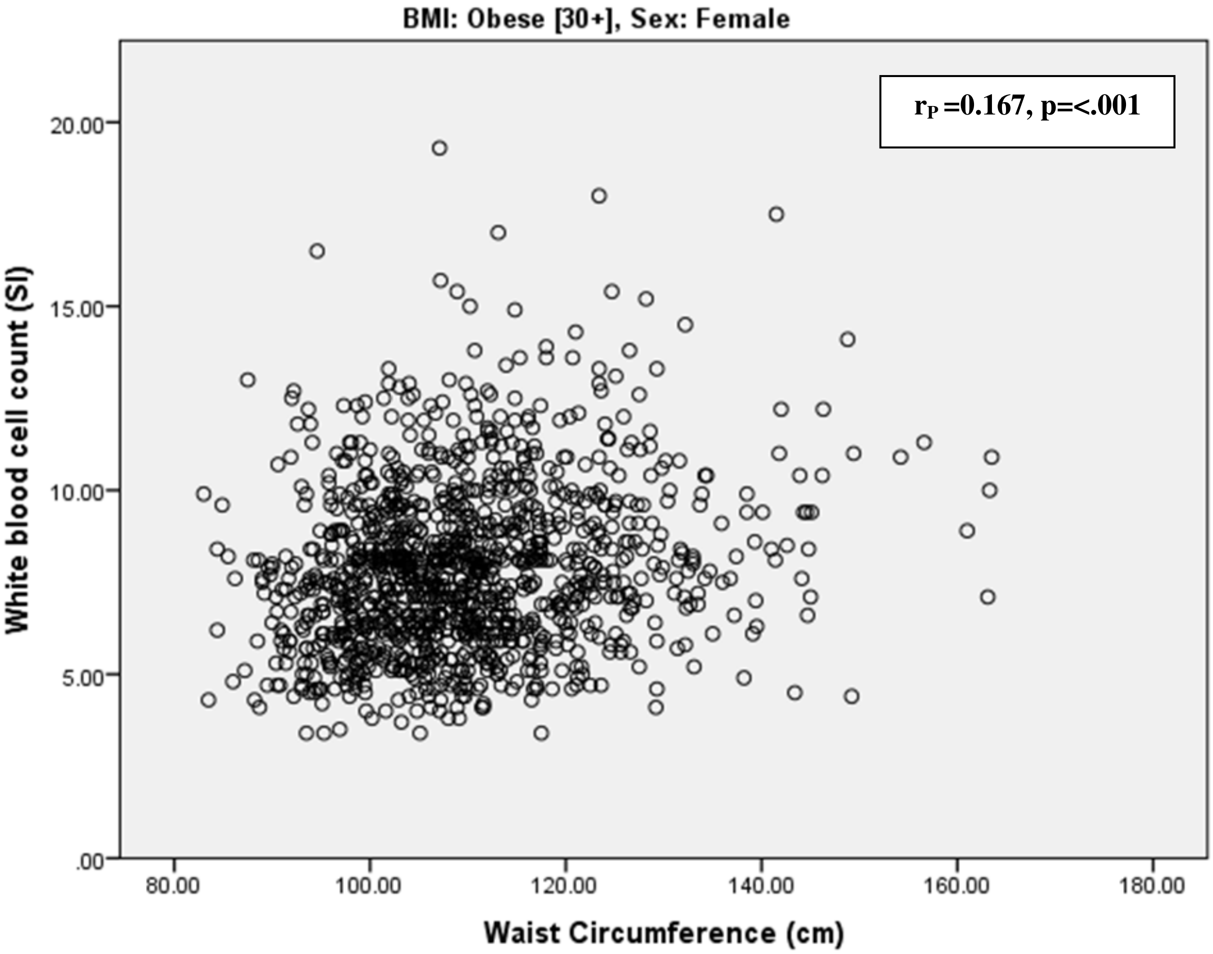

BMI: Obese [30+], Sex: Male
r_P =0.190, p=<.001
White blood cell count (SI)
20.00
15.00
10.00
5.00
.00
80.00
100.00
120.00
140.00
160.00
180.00
Waist Circumference (cm)

Figure 1F:



BMI: Obese [30+], Sex: Female
rP =0.167, p=<.001
White blood cell count (SI)
20.00
15.00
10.00
5.00
.00
80.00
100.00
120.00
140.00
160.00
180.00
Waist Circumference (cm)

Fig. 2 List of Leisure-Time Activities coded in NHANES (2001-06)

Aerobic Activities	Non-Aerobic Activities
Aerobics	Bowling
Baseball	Fishing
Basketball	Gardening
Bicycling	Golf
Dance	Hunting
Football	Kayaking
Hiking	Push-Ups
Hockey	Sit-Ups
Jogging	Skating
Racquetball	Skiing-downhill
Rowing	Stretching
Running	Weight Lifting
Skiing-cross country	Yard Work
Soccer	Horseback Riding
Softball	Martial Arts
Stairclimbing	Wrestling
Swimming	Yoga
Tennis	Cheerleading and Gymnastics
Treadmill	Children's Games-Dodgeball, Kickball, etc
Volleyball	Skateboarding
Walking	Surfing
Boxing	Trampoline Jumping
Frisbee	Other
Rope Jumping	

Fig. 3 MET Values

NHANES Code	Activity	Moderate	Vigorous
10	Aerobics	5.0	7.0
11	Baseball	5.0	6.0
12	Basketball	6.0	8.0
13	Bicycling	4.0	8.0
14	Bowling	3.0	3.0
15	Dance	4.5	6.0
16	Fishing	3.5	6.0
17	Football	5.0	8.0
18	Gardening	4.0	5.0
19	Golf	3.5	4.5
20	Hiking	6.0	7.0
21	Hockey	6.0	8.0
22	Hunting	5.0	6.0
23	Jogging	6.0	7.0
24	Kayaking	3.5	7.0
25	Push-ups	3.5	8.0
26	Racquetball	7.0	10.0
27	Rollerblading	6.0	7.0
28	Rowing	3.5	7.0
29	Running	7.0	10.0
30	Sit-ups	3.5	8.0
31	Skating	5.0	7.0
32	Skiing – cross country	7.0	9.0
33	Skiing – downhill	6.0	8.0
34	Soccer	6.0	10.0
35	Softball	5.0	6.0
36	Stair Climbing	6.0	8.0
37	Stretching	2.5	2.5
38	Swimming	6.0	8.0
39	Tennis	5.0	7.0
40	Treadmill	4.5	7.0
41	Volleyball	4.0	8.0
42	Walking	3.5	5.0
43	Weight Lifting	3.0	6.0
44	Yard Work	4.0	6.0
50	Boxing	6.0	9.0
51	Frisbee	3.0	8.0
52	Horseback Riding	4.0	6.5
53	Martial Arts	4.0	10.0
54	Wrestling	6.0	8.0
55	Yoga	2.5	4.0
56	Cheerleading and Gymnastics	4.0	6.0
57	Children's Dodgeball, Kickball, etc.	5.0	6.0
58	Rope Jumping	8.0	10.0
59	Skateboarding	5.0	6.0
60	Surfing	3.0	5.0
61	Trampoline Jumping	3.5	4.5
71	Other	4.5	7.0

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