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The Dose-Response Association of Physical Activity and the Metabolic Syndrome Among U.S. Adults: NHANES 1999-2004

James R. Churilla
University of Tennessee, Knoxville

To the Graduate Council:

I am submitting herewith a dissertation written by James R. Churilla entitled "The Dose-Response Association of Physical Activity and the Metabolic Syndrome Among U.S. Adults: NHANES 1999-2004." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Exercise Science.

Eugene C. Fitzhugh, Major Professor

We have read this dissertation and recommend its acceptance:

Edward T. Howley, Dixie L. Thompson, David R. Bassett, Lisa Jahns

Accepted for the Council:

Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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THE RELATIONSHIP BETWEEN LEISURE-TIME PHYSICAL ACTIVITY AND THE METABOLIC SYNDROME AMONG U.S. ADULTS: 1999-2004 NHANES

Presented for the Doctor of Philosophy Degree

The University of Tennessee, Knoxville

James Richard Churilla

Knoxville, Tennessee

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DEDICATION

To Mirtha, my wife, and Cameron and Tyler, my two sons. Knowing your love and support was always there, made this journey worth it. This is ours.

To my departed brother-in-law Johnny, this world will never truly reach its potential without you.

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ABSTRACT

The purpose of this study was to evaluate the current prevalence of the metabolic syndrome with an emphasis on examining the relationship between leisure time physical activity (LTPA) and the metabolic syndrome in a nationally representative sample of the United States (U.S.) adult population within the 1999-2004 National Health and Nutrition Examination Survey (NHANES). The sample for this study included adults (N=5620), 20 years and older, who attended a mobile examination center (MEC) examination in the NHANES 1999-2004. The American Heart Association and National Heart, Lung, and Blood Institute (AHA/NHLBI) AHA/NHLBI definition was used to define the metabolic syndrome based on the results of a preliminary pilot study found in Appendix A. A metabolic syndrome risk score (MSRS), ranging from 0 to 5 was created to sum cardiovascular (CV) risk factors. Accumulating a MSRS $\geq$3 designated a metabolic syndrome diagnosis, a dependent variable within this study. Physical activity (PA) was measured in two ways; a six-level measure of MET·minutes per week, comprised of PA frequency, intensity, and duration and a three-level variable (no leisure-time physical activity (LTPA), insufficient LTPA, and an LTPA level equivalent to meeting the CDC/ACSM PA recommendation) associated with the current Centers for Disease Control and American College of Sports Medicine public health PA recommendation (CDC/ACSM). SUDAAN statistical software was

used to estimate age-adjusted prevalence and logistic and multi-logistic odds risk ratios.

The overall age-adjusted prevalence of the metabolic syndrome among the U.S. adult population was 36.3%. A significant difference was found for metabolic syndrome prevalence between those meeting the current public health PA recommendation (29.0%) and those reporting no LTPA (40.0%). Adults who acquired between 736.55 and 1360.15 MET·min·wk^{-1} of LTPA were found to be 35% (OR 0.65; 95% CI 0.48-0.88) less likely to meet the AHA/NHLBI metabolic syndrome diagnosis criteria compared to those reporting no LTPA. A similar inverse association was found for an increasing the MSRS (OR 0.69; 95% CI 0.56-0.85). The strength of this inverse association increased (OR 0.55; 95% CI 0.42-0.71) when weekly LTPA MET·minutes reached >1360.15 MET·min·wk^{-1}. This inverse association was also found for an MSRS (OR 0.58; 95% CI 0.48-0.70) at this level of LTPA.

These findings estimate one in three U.S. adults have the metabolic syndrome. This study consistently showed an inverse association between LTPA and metabolic syndrome risk. Furthermore, there appeared to be a stronger inverse association between metabolic syndrome and LTPA when LTPA volume was increased. However, this additional decrease in risk associated with increasing volumes of LTPA may likely revolve around improvements in body composition. Improvements in body composition associated with varying frequencies, intensities, and duration of PA may

improve other components defining the metabolic syndrome (*i.e.* hypertension, obesity.) While this study is cross-sectional and causality cannot be inferred due to the nature of self-reported data, our findings do illustrate a strong inverse association for LTPA and the metabolic syndrome. Researchers can feel confident that if LTPA is measured using all three components (frequency, intensity, and duration) necessary to calculate MET·min·wk^{-1}, that relationships with the metabolic syndrome and its individual defining criteria will be detected. These results support the need for future longitudinal studies and randomized control trials examining PA volume and metabolic syndrome risk.

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NOMENCLATURE

cm	centimeter
d/wk	days per week
hr/d	hours per day
hr/wk	hours per week
kj/min	kilojoule per minute
m^3	meter cubed
MET/h/d	MET hours per day
$MET \cdot min \cdot wk^{-1}$	MET minutes per week
mg/dL	milligrams per deciliter
mg/g	milligrams per gram
min/wk	minutes per week
mmHg	millimeters of mercury
mmol/L	millimoles per liter
wkd/min	weekday minutes

LIST OF ABBREVIATIONS

AACE	American Association of Clinical Endocrinologists
ACE	American College of Endocrinology
ACLS	Aerobics Center Longitudinal Study
ACSM	American College of Sports Medicine
ADA	American Diabetes Association
AHA	American Heart Association
BMI	body mass index
BMR	basal metabolic rate
BP	blood pressure
CAPI	computer assisted personal interview
CDC	Centers for Disease Control and Prevention
CHHS	Canadian Heart Health Survey
CI	confidence interval
CV	cardiovascular
CVD	cardiovascular disease
EGIR	European Group for the Study of Insulin Resistance
FFM	fat free mass
HDL-C	high density lipoprotein cholesterol
HR	heart rate
HTN	hypertension
ICD-9	International Classification of Disease Vol. 9
IDF	International Diabetes Federation
IFG	impaired fasting glucose
IGT	impaired glucose tolerance
IR	insulin resistance
IRS	insulin resistance syndrome
Kcal	kilocalorie
KHANES	Korean Health and Nutrition Examination Survey
KSSO	Korean Society for the Study of Obesity
LDL-C	low-density lipoprotein cholesterol
LTPA	leisure-time physical activity
MEC	medical examination center
MET	metabolic oxygen equivalent
MRC	Medical Research Council
MSRS	metabolic syndrome risk score
MVU	masked variance unit
NCEP	National Cholesterol Education Program
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey

LIST OF ABBREVIATIONS (continued)

NHLBI	National Heart, Lung, and Blood Institute
OR	odds ratio
PA	physical activity
PAEE	physical activity energy expenditure
PAL	physical activity level
PAQ_C	physical activity questionnaire
PAQIAF	physical activity questionnaire individual activity files
PI	ponderal index
PROC CROSSTAB	procedure produces weighted frequency and percentage distributions
PROC DESCRIPT	procedure produces descriptive statistics for continuous and categorical data analysis
PROC MULTILOG	multivariate logistic regression procedure
PROC RLOGIST	logistic regression procedure
PSU	primary sampling unit
RMR	resting metabolic rate
RT	resistance training
SAS	statistical analysis software
SES	socioeconomic status
SDMVPSU	masked variance primary sampling unit
SDMVSTRA	stratum design variable
SUDAAN	software for the statistical analysis or correlated data
TC	total cholesterol
T2D	type 2 diabetes
TG	triglycerides
TV	television
U.S.	United States
VLDL	very low-density lipoprotein
VO_{2max}	maximal oxygen consumption
$V0_{2\ max\text{-}pred}$	predicted maximal oxygen consumption
WC	waist circumference
W:H	waist to hip ratio
WHO	World Health Organization
WTSAF2YR	two year fasting weights
WTSAF4YR	four year fasting weights
WTSAF6YR	six year fasting weights

PART I

INTRODUCTION

The clustering of multiple cardiovascular risk factors was first observed by Kylin (31) in 1923, when the Swedish physician reported three medical conditions occurring together that he characterized as a syndrome. These conditions included hypertension (HTN), hyperglycemia, and hyperuricemia. However, it was not until 1988 (42) that cardiovascular (CV) risk factor clustering became a common focus for researchers. At this time, Reaven (42) described a series of abnormalities called "Syndrome X", which included insulin resistance (IR), glucose intolerance, hypertension (HTN), hyperinsulinemia, elevated very low-density lipoprotein (VLDL) triglycerides, and low high-density lipoprotein cholesterol (HDL-C). Today, this constellation of cardiovascular risk factors which now includes abdominal obesity (29), is commonly known as the metabolic syndrome, and is recognized as a global public health problem (51).

The metabolic syndrome has been shown to contribute to premature morbidity and mortality resulting from cardiovascular disease (CVD) and type 2 diabetes (T2D), two of the leading causes of death worldwide (26, 38, 45). With this in mind, the United States (U.S.) medical community recognized the importance of diagnosing the metabolic syndrome by creating the International Classification of Disease (ICD-9) Code 277.7 for the Dysmetabolic syndrome (13).

Despite the recognition by the medical community, only recently has the prevalence of the metabolic syndrome in the U.S. population been widely reported (15-17). In fact, the first definition of the metabolic syndrome was published by the World Health Organization (WHO) (47) in 1999. Since the

creation of the WHO definition, there have been several definitions of the metabolic syndrome published by various medical societies (1, 13, 20, 24, 39). Nevertheless, the core components are similar across all definitions and include: IR or type 2 diabetes (T2D), central obesity, HTN, and atherogenic dyslipidemia (elevated triglycerides and low levels of high-density lipoprotein cholesterol (HDL-C)). The most recent definition of the metabolic syndrome has been developed by the American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI) (20), and represents an updated version of the National Cholesterol Education Program (NCEP) (39) definition. To date, no study has estimated the prevalence of metabolic syndrome according to the AHA/NHLBI definition.

Central to these metabolic syndrome definitions are factors highly associated with lifestyle, including smoking, alcohol consumption, diet, and physical activity (PA). The positive impact regular PA has on cardiovascular risk and overall health is well recognized (9). The Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) have established the public health recommendation that all Americans should accumulate a minimum of 30 minutes of moderate-intensity PA on most if not all days of the week or 20 minutes of vigorous-intensity PA on three days per week (41). With this PA recommendation in mind, researchers have focused on the impact of PA on individual CV risk factors (2, 21, 44, 48, 49). However, the first study examining the association of PA with the clustered risk factors of the metabolic syndrome was not conducted until 1998, when Wareham et al. (46)

reported that increasing total physical activity energy expenditure (PAEE) reduced the risk (OR 0.32, 95%CI, 0.13-0.83) of the metabolic syndrome.

Over the last decade, the body of literature examining the relationship between PA and the risk of the metabolic syndrome has flourished. Several cross-sectional (3, 5, 11, 12, 18, 19, 21, 22, 25, 28, 34-37, 40, 43, 50) and longitudinal studies (4, 14, 27, 30, 32, 33) have been conducted. An all important question within this literature is examining the relationship between the volume of PA and the potential risk reduction of the metabolic syndrome. The frequency, intensity, and duration of PA are the characteristics used to express the volume of PA necessary to elicit a certain response (23). To date, only four studies (11, 18, 40, 50) have investigated the relationship between PA and the metabolic syndrome using a national representative sample of U.S. adults. However, none of these studies included data on all the components of PA volume (frequency, duration, and intensity) necessary to fully examine the association of PA with the risk of having the metabolic syndrome.

In the first study, which utilized the 1988-1994 Third National Health and Nutrition Examination Survey (NHANES III) dataset, Park et al. (40) used a physical activity intensity score (PAIS) to define physical inactivity while examining the relationship between being inactive and having or not having the metabolic syndrome. Individuals with a PA intensity score $\leq$ 3.5 were designated physically inactive and comprised 15 and 25 percent of adult males and females respectively, in the U.S. population. In a multivariate odds ratio (OR) model adjusting for ethnicity, BMI, smoking status, alcohol intake, carbohydrate intake,

education level, household income, and menopausal status, neither men (OR 1.4; 95% CI 1.0-2.0) or women (OR 1.2, 95% CI 1.0-1.4) classified as physically inactive were found to be at an increased risk for having the metabolic syndrome. This suggests there is no relationship between physical inactivity and the metabolic syndrome.

In the second study utilizing the same NHANES III dataset, Zhu et al. (50) examined the relationship of being active, moderately active, and sedentary with the likelihood of having the metabolic syndrome as defined by National Cholesterol Education Program (NCEP) in U.S. adults. Based on a PAIS, which summated the weekly intensity in metabolic equivalents (METs) for each activity performed to get an overall total MET score. Physical activity levels were defined as follows: $\geq$15.0 (active), 3.6 to 14.9 (moderately active), and $\leq$ 3.5 sedentary. Both males and females in the active group were found to be significantly less likely to have the metabolic syndrome compared to the inactive group (OR, 0.41; 95% CI 0.31-0.54) for males and (OR, 0.25; 95% CI 0.18-0.37) for females. Following adjustments for BMI, males were 73% less likely (OR 0.27, 95% CI, 0.18-0.40) and females were 68% less likely (OR 0.32; 95% CI, 0.21-0.51) to have the metabolic syndrome if they reported being active.

Additionally, Zhu et al. found that men and women who reported being moderately active were 34% less likely (OR 0.66; 95% CI, 0.48-0.89) and 31% less likely (OR 0.69; 95% CI, 0.48-0.99) respectively, to have the metabolic syndrome. However, among females, after adjusting for age, race, education, income, and menopausal status in the model, the relationship with PA

disappeared. While these findings in both the studies by Park et al. and Zhu et al. illustrate an inverse relationship between PA and the metabolic syndrome, data on the duration was not measured in NHANES III, so quantifying PA volume was not possible.

In the third, which also used the NHANES III dataset, DuBose et al. (11) examined the relationship between PA and the metabolic syndrome by defining PA with a three-level categorical variable, (inactive, irregularly active, and regularly active) and metabolic syndrome based on the NCEP medical society definition. Respondents acquiring $\geq$ 5 d/wk of moderate PA for 30 minutes and/or $\geq$ 3 d/wk of vigorous PA for 20 minutes were considered regularly active, those who reported some PA, however not $\geq$ 5 d/wk of moderate or $\geq$ 3 d/wk of vigorous PA, were considered irregularly active. Participants who reported no PA over the last 30 days were considered inactive. Irregularly active and inactive men were found to be 52% (OR 1.52; 95% CI, 1.11-2.31) and 60% (OR 1.60; 95% CI, 1.18-1.98), respectively, more likely to have the metabolic syndrome compared to regularly active men following adjustment for age, race, gender, and education. In contrast, in women, physical inactivity was not found to be associated with increasing risk of having the metabolic syndrome (OR 0.96; 95% CI 0.72-1.27) irregularly active and (OR 1.18; 95% CI 0.87-1.59) inactive. These findings specific to women were consistent with previous studies (25, 33, 40).

In the most recent study examining the relationship between PA and the metabolic syndrome, Ford et al.(18) utilized the 1999-2000 NHANES dataset (6) and included 1,626 subjects $\geq$ 20 years of age who reported in a fasting condition

for a morning medical examination. During this examination, subjects were asked to report the frequency and duration that they spent performing 43 different leisure-time physical activities (LTPA) of moderate or vigorous intensity over the previous 30 days (6). The total PA time in minutes per week (min/wk) was calculated by summing the weekly minutes of participation for each intensity level LTPA. A three-level categorical variable was then created: 0 min/wk, < 150 min/wk, and ≥ 150 min/wk.

In this study, after only controlling for age, adults who were physically inactive were found to be 65% (OR 1.65; 95% CI, 1.01-2.65) more likely to have the metabolic syndrome than those reporting ≥ 150 min/wk of PA. However, after controlling for gender, ethnicity, education, smoking status, and alcohol intake this association was attenuated to the point of non-significance (OR 1.45; 95% CI, 0.86-2.44), yet when stratified by gender, women reporting no PA were over twice as likely to have the metabolic syndrome when compared to women reporting ≥ 150 min/wk (OR 2.35; 95% CI, 1.19-4.63). Physical inactivity was not associated with the metabolic syndrome risk in men.

While the research described above illustrates the relationship between PA and the metabolic syndrome, each study measured PA volume with only two of the necessary three components. More specifically, the duration of each bout of PA was not available in NHANES III (10), thus one of the necessary components for more accurately assessing PA volume was missing. Also, the investigators elected not to use available data on intensity (MET) level for each specific activity in the1999-2002 NHANES dataset.

An opportunity now exists to more accurately measure PA volume and its relationship with the metabolic syndrome using the most comprehensive measure of PA ever available in a nationally representative sample of U.S. adults. This measure, MET minutes per week ($MET \cdot min \cdot wk^{-1}$) includes all the necessary components to measure LTPA volume: frequency, intensity, and duration. With this in mind, the purpose of this study was to estimate the current prevalence of the metabolic syndrome while examining the relationship of LTPA with the metabolic syndrome using the most recent six years in1999-2004 NHANES (7).

Statement of the Problem

This study estimated the most recent prevalence of the metabolic syndrome using a nationally representative sample of U.S. adults utilizing the AHA/NHLBI definition. In addition, the relationship between LTPA and the risk of the metabolic syndrome was examined. Particular emphasis was placed on the relationship between LTPA and the metabolic syndrome utilizing $MET \cdot min \cdot wk^{-1}$, a more comprehensive measure of PA volume. Toward this end, these specific research questions are posed below.

Research Questions

1. What is the current prevalence of the Metabolic Syndrome in the United States adult population according to the American Heart Association/National Heart, Lung, and Blood Institute definition?

2. Is there an inverse association for LTPA and the metabolic syndrome when utilizing a measure of LTPA volume ($MET \cdot min \cdot wk^{-1}$)?
3. Is there an inverse association for LTPA and the metabolic syndrome when measuring LTPA from the parameters of the CDC/ACSM physical activity public health recommendation?

Significance of the Study

The purpose of this study is to examine the relationship between LTPA and the Metabolic Syndrome metabolic syndrome in a nationally representative sample of the U.S. adult population. This will be the first study to estimate the current prevalence of the metabolic syndrome utilizing the AHA/NHLBI definition.

Delimitations

This study population was limited to U.S. adults aged 20 years and over who participated in a fasting morning medical examination and health interview in the1999-2004 NHANES (7). The NHANES is a collaborative effort between the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC) and is designed to provide national estimates of health and nutritional status of the civilian noninstitutionalized population of the U.S. aged two months and older (8). This study is delimited to only leisure-time physical activity.

Limitations

Aspects of the1999-2004 NHANES may limit the findings in this study, therefore the findings and discussion of the findings in this study must be interpreted with caution. The limitations of this study are described below.

1. This was a cross-sectional study, thus causality cannot be established.
2. Data on PA and all covariates were measured by a self-report interview, thus frequency, intensity, and duration of LTPA is subject to recall bias.
3. Leisure-time physical activity, smoking, and alcohol responses may have been subjected to the social desirability effect (*i.e.* providing answers to impress or please interviewer).
4. Dietary factors (*i.e.*, caloric intake) were controlled in this study due to the complex nature of this data inherent to 1999-2004 NHANES.

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PART II

REVIEW OF LITERATURE

The metabolic syndrome (MetS) has been recognized as a global public health problem that is strongly linked as a seminal cause of cardiovascular disease (CVD) and type 2 diabetes (T2D), both of which are responsible for premature mortality and morbidity worldwide (108, 153, 207). The MetS is characterized by the clustering of cardiovascular risk factors including insulin resistance (IR or T2D), central obesity, hypertension (HTN), and atherogenic dyslipidemia (elevated triglycerides and low levels of high-density lipoprotein cholesterol (HDL-C)) (14, 65, 103, 155, 223). Also, depending on the medical society definition applied, microalbuminuria may also be considered another risk factor (223).

The following review of the literature will discuss 1) a historical perspective of cardiovascular risk factor clustering and the evolution of the MetS; 2) the most commonly used working medical society definitions of the MetS; 3) current international and national prevalence estimates of the MetS; 4) the effects that physical activity (PA) (or lack thereof) has on the individual components of the MetS; and 5) review of all the studies done to date that have examined the association of PA with the MetS, both cross-sectional and longitudinal.

Cardiovascular risk factor clustering and the metabolic syndrome

The constellation of metabolic risk factors and their deleterious effects on cardiovascular health are well established (29, 84, 88, 141, 173, 229). Seminal risk factor clustering for cardiovascular disease (CVD) was first reported by Kylin (128) in the early 20th century. The Swedish physician described a syndrome

involving the clustering of HTN, hyperglycemia and hyperuricemia (gout). Subsequent work by Vague (212) reported a relationship between central adiposity and diabetes, and Avogaro (11), adding obesity to Kylin's original syndrome, strengthened the relationship between the clustering of MetS risk factors and CVD. With continued interest on risk factor clustering and CVD, Camus (35) coined an ensemble of CVD risk factors *the 'deadly quintet'* and Jahnke (111) referred to a *'special metabolic syndrome'* in specific individuals. For the first time in 1977, Haller and colleagues (91, 194) applied the term "m*etabolic syndrome*" when examining the convergence of obesity, diabetes hyperproteinemia, hyperuricemia, and hepatic steatosis (fatty liver).

Reaven (173) drew immense attention to risk factor clustering and CVD in his 1988 'Banting Lecture'. Frederick G. Banting was a Nobel Prize winning physician who was one of the two men responsible for the discovery of insulin (158). The 'Banting Lecture' is given every year by an expert in the area of diabetes at the annual meeting of the American Diabetes Association (6). Reaven described a constellation of risk factors leading to development of T2D and CVD which he termed *Syndrome X*. Reaven postulated the etiology and clinical course of three major related diseases - T2D, CVD, and HTN, all having a common foundation of IR and hyperinsulinemia. However, at this time, adiposity was not considered a major etiological factor.

In 1989, Kaplan (115) coined the term *The Deadly Quartet* to describe upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. However, this addition of central adiposity was not novel. It was established 60

years ago that upper-body obesity was a major player in the risk of developing CVD (212). Subsequent work found that this quartet of conditions had a high level of agreement more commonly than by chance (5, 115). Hypertriglyceridemia, HTN, and T2D have been found to be much more prevalent in obese compared to nonobese individuals (196, 213). Modan et al. (151) found a twofold increase in obesity and T2D among individuals with HTN versus their normotensive counterparts. In addition, dyslipidemia has also been found to be associated with IR, obesity and the MetS (26, 79).

The name *Insulin Resistance Syndrome* (IRS) was first used in 1992 in a prospective analysis examining the association of hyperinsulinemia (used as proxy for IR) and incidence of HTN, T2D, and dyslipidemia over an eight year follow-up in the San Antonio Heart Study (88). The San Antonio Heart Study was a population-based study conducted in San Antonio, Texas. Mexican-American and non-Hispanic White men and nonpregnant women, aged 25-64 years, were randomly selected from all levels of socioeconomic status to examine the effects of the clustering of conditions described above on CVD incidence. This prospective analysis illustrated that hyperinsulinemia at baseline significantly increased the relative-risk of T2D five-fold, hypertriglyceridemia three-fold, HTN two-fold and the presence of low HDL-C by 60%. Zavaroni et al. (231) found similar results in a prospective study when testing the hypothesis that hyperinsulinemia was positively associated with glucose intolerance, dyslipidemia, elevated uric acid concentrations, and HTN. Interestingly, in both of

the above studies these changes were independent of level of adiposity (obesity).

Visceral obesity, IR, and dyslipidemia were assigned the name "*plurimetabolic syndrome*" by Despres (49) when examining how aerobic exercise influenced this trio of cardiovascular risk factors. In the Bruneck Study, which examined the prevalence of IR in metabolic disorders, the coexistence of IGT or T2D, dyslipidemia, hyperuricemia, and HTN were also designated the "*plurimetabolic syndrome*" (30). Given the metabolic nature of the syndrome, the name "*metabolic syndrome"* as proposed by Haller (91) has been rcognized as the most appropriate label by the clinical and research communities.

Different medical society definitions of the metabolic syndrome

In establishing an *official diagnosis* for the MetS, the American Association of Clinical Endocrinologists (AACE) championed the creation of the International Classification of Disease-9th revision (ICD-9) Code 277.7 for the MetS (65). Currently, there are currently five working medical society definitions proposed for the diagnosis of the MetS. Table 1 summarizes the various definitions published by the following medical societies: 1) World Health Organization (WHO) (223), 2) European Group for the study of Insulin Resistance (EGIR) (14), 3) American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI) definition (85) which refers to the updated National Cholesterol Education Program (NCEP) (2001) definition, 4) the American College of Endocrinology (ACE) and American Association of

Clinical Endocrinologists (AACE) consensus definition for epidemiological research (65), and 5) the International Diabetes Federation (IDF) (103).

AHA/NHLBI (updated NCEP)

The majority of the recent research focusing on the metabolic syndrome involved the use of the NCEP definition because of its clinical utility (See Table 1). The NCEP definition requires that three of the following five criteria be present for a diagnosis of the metabolic syndrome: impaired fasting glucose (IFG) represented by a fasting blood sugar $\geq$ 110 milligrams per deciliter (mg/dL), including type 2 diabetes (T2D); HDL-C < 40 mg/dL in men and < 50 mg/dL in women; triglycerides $\geq$ 150 mg/dL; an augmented waist circumference (WC) of > 102 centimeters (cm) in men and > 88 cm in women, or a blood pressure value of $\geq$ 130/85 millimeters of mercury (mmHg). The NCEP definition is unique to the other metabolic syndrome definitions in the respect that it precludes specific inclusion criteria of any one condition (e.g. IFG) in order for metabolic syndrome to be diagnosed. The most recent definition put forth by the AHA and NHLBI (85) mirrors the NCEP definition with the following modifications: medication use for those with dyslipidemia, HTN, and IFG maintains the diagnosis, and the cut-off point for IFG was lowered from 110 mg/dL to 100 mg/dL to reflect the recent changes put forth by the American Diabetes Association (ADA) for IFG (2).

WHO

The WHO metabolic syndrome definition includes at least one of the following requisite conditions: impaired glucose tolerance (IGT) following an oral glucose tolerance test (OGTT); IFG (≥ 110 mg/dL), including T2D; or insulin levels in the top quartile of the population; plus 2 of the following: HDL-C < 35 mg/dL in men or 39 mg/dL in women or elevated triglycerides (≥ 150 mg/dL), a waist to hip (W:H) ratio >0.9 for men or >0.85 for women, or body mass index (BMI) > 30 kilograms per meters squared (kg/m^2) in men or women, BP ≥ 140/90 mm/Hg, or microalbuminuria represented by a albumin creatinine ratio ≥ 30 milligrams per gram (mg/g).

EGIR

The EGIR definition requires insulin in the upper quartile of the background population, plus any 2 of the following: HDL-C < 1.0 millimole per liter (mmol/L) or 40 mg/dL or treatment for dyslipidemia, triglycerides > 2.0 mmol/L (180 mg/dL) or treatment for dyslipidemia, WC of ≥ 94 cm for men and ≥ 80 cm for women, blood pressure ≥ 140/90 mmHg or treatment for HTN, or IGT following a oral glucose tolerance test (OGTT) or IFG (≥ 110 mg/dL), but not diabetes.

IDF

The IDF definition requires an augmented WC in Europeans and Americans of ≥ 94 cm for men and ≥ 80 cm for women. However, the IDF

recommends WC cut-off points that are population and/or ethnic specific with values of ≥ 90 cm and ≥ 80 cm in South Asian and Chinese men and women, respectively, and values of ≥ 85 cm and ≥ 90 cm in Japanese men and women, respectively (234). In addition to a requisite for an augmented WC, 2 of the following conditions must be present for metabolic syndrome diagnosis: IFG represented by a fasting blood sugar ≥ 100 mg/dL, including T2D; HDL-C < 40 mg/dL in men and < 50 mg/dL in women or treatment for lipid abnormality; triglycerides ≥ 150 mg/dL or treatment for lipid abnormality; or a blood pressure value of ≥ 130/85 mmHg or treatment for HTN.

ACE/AACE

The ACE/AACE definition requires one of the following: an individual to be classified as high risk (See Table 1); BMI >25 kg/m^2 or WC of >102cm in men or >88cm in women, plus > 2 of the following: IFG (≥ 110 mg/dL) or IGT following a OGTT, but not diabetes; HDL-C < 40 mg/dL in men or < 50 mg/dL in women; elevated triglycerides (> 150 mg/dL); or a BP > 130/85 mm/Hg.

Metabolic syndrome prevalence has been shown to vary depending on which medical society definition is adopted (75, 76). Several prevalence studies have compared multiple definitions (15, 46, 51, 130, 215), however, since there is no consensus among definitions and various working definitions are continuing to be employed in both clinical and epidemiological research, comparisons between studies continues to be a difficult task. The following section will

examine the current international and national prevalence estimates of the metabolic syndrome.

Current prevalence estimates

It is estimated that close to one billion people worldwide have the metabolic syndrome (64). Global prevalence estimates of the metabolic syndrome vary considerably, depending on the population under study, definition applied, and study design utilized. The increasing number of people with the metabolic syndrome can be attributed in part to population growth, aging, excess caloric intake, and an inactive lifestyle (169). There have been numerous population based cross-sectional (7, 9, 12, 34, 58, 72, 73, 75-77, 86, 112, 123, 139, 147, 157, 165, 167, 171, 203, 215) and cohort studies (145, 148) done that have estimated the metabolic syndrome prevalence. Among these studies, only 12 have estimated the prevalence of the metabolic syndrome utilizing a nationally representative sample of adults (7, 9, 31, 33, 34, 73, 75-77, 86, 119, 161). The following section will examine all the cited prevalence studies that utilized a national representative sample, starting with the international studies, followed by the national (U.S.) studies.

International prevalence estimates

In the Australian, Obesity, and Lifestyle Study (AusDiab), which was a national population-based cross-sectional survey of the prevalence of diabetes and other cardiovascular risk factors in people aged $\geq$ 25 years, the prevalence

estimates of the metabolic syndrome were reported utilizing three different definitions (33). Overall prevalence estimates from the AusDiab were reported to be 15.9% for the EGIR definition, 18.3% for the NCEP definition, and 20.9% for the WHO definition. The same research group, utilizing the WHO and NCEP definitions, reported the prevalence estimates of the metabolic syndrome originating from a national sample of Mauritians (34). Mauritians are comprised of a mixture of Indians, Creoles, Chinese, Europeans, Zarabes, Kaffirs and Malabars living on a sub-continent off the coast of India. The metabolic syndrome prevalence estimates in this highly heterogeneous group were found to be 19.1% (WHO) and 13.8% (NCEP).

The estimated prevalence of the metabolic syndrome in Greece was reported in a cross-sectional analysis of a representative sample of Greek adults participating in the Metabolic Syndrome-Greece Multicentre Study (8). The estimated prevalence of the metabolic syndrome originating from this national sample was 23.6% utilizing the NCEP definition. In cross-sectional survey of a national representative sample of White, Black, Amerindian, and Mixed Hispanics $\geq$ 20 years of age in Venezuela, the prevalence of the metabolic syndrome and its associated risk factors was identified (73). The estimated prevalence of the metabolic syndrome was reported to be 31.2% utilizing the NCEP definition. This was the first national study examining metabolic syndrome prevalence in South America.

The International Collaborative Study of Cardiovascular Disease in ASIA (InterASIA) was a cross-sectional study of CVD risk factors in a national sample

of Chinese adults (86). Utilizing the NCEP criteria, the estimated prevalence among Chinese adults was 13.7%. However, the NCEP criteria may not be appropriate for Asian populations (93, 224). Subsequently, adjustments for the HDL-C cut-off point being ≤ 1.0 mmol/L for both men and women and WC cut-off points being lowered to > 90 cm for men and > 80 cm for women increased the metabolic syndrome prevalence estimate in Chinese adults to15.1%.

The estimated prevalence of the metabolic syndrome in Japan was recently reported in a national survey of adults aged 20-79 years (7). This study utilized the new definition released from the Japanese Committee for the Diagnostic Criteria of the metabolic syndrome. The Japanese metabolic syndrome definition requires the presence of abdominal obesity defined as a WC of ≥ 85 cm in men and ≥ 90 cm in women, plus 2 of the following: triglycerides ≥ 150 mg/dL and/or HDL-C < 40 mg/dL or treatment for dyslipidemia; blood pressure ≥ 130/85 mm/Hg or treatment for HTN; and IFG ≥ 110 mg/dL or treatment for diabetes. Participants taking medication for dyslipidemia were excluded in this study because data allowing differentiation of treatment for hypercholesterolemia or hypertriglyceridemia could not be obtained. In Japanese adults, the national metabolic syndrome prevalence was estimated to be 7.8%.

In the Korean National Health and Nutrition Examination Survey (KHANES), the prevalence of the metabolic syndrome was estimated in over 4,000 Korean adults (119). This study was conducted to compare prevalence estimates of the metabolic syndrome as defined by the IDF and NCEP, and the obesity criteria put forth by the WHO and the Korean Society for the Study of

Obesity (KSSO) (136). The WHO WC cut-points in Korean adults are ≥ 90 cm in men and ≥ 80 cm in women. The WC cut-points according to the KSSO are ≥ 90 cm in men and ≥ 85 cm in women. The WHO recommendation lowers WC cut-point in men by 5 cm and utilizes the same IDF cut-points in women. The KSSO also lowers WC recommendations to ≥ 90 cm in men; however, the women cut-point is raised 5 cm above the IDF criteria.

The age-adjusted prevalence of the metabolic syndrome within the KHANES was estimated to be 23.8% and 17.5% utilizing the modified IDF definition and WHO obesity criteria, and modified IDF definition and KSSO obesity criteria, respectively (119). The age-adjusted prevalence estimates for the NCEP modified by the WHO definition and the NCEP modified by KSSO definition were 26.7% and 23.7%, respectively. The prevalence of the metabolic syndrome as defined by NCEP, modified by the WHO, was the highest (26.7%; 95% CI, 26.0-27.4), while the prevalence of the metabolic syndrome defined by the IDF modified by the KSSO was the lowest 17.5%, 95% CI, 16.9-18.1). This study clearly illustrated how metabolic syndrome definition (and definition modification) can impact prevalence estimates.

In a study examining PA and the metabolic syndrome in Canada, the age-adjusted national prevalence of the metabolic syndrome was also estimated (31) utilizing a modified NCEP definition in the Canadian Heart Health Survey (CHHS). The CHHS was a series of national representative cross-sectional surveys of CVD risk factors in Canadians aged 18-74 years, conducted between 1986 and 1992. Data on glucose and WC values were only obtained on half of

the participants, therefore self-reported physician diagnosed T2D was substituted for glucose, and BMI was used in place of WC. The age-adjusted estimated metabolic syndrome prevalence in Canadian adults surveyed between 1986 and 1992 was 14.4%.

Prevalence estimates in the United States

In the U.S., Ford et al. (77) first reported the estimated prevalence of the metabolic syndrome in a national representative sample of adults, aged $\geq$ 20 years, utilizing data from the 1988-1994 Third National Health and Nutrition Examination Survey (NHANES III) (41). NHANES III was a cross-sectional health survey of a national representative sample of noninstitutionalized U.S. adults. The estimated age-adjusted prevalence of the metabolic syndrome utilizing the NCEP criteria was found to be 23.7%. This was the first report of metabolic syndrome prevalence estimates in the US. In a follow-up study utilizing the same NHANES III data, Ford et al. (76) reported the prevalence of the metabolic syndrome comparing two different medical society definitions, the WHO definition and NCEP definition. The estimated age-adjusted prevalence of the metabolic syndrome utilizing the WHO definition was 25.1% and the NCEP definition was 23.9%. These two prevalence estimates were not significantly different. Ford et al. reported that the reason the prevalence estimates utilizing the same data set and NCEP definition varied slightly from the first prevalence estimates (77) was due to differences in the analytical sample sizes.

The most recent prevalence estimate of the metabolic syndrome in the U.S. were reported by Ford et al. (75) utilizing the newly released IDF definition (103). This study also used 1999-2002 NHANES (39). In addition to estimating metabolic syndrome prevalence using IDF definition, this study also examined prevalence using the NCEP definition. The age-adjusted national prevalence estimates for the metabolic syndrome were found to be 39.1% (IDF) and 34.6% (NCEP). These two prevalence estimates were found to be significantly different, illustrating for the first time in a national sample of U.S. adults, how the metabolic syndrome definition applied can impact prevalence.

A cross-sectional examination of the last two releases of the NHANES (1988-1994 and 1999-2002) data illustrates a 10% increase in the prevalence of the metabolic syndrome in US adults, depending on the definition applied (75, 77). With the metabolic syndrome becoming more common in Westernized societies (64), the prevalence and incidence are anticipated to increase in line with the prevalence and incidence of obesity (152) and T2D (225).

Physical activity and defining metabolic syndrome criteria

Insulin resistance and physical activity

PA and its positive effects on blood sugar control were first observed in the early part of the twentieth century (170). Regular physical activity has been shown to improve rates of glucose uptake in a similar fashion to insulin. Muscle fiber contraction increases the number and activity of glucose transport proteins, GLUT-4, in skeletal muscle (83, 97). Thus, contracting skeletal muscle has

'insulin like effects' on glucose uptake. Furthermore, contracting skeletal muscle does not require the presence of insulin in order to take up glucose.

Reaven (172, 173) and others (45, 69) have clearly illustrated IR to be the core component of the metabolic syndrome. It has been found to be present in approximately 25% of western society (22, 45, 173). The etiology of IR involves diminishing beta-cell function over time, and has been estimated to result in IGT and eventually frank T2D approximately 30%-40% of the time (218). Saltin et al. (186) demonstrated that a low aerobic capacity, expressed per kilogram of body weight, may manifest itself as an early component of the metabolic syndrome, particularly in individuals likely to go on to develop T2D. Furthermore, histological evidence has demonstrated that IR/hyperinsulinemic individuals have attenuated mitochondrial and capillary density in skeletal muscle, accompanied by a decreased type I versus type II fiber ratio (146). Therefore, genetic abnormalities in skeletal muscle may limit aerobic capacity, thus resulting in lower levels of physical activity.

Several cross-sectional studies have illustrated that individuals who reported performing large amounts of aerobic PA on a consistent basis present with lower serum insulin levels, both in the fasting and postprandial state (21, 63, 178). Similar effects have been reported in older men and women (181, 182, 190). Therefore, regular PA also appears to insulate individuals from the deleterious effects of glucose intolerance associated with the normal aging process. When examining insulin sensitivity and glucose uptake in PA intervention studies, acute bouts of PA (28) and lifestyle changes including

regular aerobic (101, 199, 200) and strength training activities (114, 149) have been shown to enhance insulin sensitivity, thus improving glucose control in subjects with varying levels of glycemia and BMI (142, 210).

Hypertension and physical activity

Essential (*i.e.,* no known cause) HTN is a heterogeneous condition which has been shown to be associated with hyperinsulinemia (45, 68, 70, 71, 173, 176). Hypertension has been studied more than any other condition defining the metabolic syndrome (43, 67, 89, 94, 104, 174, 191, 195, 197, 232). As reported by the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) (43), approximately 25% of the US population is estimated to be hypertensive as classified by a systolic blood pressure (SBP) $\geq$ 140 mmHg, a diastolic blood pressure (DBP) $\geq$ 90 mmHg or taking anti-hypertensive medication. It has also been estimated that another 22% of the US population falls into the prehypertension category which is classified as a SBP between 120-139 mmHg or a DBP that falls between 80-89 mmHg. This prehypertension category carries with it a recommendation for lifestyle changes before introducing pharmacological treatment (43). These changes, which are also recommended for individuals with diagnosed HTN, include increasing the amount of regular PA and making healthy dietary changes (*e.g., sodium restriction)* leading to weight loss to help prevent the development of HTN.

Regular PA has been shown to be associated with more favorable blood pressure (BP) values (18, 89). Tanaka et al. (201) found a decrease in both

sitting and supine SBP in 18 previously sedentary subjects with stage 1 and stage 2 HTN following 10 weeks of supervised swimming. Dengel et al. (47) reported decreases in both SBP and DBP following nine months of aerobic PA, three days per week and gradually reaching 40 minutes per session. Similar findings were reported by Fagard (67) demonstrating a decrease in BP in both normotensive and hypertensive individuals, however the effect was more pronounced in the hypertensive group.

Ishikawa et al. (107) reported a significant drop in blood pressure in both sedentary men and women age 30-69 years with stage 1 and 2 hypertension following an eight week PA program. In addition, this study demonstrated no differences in the efficacy of PA between genders; however, the older hypertensive subjects experienced less of a reduction in BP following the exercise program than their younger counterparts. Similar reductions in both SBP and DBP were reported by Swartz et al. (200) following an eight week walking program of 10,000 steps per day in overweight women. Overall, regular PA has been shown to decrease SBP and DBP in nearly 75% of people with HTN (89).

Dyslipidemia and physical activity

Atherogenic dyslipidemia commonly associated with the metabolic syndrome is represented by elevated triglycerides and decreased levels of HDL-C, particularly HDL_2-C (25, 26, 175) which is associated with cardioprotection. The Diabetes Prevention Program (DPP) Research group (Rockville, MD) (50) reported that individuals with IGT, compared with individuals who go on to

develop T2D, were very similar. Individuals with either IGT or T2D showed minimal differences in BP; triglycerides; HDL-C or non-HDL-C; or low-density lipoprotein cholesterol (LDL-C); implying that cardiovascular risk factor profile for T2D differs very little from that of IGT. This suggests that the IR phenotype may be primarily responsible for the dyslipidemia characteristic of hyperglycemia.

Regular PA has been shown to demonstrate favorable effects on lipid profiles (61, 226, 227). PA can augment the capacity of muscle tissue to take up and oxidize non-esterified fatty acids (25, 61) and increase the activity of lipoprotein lipase (LPL) in muscle (164). Individuals who engage in regular PA, compared to those who are physically inactive, have been found to have higher levels of HDL-C and HDL_2-C, in addition to lower levels of triglycerides and LDL-C. In contrast, limited evidence exists demonstrating that individuals who are physically active possess lower levels of total cholesterol (TC) and LDL-C (121, 122, 133). Hence, some lipids and lipoproteins are more favorably impacted by exercise and PA than others (59).

There have been several studies examining the relationship between volume of PA and changes in blood lipid levels (52, 53, 120, 124, 133, 226, 227). Drygas et al. (52) found HDL-C to be approximately 6 mg/dL greater in men who were physically active when compared to the least active group. In a similar study design, Kokkinos et al. (120) reported an inverse association between miles run per week and TG levels, and a positive association between HDL-C and miles run per week in a group of middle-aged men. In women, similar results have been reported. Durstine et al. (62) reported HDL-C levels were greater in

female recreational runners and even greater in female elite runners versus their sedentary counterparts, thus demonstrating a favorable positive association. The positive association between HDL-C levels and running volume were similar for men and women, however TG and TC:HDL-C ratios remained intact (226).

The frequency of favorable changes reported in HDL-C and TG levels following regular PA suggests that these lipid values are more responsive to regular PA than TC and LDL-C (60). Although regular PA results in minimal changes in TC and LDL-C in the absence of weight loss (198), the concentrations of LDL-C, particularly small dense LDL-C has been shown to decrease, while LDL-C particle size is augmented, resulting in a less atherogenic environment (124). Regular PA has also been shown to have favorable effects on the atherogenic dyslipidemia associated with the metabolic syndrome (27, 50, 60). In addition, prospective studies (124, 204, 226, 227) have confirmed additional improvements in these lipid values with increases in the volume of PA performed, thus suggesting a potential dose-response association.

Obesity and physical activity

In a recent 2006 study, Ogden et al. (159) reports the current prevalence of overweight and obesity in the U.S. adult population to be 66.5%. The metabolic syndrome has been shown to be linked to increased levels of abdominal or central adiposity (19, 20, 45, 48, 75, 77, 116, 160, 161, 179). Upper body obesity, formerly known as *android obesity* (211) carries the highest level of cardiovascular risk and is ubiquitous among the defining criteria in all the working

definitions of the metabolic syndrome (14, 65, 85, 103, 155, 223). Regional fat distribution studies performed with computed topography (CT) scanning and dual energy x-ray absorptiometry (DEXA) have demonstrated that higher levels of visceral adiposity are related to greater degrees of IR and HTN (44, 81), thus creating a more atherogenic environment. However, these findings are not consistent across racial groups (13).

High levels of physical inactivity have been reported to be the seminal etiology in the rapid rise in obesity rates (127, 168). Regular bouts of PA have been shown to improve percent body fat and body fat distribution. In a cross-sectional study, Troisi et al. (208) found both BMI and waist to hip ratio to be inversely associated with regular PA. In NHANES III, women who met or exceeded the Centers for Disease Control and Prevention and the American College of Sports Medicine (CDC/ACSM) public health recommendation for PA (162) were found to have lower BMI, percent body fat, and waist to hip ratios compared to those not meeting the recommendation or reporting being physically inactive (96).

Folsom et al. (74) reported in a study of 25-74 year old men and women, that adults expending 2,000 kilocalories (kcals) per week in leisure time physical activity (LTPA) had significantly lower BMI values. Similar results were seen in the Bogalusa Heart Study (87). This study examined reported levels of leisure-time PA (LTPA) and physical inactivity and found LTPA to be inversely related with BMI and WC. In contrast, a cross-over design study consisting of 22 healthy, slightly overweight, sedentary men resulted in little change in body weight,

percent body fat, BMI or overall cardiovascular risk profile following 12 weeks moderate to vigorous PA (138). One explanation for this may be low levels of non-LTPA (domestic activities), which have been shown to reduce CVD risk at higher levels (221).

Findings from several prospective studies suggest that overweight and obesity may be more due to low levels of energy expenditure and not hyperphagia (118, 168, 228). Prospective studies however, have shown moderate amounts of PA result in small to moderate weight loss when compared to hypocaloric diets alone (95, 126, 137, 163, 188, 222). Nonetheless, several recent prospective studies have demonstrated that combining regular PA with a weight loss program in individuals at increased risk for developing the metabolic syndrome can have favorable effects on the metabolic profile, thus reducing the risk of the metabolic syndrome (50, 142, 210, 220). Therefore, adding PA to any prescribed weight loss program would be prudent. Including regular PA as an adjunct to a weight loss program has also been shown to result in a disproportionate amount of visceral fat loss (189). Furthermore, PA has been shown to increase as a function of body weight (209), therefore, regular weight maintenance is recommended for prevention of the metabolic syndrome (140).

Similar benefits from performing regular PA have also been observed in older adults. Favorable effects on body weight, body composition, lean body mass (LBM), and intra-abdominal adipose tissue have been observed in male and female master athletes (166, 183, 214) compared to sedentary age-matched controls. With losses of one kilogram of muscle per year after the fifth decade of

life, PA programs that include resistance training (RT) can help attenuate this process while preserving function (156).

Physical activity and the metabolic syndrome

The health benefits of regular PA are well recognized (162). A search of the peer-reviewed literature on the association between PA and the metabolic syndrome identified 25 studies, 19 cross-sectional studies (31, 32, 37, 54, 56, 78, 80, 87, 90, 105, 114, 132, 143, 144, 150, 161, 187, 217, 233) and six prospective studies (36, 66, 113, 117, 129, 131). Central to the research and literature examining the association of PA and the metabolic syndrome is the issue of PA volume. Frequency, intensity, and duration of PA are the components used to precisely measure PA volume.

The following section will discuss the 25 studies identified in the literature examining the association between PA and the metabolic syndrome. Both the cross-sectional and prospective studies identified in the literature will be presented by level of precision in which PA is measured, starting with least precise and leading to the most sensitive measures of PA. Predominantly, these studies focused on LTPA and not physical activities from the other PA domains (*i.e.*, domestic, transportation.)

Muscular strength and the metabolic syndrome

In a study examining the association of muscular strength with the risk of having the metabolic syndrome (155), Jurca et al. (114) grouped 8,570 men aged

20-75 years enrolled in the Aerobic Center Longitudinal Study (ACLS) into strength quartiles based on one-repetition maximal (1-RM) efforts on variable resistance equipment. The 1-RM tests performed to calculate a strength index were the supine bench press, seated leg-press, and leg-extension. Quartile 1 represented the lowest strength index and served as the referent group. Men in quartiles 2, 3, and 4 were found to be 38% (OR 0.62; 95% CI, 0.53-0.72), 57% (OR 0.43; 95% CI, 0.37-0.52), and 67% (OR 0.33; 95% CI, 0.28-0.40) less likely to have the metabolic syndrome, respectively after adjusting for age and smoking. However, after adding maximal treadmill time (which is used as a surrogate measure of cardiovascular fitness in the ACLS) to the model, this association was slightly attenuated, leaving only men in the top two quartiles for strength protected from the metabolic syndrome. This finding is not unusual given the positive impact cardiorespiratory fitness has on metabolic risk (1, 24, 105, 132, 135).

In a follow-up to a cross-sectional study examining the association between muscular strength and the metabolic syndrome (114), the same research group examined the association of muscular strength with incidence of metabolic syndrome in a longitudinal study (113). Subjects were 3,233 men aged 20-80 years enrolled in the ACLS at the Cooper Clinic in Dallas, Texas from 1980-1989.These men were free from CV disease(s) at baseline. Assessment of muscular strength and defined strength quartiles have been described previously (114). Quartile 1 defined the low strength category and served as the referent group.

The mean follow-up in this study was 6.7 years (range 0.1-22.0 years). A total of 480 men developed the metabolic syndrome during this time. Men in quartile 3 and quartile 4 were found to be 23% and 46% less likely to develop the metabolic syndrome compared to men in quartile 1 when controlling for age and examination date. However, following the addition of smoking status, alcohol intake, number of metabolic syndrome risk factors at baseline, family history of diabetes, HTN, and early onset coronary artery disease to the model, this association was attenuated. Following these adjustments, only men in strength quartile 4 remained at a decreased risk for developing the metabolic syndrome OR 0.76 (95% CI, 0.57-0.99). Others have also illustrated the benefits of resistance training and increases in muscular strength on metabolic risk (38, 55, 92, 99, 102, 206). Muscular fitness appears to add another level of protection against the metabolic syndrome in men (114) and may help with daily and long-term glycemic control.

Total physical activity time

In the Bogalusa Heart Study (87), self-reported levels of PA in hours and the risk of having the metabolic syndrome as identified by Reaven (173) was examined. Two questions assessing the level of PA were asked as part of a detailed health questionnaire. Anyone who replied "do not work" for the work related activity question (question 1) was not included in the analysis. Question 2 asked about PA outside of work. Both questions provided responses ranging from 1 (inactive to 5 (very active). Questions regarding frequency, intensity, time,

and type were not part of the questionnaire. Total LTPA status was divided into quintiles (1= inactive; 2=some activity; 3=moderate activity; 4=moderate-vigorous activity; and 5=vigorous activity) to assess the possible inverse association of having the metabolic syndrome. Individuals who reported being moderately to vigorously active were 44% to 69% less likely to have the metabolic syndrome compared to those who reported being inactive; OR 0.56 (95% CI, 0.36-0.87) for moderate, (OR 0.31; 95% CI, 0.16-0.58) for moderate-vigorous, and OR (0.41; 95% CI, 0.24-0.71) for vigorous. A inverse association was noted between the 3rd and 4th quintile, however no further reduction in risk was noted specific to the 5th quintile.

The association between performing PA and having the metabolic syndrome was examined in the Coronary Artery Risk in Young Adults (CARDIA) study (36). The study population was made up of over 4,000 black and white males and females without the metabolic syndrome. Incidence of metabolic syndrome was observed at baseline, 7, 10, and 15 years. Regular leisure-time and occupational physical activities were assessed by the validated Minnesota Heart Health Program questionnaire (109). Age-adjusted rate of metabolic syndrome were reported per 1,000 person years. Subjects who reported PA levels above the study population mean at all four follow-up examinations were classified as being regularly active; those with inconsistent measures over time were considered moderately active.

Over a mean of 13.6 years of follow-up, the metabolic syndrome was diagnosed in 575 participants (36). The age-adjusted metabolic syndrome rate

was 10 per 1,000 person years. This was similar in both genders; however, black women had the highest overall incidence. Following adjustments for age, race, gender, weight gain, and PA over time, participants who remained regularly active were found to be 51% (OR 0.49; 95% CI, 0.34-.070) less likely to have the metabolic syndrome compared to their sedentary counterparts. The addition of education, baseline BMI, baseline PA, smoking status, drinking status, and dietary covariates to the model attenuated this association slightly, however it remained significant (OR 0.65; 95% CI, 0.76-0.98).

In a NHANES III (41) study examining the association of LTPA and the metabolic syndrome, as defined by NCEP, in U.S. adults. DuBose et al. (54) defined LTPA as a three level categorical variable. PA was assessed by questionnaire, however, duration of each bout of LTPA was not assessed in NHANES III, and therefore, the quantification of LTPA energy expenditure was not possible. LTPA was categorized into 3 levels: inactive, irregularly active, and regularly active in order to assess the possible dose-response characteristics of LTPA. Moderate LTPA was defined as activity ranging from 3-6 METs, and vigorous activity was defined as > 6 METs. Each activity was then assigned an intensity level (3). Frequency of LTPA was recorded as days per week (d/wk) and dividing the number days per month of LTPA by 4.3 weeks. Those completing $\geq$ 5 d/wk of moderate LTPA and/or $\geq$ 3 d/wk of vigorous LTPA were considered regularly active, those who reported some LTPA, however not $\geq$ 5 d/wk of moderate or $\geq$ 3 d/wk vigorous, were considered irregularly active. Participants who reported no LTPA over the last 30 days were considered inactive. Irregularly

active and inactive men were found to be 52% (OR 1.60; 95% CI, 1.11-2.31) and 60% (OR 1.52; 95% CI, 1.18-1.98) more likely to have the metabolic syndrome compared to regularly active men after adjustment for age, race, gender, and education. These findings illustrate a protective association for participating in regular LTPA in men. In contrast, physical inactivity was not found to be associated with the risk of having the metabolic syndrome in women. These findings were consistent with previous studies examining the level of LTPA and risk of having the metabolic syndrome in women (105, 131, 161).

In the first two years of most recent NHANES (1999-2000) (40), a nationally representative sample of the noninstitutionalized U.S. population, the association between sedentary behavior, PA, and the metabolic syndrome (155) was examined (78). 1,626 participants, $\geq$ 20 years of age, who reported for a morning medical examination were included in the study. During this examination, subjects were asked to report the frequency and duration that they spent performing 43 different leisure-time physical activities and any type of domestic physical activities of moderate or vigorous intensities (40), however, available data on absolute intensities for each activity (METs) were not utilized in this study. The total PA time in minutes per week (min/wk) was calculated by summing the weekly minutes of participation for each activity. A three level categorical variable was then created: 0 min/wk; < 150 min/wk; and $\geq$ 150 min/wk. Time spent watching TV or playing video games was assessed and a three level categorical variable was developed for part of the analysis: $\leq$ 1hour

per day (hr/d), 2 to 3 hr/d, and ≥ 4 hr/d; and a five level categorical variable for another part of the analysis: < 1 hr/d, 2 hr/d, 3 hr/d, and ≥ 4 hr/d.

In this study, men and women who were physically inactive were found to be 63% (OR 1.65; 95% CI, 1.01-2.65) more likely to have the metabolic syndrome after controlling for age, than those reporting ≥ 150 min/wk of PA. However, after adding gender, ethnicity, education, smoking status, and alcohol intake to the model this association was attenuated and became non-significant (OR 1.45; 95% CI, 0.86-2.44). When stratified by gender, women were over twice as likely to have the metabolic syndrome when reporting no PA compared to women reporting ≥ 150 min/wk (OR 2.35; 95% CI, 1.19-4.63). Physical inactivity was not associated with the metabolic syndrome in men following stratification. Participants reporting watching TV and/or playing video games ≥ 4 hr/d were found to be twice as likely to have the metabolic syndrome when compared to those reporting these activities for < 1 hr/d. Following stratification by gender, women were almost three times as likely to have the metabolic syndrome if they reported watching TV or playing video games ≥ 4 hr/d when compared to women reporting < 1 hr/d of these activities. Regardless of their level of TV viewing or video game playing, men were not found to be at an increased risk for the metabolic syndrome.

The 1999-2000 AusDiab Study collected data from a national representative sample of over 11,000 adults in Australia (57). From this population, 7,821 adults > 35 years of age who had complete data on metabolic syndrome criteria, television (TV) viewing time, and PA time were enrolled in a

study to examine the association of time spent watching TV and hours per week (h/wk) engaging in moderate or vigorous PA with the likelihood of having the metabolic syndrome (56, 223). Subjects, using a previously validated tool (184), reported total TV viewing time or time spent playing video games over the previous seven days. A three level categorical was created for TV viewing: 0-7 hours per wk (hr/wk), 7.1-14 hr/wk, and > 14 hr/wk. The validated Active Australia Survey Questionnaire (10) was utilized to collect data on subjects frequency and duration of PA over the previous seven days. This included activities like walking for exercise or transportation, 'other' moderate activities and vigorous activity. The total PA time was summed by adding time spent walking and performing 'other' moderate activities and then adding double the time spent performing vigorous PA. The 'Active Australia' method takes into account the higher physical activity energy expenditure (PAEE) per unit of time associated with higher intensity PA (10).

In this study, men were found to be 64% more likely to have the metabolic syndrome and women were found to be over two times as likely to have the metabolic syndrome if they reported watching TV or playing video games > 14 hr/wk. However, after controlling for age, education, family history of diabetes, smoking status, and dietary covariates, only women remained at risk. Men and women reporting participating in $\geq$ 2.5 hr/wk of total PA were found to be 28% (OR 0.72 95% CI, 0.58-0.90) and 47% (OR 0.53; 95% CI, 0.38-0.74) less likely to have the metabolic syndrome, respectively, after controlling for all confounders. Furthermore, women were 38% (OR 0.62; 95% CI, 0.41-0.95) less likely to have

the metabolic syndrome if they reported walking or 'other' moderate PA and 68% (OR 0.32; 95% CI, 0.13-0.78) less likely to have the syndrome if they reported ≥ 60 min of vigorous PA per week. Men only received protection from total of ≥ 2.5 hr/wk of PA performed. One explanation for this may be women have been found to report PA more accurately than men (205). Also, limitations of the measurement tool, which excluded both domestic and occupational domains of PA, must be considered.

Physical activity energy expenditure (PAEE)

Some investigators have utilized total PAEE when examining potential associations between PA and the metabolic syndrome. Determining the effects of PAEE on the risk of having the metabolic syndrome (223) is paramount, due to the fact that it may be easier to get people to make small changes in their total energy expenditure than trying to improve their fitness level (80). In a study analyzing the relationship between habitual energy expenditure, fitness and the metabolic syndrome, the physical activity level (PAL) was developed to measure PA (217). The PAL was derived from estimating total kcal energy expenditure using the HRFlex method (42) and basal metabolic rate (BMR) to examine the association with the metabolic syndrome as defined by Reaven (173). The oxygen consumption-heart rate (HR) relationship was assessed at rest (217). Subjects were asked to come into the laboratory and cycle on an ergometer at 0 watts (W), 37.5 W, 75 W, and 125 W. Data on HR and oxygen and carbon

dioxide subfractions were collected. Energy expenditure was designated in kilojoules per minute (kj/min).

Flex HR, which is the point used to differentiate between inactivity and exercise was calculated as a mean of the highest resting pulse and the lowest HR during exercise. Mean resting energy expenditure was calculated and basal metabolic rate was predicted (82). Cardiorespiratory fitness ($V0_{2\,max}$) was predicted as oxygen uptake at maximal HR determined from a regression line during the individual HR calibration. Heart rate monitors were worn for four days and PAL was derived from subtracting the average energy expenditure at rest, from total energy expenditure. This was expressed in units of fat free mass (FFM). PAL was divided into quartiles with the lowest PAL defining the referent group. Utilizing multiple-logistic regression analysis, the overall association treating PAL quartile as a ranked categorical variable for the metabolic syndrome was 0.64 (95% CI 0.43-0.94) per quartile. The OR following adjustments for sex and BMI was 0.62 (95% CI, 0.42-0.92).

In a cross-sectional study of 874 healthy Caucasian participants from the Medical Research Council (MRC) Ely Study (216), the association of habitual PA expressed as PAEE and the likelihood of having the metabolic syndrome was evaluated (80). In addition, cardiorespiratory fitness levels were obtained to examine whether PA or fitness provided more protection from the metabolic syndrome. The HR Flex methodology for this study is described above (217). Following adjustments for age, gender and $V0_{2\,max}$, the association between PAEE expressed in kj/kg_{FFM} and the metabolic syndrome were three times

stronger than the associations for $V0_{2\ max\text{-}pred}$. These data also illustrate that those below the mean level of fitness ($V0_{2\ max\text{-}pred}$) are less likely to have the metabolic syndrome if they acquired an adequate level of PAEE. With PAEE divided into quartiles, a clear inverse association was observed for increasing levels of PAEE and the likelihood of having the metabolic syndrome. Also, these data suggest that increasing levels of PAEE may be more effective in less fit individuals.

Ekelund et al. (66), in the MRC Ely Study (217), examined whether PAEE and aerobic fitness (VO_{2max}) predicted the development of the metabolic syndrome (223) in a group of middle-aged healthy Caucasian men over a 5.6 year time frame. PAEE was measured using the flex heart method described previously (80) and aerobic fitness (VO_{2max}) was predicted by extrapolation and expressed per unit of FFM (80).

PAEE was divided into quartiles: < 44 kilojoule (~ 10.5 kcal) per kg of FFM per day ($kJ/kg_{FFM}/d$); 44-70 (~ 10.5-17 kcal) $kJ/kg_{FFM}/d$; 71-100 (~17-24 kcal) $kJ/kg_{FFM}/d$; and > 100 (~24 kcal) $kJ/kg_{FFM}/d$. The PAEE at baseline significantly predicted progression toward metabolic syndrome at 5.6 years. There was a significant difference found between the first and second quartile of the PAEE and the likelihood of having the metabolic syndrome. However, no additional decrease in risk was observed in other quartiles, thus suggesting a threshold effect for a PAEE of $\geq$ 44 $kJ/kg_{FFM}/d$ or 10.5 kcals per every 2.2 pounds of FFM per day. This association was unchanged after adjusting for level of adiposity as measured by WC or percent body fat. This was the first population-based

prospective study that used a validated objective measure to examine the association between PAEE and the metabolic syndrome (80).

The association between LTPA and the likelihood of having the metabolic syndrome was examined in the CHHS, which is a national representative sample of Canadian adults surveyed between 1986 and 1992 (31). Participants were classified as physically inactive or active in accordance with their levels of self-reported LTPA. A participant was considered active if they reported performing at least 30 minutes of LTPA that induced sweating, once a week over the last 30 days. If they did not meet these criteria, they were considered inactive. The information provided on intensity (sweating) was not enough to determine whether moderate or vigorous LTPA was performed. Men, but not women who reported at least 30 minutes of LTPA that induced sweating four times over the last month were found to be less likely (OR 0.45; 95% CI, 0.29-0.69) to have the metabolic syndrome, however, women did not receive the same protection (OR 0.67; 95% CI, 0.44-1.02). However, without information regarding LTPA intensity, LTPA volume was unable to be determined. Having information on intensity may have helped elucidate why there was no protective association found between LTPA and the metabolic syndrome in women in this study.

Metabolic equivalents (METs) of physical activity

A more sensitive measure for expressing total volume of PA includes utilizing a measure of absolute intensity expressed in METs. METs are obtained by dividing the oxygen uptake in $mL \cdot kg^{-1} \cdot min^{-1}$ by 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ (100). This

can also be expressed in MET·min ·wk^{-1}; for example, an individual running 5 times per week at an intensity level of 4 METs for 30 minutes would accumulate 600 MET·min·wk^{-1} of PA:

(5 times/week) * (4 METs) * (30 minutes) =600 MET·min·wk^{-1}

Recently, physical activity epidemiology studies examining the metabolic syndrome and the role of PA (105, 129, 131, 144, 177) have been able to utilize a more sensitive measure of PA by assigning a specific MET level to the activity performed (3). This allows investigators to more easily quantify self-report PA data collected by questionnaires and examine potential inverse relationships.

Two studies identified in the literature utilized a *PA intensity score* (PAIS) (161, 233) to define the PA level and examine the association with the metabolic syndrome utilizing the NCEP definition. PAIS is defined by the ratio of work metabolic rate (METs) to resting metabolic rate (RMR) obtained by a self-report recall of participation in one or more of the following activities during the past month: walking, jogging or running, cycling, swimming, resistance training, exercise classes, or yard work (41). PA was categorized based on the participants, PAIS (MET equivalent) over the last 30 days. A PAIS of $\leq$ 3.5 was classified as inactive, 3.6 -14.9 was classified as moderately active, and $\geq$ 15 was classified as active for both men and women. These specific values designated the 15th and 65th percentile of PA for men and the 25th and 75th percentile of PA for women in the US (154).

In the Third National Health and Nutrition Examination Survey (NHANES III), Park et al. (161) utilized the PAIS to define physical inactivity while examining the relationship of being inactive with the metabolic syndrome. Individuals with a PA intensity score $\leq$ 3.5 were designated physically inactive and identified the 15th and 25th percentiles of adult males and females respectively in the U.S. population. In a multivariate odds ratio (OR) model adjusting for ethnicity, BMI, smoking status, alcohol intake, carbohydrate intake, education level in years, household income, and menopausal status, neither men (OR 1.4; 95% CI 1.0-2.0) or women (OR 1.2, 95% CI 1.0-1.4) classified as physically inactive by a PAIS of $\leq$ 3.5 were found to be at an increased risk for having the metabolic syndrome. Therefore, suggesting no relationship between physical inactivity and the metabolic syndrome.

In another study utilizing the same NHANES III dataset and PAIS, Zhu et al. (233) examined the relationship of being active, moderately active, and inactive based on a PAIS $\geq$ 15.0 (active), $\geq$3.6 to 14.9 (moderately active), and $\leq$3.5 respectively, with the likelihood of having the metabolic syndrome. Both males (OR, 0.41 95% CI 0.31-0.54) and females (OR, 0.25, 95% CI 0.18-0.37) in the active group were found to be less likely to have the metabolic syndrome compared to the inactive group. Following adjustments for BMI, males were 73% less likely (OR 0.27, 95% CI, 0.18-0.40) and females were 68% less likely (OR 0.32; 95% CI, 0.21-0.51) to have the metabolic syndrome if they reported being active. In men and women who reported being moderately active they were found to be 34% less likely (OR 0.66; 95% CI, 0.48-0.89) and 31% less likely

(OR 0.69; 95% CI, 0.48-0.99) to have the metabolic syndrome respectively. These findings illustrate a potential inverse association between PA and the metabolic syndrome. However among females, after adding age, race, education, income, and menopausal status to the model, the protective effect of PA disappeared.

In a cross-sectional sample of 711 white males, Carroll et al. (37) utilized a leisure-time *physical activity index* (PAI) (192) to examine the association between LTPA and the metabolic syndrome using the criteria originally put forth by Reaven (173). Data from a 4-week history of LTPA was available for 697 of the original 711 men. These men were asked about their usual LTPA patterns, designating regular walking in minutes per weekday (min/wkd), cycling activity in minutes per day (min/d), recreational activity in hours per weekend (h/weekend), and vigorous activity in times per month (times/m). A PAI score was calculated based on frequency, duration, and intensity of each activity. Scores were assigned for each mode of activity and time spent performing the activity based on the intensity and energy requirement of each activity reported (202, 230). These men were grouped into four categories: inactive (0-2 consisting of no LTPA); occasional/light (3-8 consisting of walking and some more vigorous activities); moderate/moderate vigorous (9-20 consisting of cycling or frequent sporting activities); and vigorous ($\geq$ 21 consisting of very frequent sporting and recreational activities.)

When compared to the inactive group, men with a PAI of 3-8 were found to be 44% less likely (OR 0.56; 95% CI, 0.33-0.96) to have the metabolic

syndrome. This would equate to performing LTPA 2-3 times per week at 3-4 MET level for 30-40 minutes per session, or approximately 300 MET·min·wk^{-1}. Men with a PAI of 9-20 were found to be 67% less likely (OR 0.37 95% CI, 0.19-0.71) to have the metabolic syndrome. This would equate to performing LTPA 3-4 times per week at a 5-6 MET level for 30-45 minutes per session, or approximately 700 MET·min·wk^{-1}. Men with a PAI $\geq$ 21 were found to be 88% less likely (OR 0.12; 95% CI, 0.03-0.50) to have the metabolic syndrome and this would equate to performing LTPA 4-5 times per week at $\geq$ a 6.5 MET level for 45-60 minutes per session, or approximately 1530 MET·min·wk^{-1}. A clear inverse association was noted for each increase in PAI score.

Misra et al. (150) reported the association between LTPA and the metabolic syndrome in a study of Asian Indian immigrants living in Northern California. In this study, LTPA was expressed as a score of *activity metabolic index* (AMI) utilizing a Taylor intensity code (202) reported for each type of LTPA performed over the last 12 months. When examining the risk of metabolic syndrome as defined by NCEP, an AMI was calculated for light, moderate, heavy, and total LTPA over the last year:

$$\text{Total AMI} = \sum (\text{intensity*months/year}) * (\text{frequency/month}) * (\text{time/session})$$

This study found that compared to women, men were twice as likely to be active. Also, men and women with the metabolic syndrome reported the lowest

levels of LTPA estimated by the AMI. Men engaging in moderate LTPA of approximately 88 MET·min·wk^{-1} and high intensity PA of approximately 180 MET·min·wk^{-1} for a total of 268 MET·min·wk^{-1} were found to be significantly less likely to have the metabolic syndrome than men performing only light LTPA. This association was not seen in women. Women reported performing activities of similar intensity to men; however the total number of MET·min·wk^{-1} of LTPA performed by women was less than half of that performed by men. Women reported engaging in approximately 203 MET·min·wk^{-1} of PA or 50 total minutes of LTPA per week, while men reported engaging in approximately 533 MET·min·wk^{-1} of accumulated LTPA or 124 total minutes of LTPA. This illustrated an inverse association between PA and the risk of being diagnosed with the metabolic syndrome.

In a study of Aboriginal (native) Canadians examining non-traditional cardiovascular risk factors and their association with the metabolic syndrome as defined by three different medical societies (103, 155, 223), the association of PA with the syndrome was also evaluated (144). The lifestyle for Aboriginal people traditionally involved activities of daily living (ADLs) being of the vigorous nature, however, over the last 20 years many Aboriginals have drastically reduced their daily PA levels. Data was collected on 360 non-diabetic adults participating in a study of Aboriginal Canadians. A previously modified PA questionnaire (125) was used to assess PA. Participant PA levels were determined by LTPA and occupational activities over the past 12 months. Activity intensity was estimated so PA could be expressed in MET hours per week (MET·h/wk^{-1}). In addition,

cardiorespiratory fitness level was estimated utilizing a validated step protocol (193) and expressed in $mL \cdot kg^{-1} \cdot min^{-1}$.

In a multiple logistic regression model controlling for age, percent body fat, smoking status, and fitness level, men who reported engaging in regular PA were found to be 4% less likely to have the metabolic syndrome, (OR 0.96; 95% CI, 0.93-0.99) for every 5 $MET \cdot h/wk^{-1}$ increase in PA. This relationship not observed in women (OR 1.00; 95% CI, 0.98-1.03). However, in the same model with the substitution of PA level for CV fitness, men and women were found to be 84% and 66% respectively, less likely to have the metabolic syndrome for every 10 $mL \cdot kg^{-1} \cdot min^{-1}$ increase in cardiorespiratory fitness. The stronger association for fitness over PA is difficult to explain, but is most likely due to the objective nature in which cardiorespiratory fitness was measured compared to the self-report assessment of PA (23). In addition to utilizing the WHO (223) definition, these investigators when applying the NCEP (155) and IDF (103) definitions did not detect any changes in the results.

In a national study of over 50,000 Chinese, aged 15- 96, the association between low, moderate, and high levels of PA performed at varying intensities and the risk of having the metabolic syndrome as defined by the Chinese Medical Association was examined (143). Following adjustments for gender, age, smoking status, alcohol intake, and BMI, those who reported performing 900 $MET \cdot min \cdot wk^{-1}$ of low-level PA for were found to 55% less likely to have the metabolic syndrome when compared to those who reported performing 450 $MET \cdot min \cdot wk^{-1}$ of low-level PA. In addition, Chinese men and women who

reported engaging in ≥ 360 MET·min·wk^{-1} of vigorous PA were found to be 25% less likely to have the metabolic syndrome than those reporting < 360 MET·min·wk^{-1} of vigorous PA.

The association between MET hours per week (MET·hr·wk^{-1}) of LTPA and the likelihood of having the metabolic syndrome was examined in the Whitehall II study of civil servants aged 45-68 years (177). The metabolic syndrome was defined as meeting the cut-off points for the sex-specific top quintile, or bottom quintile in the case of HDL-C for three or more of the following: post-glucose load; SBP; fasting triglycerides; fasting HDL-C; and waist to hip ratio. This was done due to the fact that no medical society definition for the metabolic syndrome had yet been published, and these quintile cut points were thought to representative of a level of increased risk for CVD. Utilizing a modified version the Minnesota leisure-time physical activity questionnaire (202), data on 20 different activities were collected. Activity patterns over the last month were ascertained in order to get a notion for habitual activity. Activities were assigned a MET value (3) to calculate MET hours per week (MET·h/wk^{-1}). MET values for activities were grouped into two categories: moderate (METs ≥ 3 to < 5 METs), this included walking and yard work, and vigorous (METs ≥ 5). Moderate activity was then divided into two categories consisting of < 24 MET·h/wk^{-1} and ≥ 24 MET·h/wk^{-1}. Vigorous activity was divided into four categories: no vigorous LTPA, < 5 MET·h/wk^{-1}, ≥ 5 and < 12.5 MET·h/wk^{-1}, or ≥ 12.5 MET·h/wk^{-1}.

Following adjustment for age, gender, smoking status, alcohol intake, and job grade (grade 1 represented the highest job status and grade 6 represented

the lowest job status), individuals reporting ≥ 24 MET·h/wk^{-1} of moderate LTPA were found to be 22% less likely (OR 0.78; 95% CI, 0.63-0.96) to have the metabolic syndrome when compared to those reporting < 24 MET·h/wk^{-1} of LTPA. Those who reported performing some vigorous LTPA, but accumulated < 5 MET·hr·wk^{-1} were found to be 31% less likely (OR 0.69; 95% CI, 0.52-0.91) to have the metabolic syndrome, while those reporting ≥ 5 METs, but < 12.5 METs of vigorous LTPA were found to be 23% less likely (OR 0.77; 95% CI, 0.60-0.99), and those who reported engaging in ≥ 12.5 MET·hr·wk^{-1} of vigorous LTPA were found to be 48% less likely (OR 0.52; 95% CI, 0.40-0.67) to have the metabolic syndrome compared to those reporting no vigorous activity LTPA.

In a study of 107 middle-aged men participating in the KIHD Study, LTPA and the development of the metabolic syndrome as defined by the WHO was examined (131). The inclusion of microalbuminuria in the WHO definition as a component of the metabolic syndrome had been challenged (14, 110), therefore it was excluded from the analysis. The KIHD 12 month LTPA Questionnaire (134) was utilized to assess the duration, frequency, and average intensity of the most commonly performed physical activities. Low LTPA was defined as < 4.5 METs, moderate LTPA was defined as ≥ 4.5 METs, and the cut-off point for vigorous LTPA was ≥ 7.5 METs. The total time in minutes per week (min·wk) for these three levels of LTPA was summed. The odds risk ratios for total LTPA, low-intensity LTPA, moderate and vigorous LTPA, and vigorous LTPA and the likelihood of having the metabolic syndrome were calculated.

At the 4-year follow-up, and adjusting for age and BMI, men reporting engaging in a total amount of LTPA $\geq$ 487 min·wk^{-1} were found to be 47% less likely (OR 0.53; 95% CI, 0.31-0.92) to have the metabolic syndrome compared to men reporting < 270 min·wk^{-1} (referent group). In the same model, similar reductions in risk were observed in men reporting $\geq$ 180 min·wk^{-1} or approximately 720 MET·min·wk^{-1} of moderate (OR 0.52; 95% CI, 0.30-0.90) and vigorous (OR 0.37; 95%CI, 0.21-0.66) LTPA. For vigorous activity, men reporting a total of $\geq$ 60 min·wk^{-1} or 450 MET·min·wk^{-1} of LTPA were found to be 64% (OR 0.36; 95% CI, 0.19-0.70) less likely to have the metabolic syndrome compared to men reporting < 10 min·wk^{-1} of vigorous activity (referent group). No association between moderate LTPA and metabolic syndrome was observed. This was the first longitudinal study reporting the association of LTPA with the development of the metabolic syndrome (131).

In another study utilizing the measure of MET·min·wk^{-1} of LTPA, the same group (131) examined the association between vigorous LTPA and the development of the metabolic syndrome (223) among low birth weight men (129). Data on birth weight and length was gathered on 462 men aged 42, 48, 54, or 60 years at baseline, in the previously described KIHD Study (185). The researchers used the ponderal index (PI) which was computed as birth weight in kg/length (m^3) (180). The assessment of LTPA and the classification of the vigorous LTPA were described previously (131).

Men who were underweight at birth according to the PI were two times more likely (OR 1.98; 95% CI, 1.09-3.60) to have the metabolic syndrome than

men with a normal PI. However, the risk of having the metabolic syndrome among low-birth weight men was nullified in those reporting $\geq$ 25 min·wk^{-1} or 188 MET·min.wk^{-1} of vigorous LTPA when compared to men reporting < 25 min·wk^{-1} or 188 MET·min.wk^{-1} of vigorous LTPA. This association remained following adjustments for child or adult socioeconomic status (SES) and BMI. These results illustrate that an active lifestyle can modify health outcomes in what some consider a *thrifty phenotype* (17, 98). Individuals with a thrifty phenotype have a smaller body size and lower RMRs, thus making them more susceptible to metabolic disorders, particularly in affluent societies (16).

Physical activity and the risk of the metabolic syndrome as defined by NCEP was examined in a sample of tri-ethnic females (105). This study had 146 subjects who were enrolled in the Cross-Cultural Activity Participation Study (4, 106). The Cross-Cultural Activity Participation Study is a study designed to examine PA patterns of women > 40 years of age of varying race and ethnic backgrounds. A total of 51 white women, 49 African-American women, and 46 Native-American women participated with PA records obtained two times, 30 days apart. Each activity had the type, duration, and intensity recorded and was used to calculate MET minutes per day (MET·min/d^{-1}) for moderate and vigorous LTPA. Utilizing the compendium of physical activities (3), each activity had a MET value assigned to it. This allowed the absolute intensity of the LTPA to be measured. Women reporting 491 MET·min/d^{-1} to 1351 MET·min/d^{-1} of moderate intensity LTPA were found to be 82% (OR 0.18; 95% CI, 0.03-0.90) less likely to have the metabolic syndrome than women in the least active group. Women

reporting any vigorous LTPA were also less likely to have the metabolic syndrome compared to their inactive counterparts; however, due to a power issue related to the inverse association observed with vigorous LTPA, this did not reach significance.

In the Kuopio Ischemic Heart Disease Study (132) (KIHD) a cross-sectional association of self-reported LTPA and the risk of having the metabolic syndrome as defined by the WHO (223) was examined. The KIHD included 1,069 middle-aged men free of diabetes and CVD at baseline. The validated KIHD 12-month LTPA questionnaire assessed the duration, frequency, and mean intensity of LTPA over the previous year. LTPA was defined as low-intensity which corresponded to < 4.5 metabolic equivalents (METs), and *at least* moderate intensity, which was defined as ≥ 4.5 METs. Three Categories of LTPA were then created with tertiles of LTPA in minutes per week (min/wk) in each category: total minutes of LTPA, MET·min·wk^{-1} of low-intensity LTPA, and MET·min·wk^{-1} of moderate and vigorous LTPA.

After adjusting for age, men reporting < 217 min/wk^{-1} of total LTPA were found to be 64% more likely (OR 1.64; 95% CI, 1.08-2.49) to have the metabolic syndrome than men reporting ≥ 409 min/wk^{-1} of total LTPA . Low-intensity LTPA was not found to be associated with the metabolic syndrome. However, men reporting < 360 MET·min·wk^{-1} of at least moderate and vigorous LTPA were found to have a similar increase in risk for having the metabolic syndrome as men reporting < 217 min/wk^{-1} of total LTPA (OR 1.63; 95% CI, 1.07-2.48). Thus,

men reporting engaging in low-levels of LTPA, regardless of the intensity level, were found to be at an increased risk for having the metabolic syndrome.

In a sample from the HERITAGE Family Study (117), the efficacy of a 20 week aerobic exercise training program was evaluated for treating the metabolic syndrome (117, 155). There were 621 black and white participants, aged 17 to 65 years, who met the inclusion criteria of being healthy and sedentary adults with BP <160/100 mmHg. The metabolic syndrome prevalence was calculated at baseline and at the end of the 20 week exercise program. Participants began exercising three times per week, 30 minutes per session at 55% of their $VO_{2\ max}$, or approximately 360 MET·min·wk^{-1} for the first two weeks and eventually progressed in the 20 week program to exercising three times per week for 30 minutes at 75% $VO_{2\ max}$, or approximately 550 MET·min·wk^{-1}. Following baseline analysis, 105 of the 621 participants were found to have the metabolic syndrome, thus the prevalence was 16.9% for the entire study sample. The prevalence of the metabolic syndrome was similar for black men, white men, and black women, however, white women were found to have a lower prevalence.

Following the 20 week exercise program, 32 of the 105 participants classified with the metabolic syndrome at baseline no longer had the syndrome. In addition, there were no differences between the 32 participants who no longer had the metabolic syndrome and the remaining 73 participants who still had the syndrome in terms of age or current fitness level. Consequently, the prevalence in this study sample dropped from 16.9% to 11.8%. This was the first study to

report the usefulness of regular PA in the simultaneous improvements of the constellation of risk factors that make up the metabolic syndrome.

Santos et al. (187) evaluated the association between PA, hours spent sleeping, alcohol and smoking habits with the risk of the metabolic syndrome. Self-report data was collected on 2,164 adults (1,332 women; 832 men), aged 18-92 years. PA data was collected from occupational (included transport to and from work), domestic and LTPA domains over the previous 12 months. A MET level was assigned to each group of activities and these groups were categorized as very light, light, moderate and heavy activities with the corresponding mean MET values of 1.5, 2.5, 5.0 and 7.0 respectively. MET values were then multiplied by the duration of each activity in minutes per day. Participants MET hours per day (MET/h/d) were then divided into tertiles for all three domains of PA and total PA.

Following adjustment for age, education, smoking, and alcohol intake women in the upper tertile of total PA (1.54-3.46 MET/h/d) were found to 37% less likely (OR 0.63; 95% CI, 0.43-0.94) and men in the upper tertile of total PA (1.59-4.29 MET/h/d) were found to be 45% (OR 0.55; 95% CI, 0.33-0.91) less likely to be diagnosed with the metabolic syndrome compared those in the lowest tertile. When examining the other three PA domains individually, there was no association found in men for occupational, domestic, or LTPA with the metabolic syndrome. However, women received the same level of protection from upper tertile of occupational PA (OR 0.63; 95% CI, 0.40-0.99) as they did from the

upper tertile of total PA (OR 0.63; 95% CI, 0.43-0.94). There was no association found in women for domestic or LTPA with the metabolic syndrome.

These results suggest that LTPA by itself may not be sufficient in reducing the risk of being diagnosed with the metabolic syndrome. Total PA accumulated from all domains may be more important in attenuating metabolic syndrome risk. Also, women with physically active jobs may receive protection from the metabolic syndrome.

The association between regular PA and the risk metabolic syndrome has also been examined in older adults (90). In a cross-sectional study examining PA and its association with the metabolic syndrome as defined by NCEP, over 4,000 men and women, 60 years of age and older were surveyed. PA over the past 12 months was categorized into four groups: 1) Low PA of < 240 MET·min·wk^{-1} representing a sedentary lifestyle; 2) Light PA (≥240 MET·min·wk^{-1}, generally without sweating, although not a good marker for PA intensity (219)); 3) moderate PA (approximately 360 MET·min·wk^{-1}, regularly active one to two times per week for at least 30 minutes per session); and 4) High PA (≥360 MET·min·wk^{-1}.) The results of this study indicated an inverse association between regular PA and the metabolic syndrome. Compared to group 1 (< 240 MET·min·wk^{-1}), participants reporting at least 240 MET·min·wk^{-1} (group 2) of PA were found to be 50% less likely (OR 0.50; 95% CI, 0.40-0.64) to have the metabolic syndrome. Those reporting at least 360 MET·min·wk^{-1} (group 3) were found to be 57% less likely (OR 0.43; 95% CI, 0.32-0.58), and those reporting ≥ 360 MET·min·wk^{-1} were found to be 67% less likely (OR 0.33; 95% CI, 0.22-0.51)

to have the metabolic syndrome. Hence, a clear inverse association between PA and the metabolic syndrome was seen in this study of older adults.

Summary of physical activity and the metabolic syndrome literature

In the literature, there is a consistent inverse association found between participation in regular PA and the likelihood of having the metabolic syndrome. An inverse association between PA and the likelihood of having or developing the metabolic syndrome was observed in more than half the studies cited in this review. Physically active study participants were found to be 4% to73% less likely to have the metabolic syndrome compared to their inactive peers. This association is influenced by the study population, study design, and how PA is measured. The minimum effective dose is not well defined, but a total of $\geq$ 150 min·wk of moderate PA or $\geq$ 60 min·wk^{-1} of vigorous PA appears to be associated with a reduced risk of having or developing the metabolic syndrome. When examining absolute volume of PA with metabolic syndrome risk, protection appears to start at approximately 300 MET·min·wk^{-1}, which could be accomplished by taking a 30 min walk at a moderate intensity (3-4 METs) three of four times per week.

There were many limitations reported in these studies. The lack of data on frequency, duration, intensity, and mode of PA was not available in many studies, thus excluding a true absolute measure of PA volume from being utilized. The self-report nature of survey (questionnaire) data is subject to recall bias. The PA questions in most of these studies focused on LTPA only. Some questionnaires

utilized in these studies have not been validated. Three-quarters of the studies identified were of the cross-sectional nature, thus causality is unable to be established. To date, there have only been two studies examining muscular strength and the risk of the metabolic syndrome, and they were both in men.

Future physical activity and metabolic syndrome research needs

Studies of PA and metabolic syndrome risk should focus on the strength of the inverse association. It has been established that approximately 30 minutes of moderate activity on most days of the week or approximately 60 min of vigorous activity performed at least 3 days per week will reduce the risk of the metabolic syndrome. Furthermore, some studies appear to show different associations for PA and metabolic syndrome risk between genders. Future studies are needed to examine the association disparity between genders. Furthermore, the effects of resistance training (*i.e.*, muscular strength) on metabolic syndrome risk, warrant continued investigation in men and need to be evaluated in women.

Summary

The current prevalence estimates of the metabolic syndrome around the world range from a low of 7.8% (7) to a high of 39.1% (75). These prevalence estimates vary depending on the population being studied and the metabolic syndrome definition utilized. Prevalence appears to greater in men and increases with age. The greatest impact on metabolic syndrome prevalence is the medical

society definition applied to a study population. Several studies have utilized various definitions of the metabolic syndrome, thus making it difficult to make comparisons between studies. The core components (glucose, obesity, dyslipidemia, and HTN) are similar in all the commonly utilized working definitions (46, 85); however, the cut-off points for each condition are not consistent among definitions. With comparison of two different definitions in the same population, prevalence estimates of the metabolic syndrome have been shown to differ (75, 76), thus definition utilized has been shown to have an impact on prevalence.

In all 25 studies identified in the literature that have examined the association of PA with the metabolic syndrome, a consistent inverse association or suggestion of potential protection was found between participating in regular PA and the likelihood of having or developing the metabolic syndrome. Some of these studies found the favorable effects of PA to be limited to a specific gender (54, 78). However, in the majority of the studies that included both men and women, some level of protection from being physically active was observed. Overall, it appears as the volume of PA increases, the likelihood of having or developing the metabolic syndrome decreases. The precise amount of PA necessary to elicit a reduced risk of the metabolic syndrome is not well defined, however, current research illustrates that meeting the recent public health recommendation for PA (162) would be prudent.

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PART III

METHODOLOGY

The purpose of this study was to examine the relationship between Leisure-Time Physical Activity (LTPA) and the likelihood of having the Metabolic Syndrome in a nationally representative sample of the United States (U.S.) adult population. The following section furnishes a detailed description of the methodology that was utilized in this study. The study employed secondary data analysis of the most recent release of the 1999-2004 National Health and Nutrition Examination Survey (NHANES). This section includes a discussion of the subjects, a description of NHANES 1999-2004, variables of interest, and data analysis.

Subjects

The subjects included in this study participated in the 1999-2004 NHANES (6). NHANES is conducted by the National Center for Health Statistics (NCHS) and is a continuous survey that regularly releases public use data as smaller component-specific files (3). The most recent survey was conducted from 1999 through 2004 and represents the eighth series of NHANES. The total sample N for the most recent six years of data released from NHANES was 31,126 and included individuals two months of age and above. The final sample for this study was 5,620 U.S. adults $\geq$ 20 years of age who were given a clinical exam following an overnight fast (minimum 8 hours).

The sample for this study met the following conditions: 1) adult men and women $\geq$ 20 years of age; 2) attending a morning MEC examination following an

overnight fast; 3) if a women, not pregnant; and 4) had provided complete data on all the variables of interest.

Data Collection

Data were collected from a nationally representative sample of U.S. adults, ≥ 20 years of age (N= 31,126) living in residences that were selected in NHANES 1999-2004. All eligible study participants, or their guardians, were provided with and signed an informed consent describing the details of the survey. All information collected was kept confidential in accordance with the Public Health Service Act and the Privacy Act of 1974 (15). The main objectives of NHANES are to estimate the prevalence of various diseases and risk factors in the U.S. population in order to monitor trends for treatment and control (6). NHANES also provides information on risk factors for known diseases in order to study the relationship between behavior, environment, and health.

The NHANES studies are conducted by the NCHS, which is a federal agency that collects health data for the U.S. (3). The NHANES survey design is a stratified, multistage probability sample of the noninstitutionalized U.S. civilian population over the age of two months. The stages of the sample selection include the following: 1) primary sampling unit (PSU) selection; 2) selection of PSUs in each segment; 3) selection of residence in each PSU; and 4) interviewing at least one person in each household. The 1999-2004 NHANES over-sampled low-income persons, adolescents, persons 60 years of age and older, and minorities (3). Previously, NHANES were conducted on a periodic

basis and data were released in single data set covering multiple years. Beginning in 1999, NHANES has been conducted as a continuous survey, releasing public use data continuously as smaller component-specific data in two-year phases. For example, NHANES 1999-2004 data were released as NHANES 1999-2000, NHANES 2001-2002, and NHANES 2003-2004.

Each year nearly 7,000 people are interviewed by trained interviewers in the participants' place of residence. Approximately 5,000 of the people interviewed in their homes also complete a health examination survey conducted in a mobile examination center (MEC). If an individual is unable to attend the MEC, they may receive a health examination at home (6). All interviews are recorded using a computer assisted personal interview (CAPI) system. Eligible participants who are 16 years of age or older are interviewed without a guardian, but those participating in the survey under the age of 16 are interviewed with a parent or guardian (5). These health surveys include questions regarding a wide breadth of health and nutrition related issues (*e.g.,* has you doctor ever told you that you have diabetes?).

Participants, who attend the MEC for the health examination component, are examined by a wide range of health professionals. Each MEC team is made up of one doctor, one dentist, two dietary personal, three certified medical technologists, five health technicians, one phlebotomist, two trained interviewers, and a data manager (6). Standardized medical examinations are completed including measurements directly associated with the metabolic syndrome and

PA. These measures include blood pressure, lipoprotein values, glucose levels, waist circumference, and urinanalyis.

Measures

Dependent measure(s): The Metabolic Syndrome

The dependent variable in this study was a positive diagnosis of the metabolic syndrome based on the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria (9). In 2005, the American Heart Association and the National Heart, Lung and Blood Institute issued a new definition which serves as an updated version of the NCEP criteria (9). The majority of research that has been done on the metabolic syndrome and PA has involved the use of the NCEP (14) criteria, which preceded the AHA/NHLBI definition.

The AHA/NHLBI definition requires that three of the following five risk factors be present for a diagnosis of the metabolic syndrome: 1) impaired fasting glucose (IFG) $\geq$ 100 milligrams per deciliter (mg/dL) or undergoing pharmacological treatment; 2) low high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL in men or < 50 mg/dL in women, or undergoing pharmacological treatment; 3) triglycerides $\geq$ 150 mg/dL or undergoing pharmacological treatment; 4) a waist circumference (WC) > 102 centimeters in men or > 88 cm in women; and, 5) blood pressure $\geq$ 130/85 mm/Hg or undergoing pharmacological treatment for hypertension (HTN). The AHA/NHLBI definition is unique in the respect that it precludes specific inclusion criteria of any one condition (*e.g.,* IFG)

in order for metabolic syndrome to be diagnosed. This most recent definition put forth by the AHA and NHLBI mirrors the NCEP definition with the following modifications: pharmacological treatment for those with dyslipidemia, HTN, and IFG are positively identified to the respective criteria for diagnosis. In addition, the cut-off point for IFG was lowered from 110 mg/dL to 100 mg/dL to reflect the recent changes issued by the American Diabetes Association (ADA) for IFG (1). A comparison of this definition to other metabolic syndrome medical society definitions can be found in Table A-1 in Appendix A.

In creating a dependent variable based on a positive diagnosis of the metabolic syndrome utilizing the AHA/NHLBI definition (METyes), data on blood pressure, fasting glucose, lipoprotein values, and WC measurements were utilized from the MEC related data from the health examination component of the survey. Each criterion was dichotomized with the demarcation being the cut-off value for inclusion as a component of the metabolic syndrome. For example, the following is a recode for blood pressure (BP) that was utilized in our study:

If 130<=bpxsar or 85<=bpxdar or bpq050a=1 then AHAHTN=1;
else if bpxsar<130 and bpxdar<85 or bpq050a=2 then AHAHTN=0;

If a person was found to have a systolic BP (code=bpxsar in NHANES data file) $\geq$ 130 or a diastolic BP (code=bpxdar in NHANES data file) $\geq$ 85 or undergoing pharmacological treatment for HTN (code=bpq050a in NHANES data file) they were coded a 1 for having HTN.

Metabolic syndrome risk score (MSRS):

In creating a dependent variable based on a positive diagnosis of the MetS utilizing the AHA/NHLBI definition, data on blood pressure, fasting glucose, lipoprotein values, and WC measurements were utilized from health examination component of the NHANES. Each CV risk factor was dichotomized with the demarcation being the cut-off value or pharmalogical treatment for inclusion as a component of the MetS (0= no risk; 1= risk). Risk factors were summed and a total metabolic syndrome risk score (MSRS) was calculated which ranged from 0 (no risk factors) to five (all five risk factors present). Those subjects with a score of 0-2 risk factors were determined not to have the MetS and those respondents with a score of 3 to 5 risk factors were determined to have the MetS.

Independent measures

A variety of variables were utilized as independent factors in this study. The primary independent measure of in this study was LTPA. All other independent measures were treated as controlling measures.

Leisure-Time Physical activity (LTPA): Data utilized to measure PA were collected from two distinct NHANES files. The PA and physical fitness file (PAQ_C) and the PA individual activities file (PAQIAF) from the household questionnaire and MEC interview (4). The PAQIAF is the second of two files on PA and includes more detailed information regarding 43-specific types of moderate and vigorous leisure-time activities. This study utilized LTPA data from the PAQIAF. The following codes were used to identify the characteristics of PA:

- PADACTIV: Numeric code for specific type of PA reported.
- PADTIMES: Frequency reported for the activity over the past 30 days.
- PADDURAT: Average amount of time (in minutes) spent during each activity session.
- PADMETS: Metabolic equivalent (MET) score assigned to each activity utilizing the compendium of physical activities (2).

The information from the PAQIAF allowed us to create a sensitive measure of PA to examine the relationship with the metabolic syndrome. Taking the number of times an activity was done over the last 30 days and calculating how many times per week the activity was performed provided a frequency per week. Utilizing the compendium of PA and assigning the appropriate MET level to the type of activity performed provided us with the intensity of the specific activity. METs represents the oxygen uptake for that activity in $mL \cdot kg^{-1} \cdot min^{-1}$ divided by 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ (10). Then, taking the average duration (minutes per session), the average frequency (number of sessions per week) and the intensity level (MET-level) assigned to the activity, we calculated MET minutes per week ($MET \cdot min \cdot wk^{-1}$). This was done for each LTPA performed. The sum of all $MET \cdot min \cdot wk^{-1}$ performed produced a "total $MET \cdot min \cdot wk^{-1}$" measure. The following is an example of a calculated LTPA $MET \cdot min \cdot wk^{-1}$ value from an earlier pilot study that examined the relationship of LTPA with the metabolic syndrome according to the NCEP definition (See Appendix B):

Frequency (5 sessions per week) x Intensity (4 METs) x (Duration 30 minutes/session)

$= 600\ MET \cdot min \cdot wk^{-1}$

In order to examine a possible inverse association for LTPA and the metabolic syndrome, $MET \cdot min \cdot wk^{-1}$ was divided into a six-level ordinal variable. The first level represented those who were physically inactive, the referent group for this study. This level included all individuals who reported no moderate or vigorous LTPA. Thus, they were assigned a score of "0" $MET \cdot min \cdot wk^{-1}$. In calculating the remaining five levels of this measure, the $Met \cdot min \cdot wk^{-1}$ was divided into quintiles from the $MET \cdot min \cdot wk^{-1}$ measure. This was done for two reasons: 1) to account for the non-normally distributed and skewed data that is inherent to national population surveys (11), and 2) to provide a greater level of precision when looking for a potential inverse association.

A second measure used focused on whether this possible inverse association transfers over to a three-level categorical variable based on the Centers for Disease Control and Prevention and the American College of Sports Medicine (CDC/ACSM) public health recommendation (18). Individuals who were found to meet the CDC/ACSM PA recommendation of five days per week of moderate intensity LTPA for 30 minutes, or three days per week of vigorous intensity LTPA for 20 minutes were classified as meeting the public health recommendation; individuals who were found to engage in LTPA at least one time per week but not meeting the CDC/ACSM recommendation were classified

in the some, but insufficient category. Those who reported performing no LTPA were classified as inactive.

Other independent measures

Additional factors that were controlled for included five demographic variables; age, race/ethnicity, and two markers of socioeconomic status (SES), education and income.

Age

Age was categorized into seven, 10-year age-groups: 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, and $\geq$ 80. The division of age into 10-year age-groups allowed testing for a more precise possible inverse association of PA.

Education

Education was divided into three categories. Completing less than 12^{th} grade (referent group), completing 12^{th} grade, or education beyond 12^{th} grade.

Income

Income was categorized as percent of poverty thresholds (< 100%, 100% to 199%, 200% to 299%, 300% to 399%, > 400%). The standardized poverty threshold represents dollar amounts that define poverty status while accounting for family size

(www.census.gov/hhes/www/poverty.html). Falling below a poverty threshold of 100% demarcates living in poverty.

Further adjustments were made for alcohol consumption, smoking status, and family history of chronic disease, including heart disease and diabetes. All of these preceding variables may impact the cardiovascular disease risk factors that define the metabolic syndrome, and will be briefly discussed below.

Alcohol intake

Alcohol intake in moderation has been shown to have favorable effects in people with the metabolic syndrome (8). In NHANES, alcohol intake is assessed over the previous 12 months. Moderate alcohol intake is classified as one drink or less per day in women, and two drinks or less per day in men. In this study, a three level categorical variable was created; 1) above moderation drinker, 2) moderate drinker, and 3) non-drinker.

Smoking

Smoking is a primary risk factor for coronary heart disease (16, 21), however, the effects of smoking on the metabolic syndrome are equivocal (13, 17). In this study, smoking status was divided into three categories: 1) current smoker, 2) previous smoker, and 3) non-smoker. The three categories allow a more precise examination of the potential effects of smoking versus using a dichotomized variable.

Family history of chronic diseases

Family history of chronic diseases included two conditions; heart disease and diabetes. The initial definition put forth by NCEP (14) and the updated AHA/NHLBI (9) definition were created to help identify those at high-risk for these two conditions. For a subject to be classified with a positive family history for heart disease or diabetes, he/she must have reported that either a parent and/or sibling have had the condition. These two variables were dichotomized, family history yes/family history no.

Data Analysis

Weighting

A variety of procedures were used to prepare the data for analysis. This section discusses data preparation, data management, and recoding. Weighting issues, as well as statistical analysis were run in SUDAAN (19) due to the correlated multi-stage design inherent in NHANES.

NHANES is a complex survey sample (5). The design and weighting methods utilized in NHANES have been similar over the history of the survey. Sampling weights must be used to account for: 1) probability selection (multi-stage), 2) over-sampling of non-Hispanic Blacks, Mexican-Americans, low-income persons, adolescents aged 12-19 years, and persons over 60 years of age, 3) and non-response rates to interview and examination components (*i.e.,* missing data). Sampling weights produce unbiased national estimates (3). "The

sample weight of a sampled person is the estimated number of individuals in the population which the person represents" (12).

A six-year weight for each person who attended the MEC following a morning fast was created for this study. Fasting weights provide national representative population estimates based on a sub-sample who attended the morning MEC examination in fasting conditions. Using a provided fasting weight variable in the NHANES data set, the six-year weight variable was created by taking 2/3 of the four year weight for each person sampled in 1999-2002 (WEIGHT6=2/3*WTSAF4YR) and 1/3 of the two year weight for each person sampled in 2003-2004 (WEIGHT=1/3*WTSAF2YR). The final six-year weight variable was WTSAF6YR (3).

Variance estimation

Variance estimation or sampling errors were also addressed. Following the NHANES 1999-2000 release of the data as public use files, confidentiality principles prohibited the release of the PSU variable. In the 1999-2000 NHANES, replicate weights were produced and a jackknife procedure was recommended for variance estimation (7). However, this procedure was not applicable for multiple two-year data sets. The new method for variance estimation protects confidentiality and allows the use of PSUs. This novel approach creates Masked Variance Units (MVUs) which can be used to estimate sampling errors. These MVUs have been developed in a way that permits them to be utilized with any

combination of data without recoding. Data were sorted by the design variables SDMVSTRA and SDMVPSU before analysis (3).

Statistical Analysis

A total of 54 data files were downloaded and managed in this study. The data were initially managed utilizing SAS 9.1 (20). SAS was used to conduct both complex variable recodes and data coding validation.

SAS-callable SUDAAN (19) was then utilized to conduct the analysis regarding the three research questions posed in this study. SUDAAN incorporates sampling weights within the context of the correlated multi-stage complex sampling design inherent to NHANES (3). Research question 1: "What is the current prevalence of the Metabolic Syndrome in the United States adult population according to the National Heart, Lung, and Blood Institute definition?" will be answered using PROC DESCRIPT. PROC DESCRIPT allows age-adjusted prevalences to be estimated. The age-adjusted prevalence of the metabolic syndrome was computed using the direct method based on the 2000 U.S. population (22).

Logistic regression using PROC RLOGIST was used to estimate odds ratios for being diagnosed with the metabolic syndrome (metabolic syndrome yes versus metabolic syndrome no) in addressing research questions 2 and 3. For research question 2, "Is there an inverse association for LTPA and the metabolic syndrome when utilizing a measure of LTPA volume ($MET \cdot min \cdot wk^{-1}$)?" a logistic regression model was utilized for the six-level $MET \cdot min \cdot wk^{-1}$ independent

measure to focus on a possible inverse association. Research question 3, "Is there an inverse association for physical activity and the metabolic syndrome when measuring physical activity from the parameters of the CDC/ACSM physical activity public health recommendation?" PROC RLOGIST was also utilized to estimate the likelihood of having the metabolic syndrome based on meeting the current public health PA recommendation (18), being active but not meeting the recommendation, and being physically inactive. Multiple logistic regression (PROC MULTILOG) was then used to estimate the OR and 95% CI of accumulating additional CV risk factors using the MSRS as the dependent variable with LTPA being the primary independent variable.

Limitations

Aspects of the NHANES 1999-2004 may limit the findings in this study. The most recent data from NHANES were collected from 1999 to 2004, thus the prevalence estimates of the metabolic syndrome and the association with PA may not reflect the association in the current U.S. population. PA data was self-report over the past 30 days, thus frequency, intensity, duration, and type of PA is subject to recall bias. While cognitive testing has been done, the reliability and validity of the PA has not been tested. Furthermore, this was a cross-sectional study, thus causality cannot be established.

Summary

The three research questions in this study were: 1) "What is the current prevalence of the Metabolic Syndrome in the United States adult population according to the AHA/NHLBI definition?", 2) "Is there an inverse association for LTPA and the metabolic syndrome when utilizing a measure of LTPA volume ($MET \cdot min \cdot wk^{-1}$)?", and 3) "Is there an inverse association for physical activity and the metabolic syndrome when measuring physical activity from the parameters of the CDC/ACSM physical activity public health recommendation?" The questions are presented to estimate the current prevalence of the metabolic syndrome and to examine the relationship between LTPA and the metabolic syndrome according to the AHA/NHLBI definition in the U.S. adult population.

This is the first study to estimate metabolic syndrome prevalence and to utilize the most sensitive measure of LTPA volume ($MET \cdot min \cdot wk^{-1}$) to examine the possible inverse association of LTPA with the METs in the U.S. adult population using the most recent metabolic syndrome definition put forth by the AHA and the NHLBI.

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PART IV

The Relationship Between Leisure-Time Physical Activity and the Metabolic Syndrome Among U.S. Adults: NHANES 1999-2004

ABSTRACT

Healthy People 2010 identifies the metabolic syndrome metabolic syndrome as an emerging health issue within the realm of cardiovascular (CV) disease. The metabolic syndrome is a clustering of five CV risk factors that include poor glucose control or diabetes, overweight/obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), and hypertension (HTN). An individual that possesses three or more of these CV risk factors would be classified as having the metabolic syndrome (15). The prevalence of metabolic syndrome in adults is reaching epidemic proportions in the United States (U.S.) and worldwide. **Purpose:** The purpose of this study was to two-fold. First, this study examined the possible inverse relationship between leisure-time physical activity (LTPA) and the metabolic syndrome. Secondly, this study evaluated the current prevalence of the metabolic syndrome metabolic syndrome in a nationally representative sample of the (U.S.) adult population within the 1999-2004 National Health and Nutrition Examination Survey (NHANES). **Methods:** The sample for this study-included adults, 20 years and older, (N=5,620) who completed the mobile examination center (MEC) examination in the 1999-2004 NHANES. The American Heart Association and National Heart, Lung, and Blood Institute (AHA/NHLBI) definition was used to define the metabolic syndrome. A metabolic syndrome risk score (MSRS) ranging from 0 (no risk factors present) to 5 (all five risk factors present) was created to sum CV risk factors in which accumulating a MSRS $\geq$3 confirmed a metabolic syndrome diagnosis. Physical activity (PA) was measured in two ways: a six-level measure based upon those

reporting no LTPA (0 MET·minutes per week) and quintiles of LTPA, and a three-level measure (no LTPA, insufficient LTPA, and LTPA level meeting CDC/ACSM PA recommendation) associated with the current Centers for Disease Control and American College of Sports Medicine public health PA recommendation. SUDAAN statistical software was used to estimate age-adjusted metabolic syndrome prevalence with logistic and multi-logistic odds risk ratios used to examine the possible inverse association between LTPA and the metabolic syndrome. **Results:** The overall age-adjusted prevalence of the metabolic syndrome among the U.S. adult population was 36.3%. Adults who acquired between 736 and 1360 MET·min·wk^{-1} of LTPA were found to be 35% (OR 0.65; 95% CI 0.48-0.88) less likely to meet the AHA/NHLBI metabolic syndrome diagnosis criteria compared to those reporting no LTPA. A similar inverse association was found against an increasing MSRS (OR 0.69; 95% CI 0.56-0.85). A stronger inverse relationship was noted for those accumulating a weekly level of LTPA MET·minutes coinciding with 60 minutes per day of moderately intense PA (OR 0.55; 95% CI 0.42-0.71). Similarly, this inverse association was also (OR 0.58; 95% CI 0.48-0.70) found at the same level of LTPA against an increasing MSRS. Furthermore, a significant inverse association (OR 0.61; 95% CI 0.48-0.77) was also found for the metabolic syndrome when examining LTPA by the CDC/ACSM public heath PA recommendation. Similar to LTPA MET·minute volume, this inverse association (OR 0.64; 95% CI 0.53-0.77) carried over to the MSRS. **Conclusion:** Findings estimate one in three U.S. adults have the metabolic syndrome which is consistent with other recent studies

conducted using NHANES. This study consistently showed an inverse association between LTPA the metabolic syndrome and underlying CV risk factors. While this study is cross-sectional and causality cannot be inferred, our findings do illustrate an inverse association between LTPA and the metabolic syndrome. These results support the need for future longitudinal studies and randomized control trials examining PA volume and metabolic syndrome risk.

Introduction

Healthy People 2010, the national health objectives for the United States, identifies the metabolic syndrome metabolic syndrome as an emerging health issue within the realm of cardiovascular (CV) disease (27). The metabolic syndrome is a clustering of five CV risk factors that include poor glucose control or diabetes, overweight/obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), and hypertension (HTN). An individual that possesses three or more of these CV risk factors would be classified as having the metabolic syndrome. The prevalence of metabolic syndrome in adults is reaching epidemic proportions worldwide (14) and it has recently been reported that one in three American adults currently have the metabolic syndrome (11). This is important because a metabolic syndrome diagnosis carries a two-fold increase in coronary heart disease mortality (CHD) (12, 22) and a 40% increase in all-cause mortality (22).

Researchers studying the metabolic syndrome and its underlying CV risk factors have, to a large degree, focused on identifying the lifestyle behaviors that might put a person at risk. One lifestyle-related behavior, physical activity (PA), has been found to be consistently and inversely associated with metabolic syndrome risk. As noted in a recent review by Ford et al. (14), a large contribution to our knowledge of a beneficial inverse relationship found between PA and metabolic syndrome comes from research that has used nationally representative population-based surveillance systems – one of which is the National Health and Nutrition Examination Survey (NHANES) (7). NHANES (7) is

one of only a few surveillance systems around the world using a nationally representative sample that simultaneously measures all of the CV risk factors making up the metabolic syndrome, in addition to measuring PA. To date, four studies have utilized the NHANES to explore the relationship between PA and the metabolic syndrome (9, 13, 23, 28).

Three studies utilized data from the 1988-1994 NHANES III. Unfortunately, these PA and metabolic syndrome studies were limited in that the assessment of PA only focused on the frequency and intensity of LTPA, with the duration of LTPA being absent. Despite this limitation, we still gained some insight into the relationship of the metabolic syndrome with PA. Park et al. (23) was the first to explore the association of PA with the metabolic syndrome utilizing a physical activity intensity score (PAIS) to measure the volume of LTPA. The PAIS was defined by the ratio of work metabolic rate (METs) to resting metabolic rate (RMR) obtained by a self-report recall of participation in various types of LTPA over the previous 30 days (8). Creating a dichotomized variable for LTPA (active versus inactive) based on the PAIS, neither physically inactive men (OR 1.4; 95% CI 1.0-2.0) or women (OR 1.2, 95% CI 1.0-1.4) were found to be at an increased risk for having the metabolic syndrome.

In another study utilizing the same NHANES III dataset and the LTPA PAIS, Zhu et al. (28) created a three-level categorical variable: active (PAIS $\geq$ 15.0), moderately active (PAIS $\geq$3.6 to 14.9), and inactive (PAIS $\leq$3.5) to allow a broader range of LTPA volume to be examined. After controlling for lifestyle-related risk factors, males (OR 0.41; 95% CI 0.31-0.54) and females (OR 0.25;

95% CI 0.18-0.37) in the most active PA group were found to be significantly less likely to have the metabolic syndrome compared to the inactive group. Adults in the moderately active group were not associated with a reduced risk for the metabolic syndrome.

More recently, DuBose et al. (9) utilizing data from NHANES III examined the relationship between LTPA and the metabolic syndrome using a three level categorical variable to define LTPA (inactive, irregularly active, and regularly active) with the regularly active level of LTPA representing the Centers for Disease Control and Prevention and the American College of Sports Medicine CDC/ACSM PA public health recommendation (24). Adults reporting being inactive (no LTPA) were found to be 45% (OR 1.45; 95% CI 1.17-1.79) more likely to have the metabolic syndrome compared to those reporting being regularly active.

The most recent NHANES, beginning in 1999, measured PA from three domains; LTPA, transportation, and domestic (7). In addition, this current NHANES collected more detailed information on PA, including frequency, intensity, and duration. As a result, the current NHANES allows for a more precise examination of PA volume with the metabolic syndrome and other chronic diseases. Ford et al. (13), using data from NHANES 1999-2000 utilized the sum of moderate/vigorous LTPA with domestic PA minutes per week (min/wk) to create a three level PA variable (0 min/wk; < 150 min/wk; and $\geq$ 150 min/wk). PA participation at any level was not found to be associated with the metabolic syndrome (13).

These conflicting NHANES results that illustrate the relationship between PA and the metabolic syndrome might be related to the varying level of precision by which PA volume was measured or utilized by researchers. For example, in the three studies using NHANES III (8), duration was not collected in the PA self-report interview, thus one of the three necessary components for accurately assessing PA volume was missing. Also, in the NHANES 1999-2000 study (13), the researchers elected not to use data on intensity linked to each specific activity which would have allowed MET·minutes per week to be calculated.

Utilizing data from the most recent NHANES, an opportunity now exists to more accurately measure LTPA volume and its relationship with the metabolic syndrome using a more comprehensive and precise measure of LTPA volume. This measure, MET minutes per week ($MET \cdot min \cdot wk^{-1}$) includes all the necessary components to precisely measure PA volume: frequency, intensity, and duration. With this in mind, the primary purpose of this study was to determine the relationship between LTPA volume and metabolic syndrome risk, and the secondary purpose of this study was to estimate the current prevalence of the metabolic syndrome in a nationally representative sample of the U.S. adult population utilizing the most recent 1999-2004 NHANES.

Methods

This study utilized six years of data from the most recent 1999-2004 NHANES, a continuous survey conducted by the National Center for Health Statistics (7). NHANES was designed to provide national estimates of the health

and nutritional status of noninstitutionalized U.S. civilians over the age of two months (7).

Sample

For the most recent six years of NHANES, the total sample N is 31,126, ages two months and above. For this study, the final sample consisted of 5,620 U.S. adults ≥ 20 years of age. The final sample met the following conditions: 1) adult men and women ≥ 20 years of age; 2) attended a morning medical examination center (MEC) examination following an overnight fast (minimum of eight hours); 3) if female, non-pregnant; and 4) had complete data on all the variables of interest.

Measures

AHA/NHLBI Metabolic syndrome definition

The dependent variable in this study was a positive diagnosis of the metabolic syndrome based on the American Heart Association and National Heart, Lung, and Blood Institute (AHA/NHLBI) definition (15). The AHA/NHLBI definition requires that three of the following five CV risk factors be present for a diagnosis of the metabolic syndrome: 1) impaired fasting glucose (IFG) ≥ 100 milligrams per deciliter (mg/dL) or undergoing pharmacological treatment for IFG; 2) low high-density lipoprotein cholesterol (HDL-C) (< 40 mg/dL in men or < 50 mg/dL in women) or undergoing pharmacological treatment for an abnormal HDL-C level; 3) triglycerides ≥ 150 mg/dL or undergoing pharmacological

treatment for hypertriglyceridemia; 4) a waist circumference (WC) ≥ 102 centimeters in men or ≥ 88 cm in women; and, 5) blood pressure ≥ 130/85 mm/Hg or undergoing pharmacological treatment for hypertension (HTN). The AHA/NHLBI definition is unique in the respect that it precludes specific inclusion criteria of any one condition found in all other medical society definitions of the metabolic syndrome (15).

In creating a dependent variable based on a positive diagnosis of the metabolic syndrome utilizing the AHA/NHLBI definition, data on blood pressure, fasting glucose, lipoprotein values, and WC measurements were utilized from the MEC, the health examination component of the NHANES. Each CV risk factor was dichotomized with the demarcation being the cut-off value or pharmalogical treatment for inclusion as a component of the metabolic syndrome (0= no risk; 1= risk). Risk factors were summed and a total metabolic syndrome risk score (MSRS) was calculated which ranged from 0 (no risk factors) to five (all five risk factors present). Those subjects with a score of 0-2 risk factors were determined not to have the metabolic syndrome and those respondents with a score of 3 to 5 risk factors were determined to have the metabolic syndrome. In this study, the MSRS served as a secondary dependent measure utilized to examine the relationship of LTPA to the metabolic syndrome.

Physical Activity

Data utilized to measure LTPA was accessed from the 'physical activities individual activities file' (PAQIAF) (5). The PAQIAF is one of the two files

measuring LTPA and includes more detailed information regarding 43-specific types of moderate and vigorous LTPA. The first measure, based upon LTPA MET-minutes per week, took the number of times an activity was done over the last 30 days and calculated an overall LTPA frequency per week. The compendium of PA (1) was used to assign an appropriate MET level to each type of activity performed. Then the average duration (minutes per session), was used in combination with the average frequency (number of sessions per week) and the intensity level (MET-level) to calculate the MET minutes per week ($MET \cdot min \cdot wk^{-1}$) specific to each LTPA activity. With the sum of all LTPA $MET \cdot min \cdot wk^{-1}$ performed, we created a "Weekly LTPA MET·minutes" measure.

In order to be able to examine a possible inverse association between LTPA and the metabolic syndrome, $MET \cdot min \cdot wk^{-1}$ was divided into a six level ordinal variable. The first level represented those who reported performing no LTPA during the past month, the referent group for this study. This level included all individuals who reported no moderate or vigorous LTPA. Thus, they received a score of "0" $MET \cdot min \cdot wk^{-1}$. In calculating the remaining five levels of this measure, the $MET \cdot min \cdot wk^{-1}$ were divided into quintiles from the $MET \cdot min \cdot wk^{-1}$ measure: 1st quintile >0.0-≤156.24 $MET \cdot min \cdot wk^{-1}$; 2nd quintile >156.24-≤393.10 $MET \cdot min \cdot wk^{-1}$; 3rd quintile >393.10-≤736.55 $MET \cdot min \cdot wk^{-1}$; 4th quintile >736.55-≤1360.15 $MET \cdot min \cdot wk^{-1}$; 5th quintile >1360.15 $MET \cdot min \cdot wk^{-1}$. This was done to account for the non-normally distributed and skewed PA measures inherent in national population surveys (17).

A second LTPA measure used to examine the possible inverse association with the metabolic syndrome was a three-level categorical variable based on the CDC/ACSM PA public health recommendation (24). Individuals who met the CDC/ACSM PA recommendation of five days per week of moderate intensity PA for 30 minutes, or three days per week of vigorous intensity PA for 20 minutes were classified as meeting the public health recommendation; individuals who engaged in LTPA at least one time per week at any duration or intensity but not meeting the CDC/ACSM recommendation were classified in the some, but insufficient category; and those who reported performing no LTPA were classified as inactive.

Other Measures

Other measures used in this research included demographic variables of age and race/ethnicity, and two markers of socioeconomic status (SES), *i.e.* education and income. Education was categorized as completing less than 12^{th} grade, completing 12^{th} grade, or education beyond 12^{th} grade. Income was categorized as a percent of the poverty threshold (< 100%, 100 to 199%, 200 to 299%, 300 to 399%, > 400%). The standardized poverty thresholds represent dollar amounts that define poverty status while accounting for family size (6). Falling below a poverty threshold of 100% demarcates living in poverty. In addition, we used measures associated with alcohol consumption, smoking status, and family history of chronic disease(s), including heart disease and diabetes.

Statistics

The data in this study were initially managed using SAS 9.1 (26). SAS was used to conduct both complex variable recodes and data coding validation. SAS-callable SUDAAN (25) was then used to conduct the analysis, incorporating sampling weights within the context of the correlated multi-stage complex sampling design inherent to NHANES (4). Age-adjusted prevalence estimates were calculated used PROC DESCRIPT for demographic characteristics and the additional covariates. For all prevalence estimates, non-overlapping 95% CIs will indicate significance. Logistic regression (PROC RLOGIST) analysis was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the metabolic syndrome (dependent variable (DV)) and both measures of LTPA. Multiple logistic regression (PROC MULTILOG) was then used to estimate the OR and 95% CI of accumulating additional CV risk factors using the metabolic syndrome risk score as the DV with both measures of LTPA.

Results

Metabolic syndrome prevalence

Applying the AHA/NHLBI definition, the overall age-adjusted prevalence of the metabolic syndrome among the U.S. adult population was 36.3%; and the prevalence was similar for men 36.9% (95% CI 34.4%-39.4%) and women 35.6% (95% CI 33.2%-38.0%) (See Table 1). The prevalence of the metabolic syndrome increased with age; 14.9% among those aged 20-29 years and 60.0% among those 70-79 years of age. Specific to race/ethnicity, Non-Hispanic Blacks

Table 1. Metabolic Syndrome Prevalence According to the AHA/NHLBI Criteria by Demographic Characteristics and Other Lifestyle-Related CV Risk Factors Among U.S. Adults ≥20 Years - NHANES 1999-2004.

	Sample N	Weighted Ratio	Age-adjusted prevalence %	95% CI
	5620		36.3	34.5, 38.1
Gender				
Male	2837	49.3	36.9	34.4, 39.4
Female	2783	50.7	35.6	33.2, 38.0
Age				
20-29	871	17.9	14.9	11.6, 18.2
30-39	917	21.1	23.5	20.4, 26.5
40-49	1007	22.0	34.8	30.1, 38.7
50-59	763	16.7	48.7	44.6, 52.9
60-69	949	11.2	59.6	56.3, 63.0
70-79	645	7.3	60.0	54.7, 65.3
≥80	468	3.8	48.3	42.7, 54.0
Race/Ethnicity				
Non-Hispanic White	2934	72.0	36.7	34.3, 39.2
Non-Hispanic Black	1016	10.6	30.8	27.9, 33.7
Mexican-American	1291	7.2	41.2	37.9, 44.4
Other	379	9.2	37.3	31.5, 43.0
Education				
<High school	1792	20.3	40.3	37.0, 43.6
High school	1302	26.0	40.9	37.2, 44.7
>High school	2515	53.7	32.6	29.9, 35.4
Income (%poverty level)				
<0 - <100	874	12.8	38.5	33.9, 43.2
≥100 - <200	1342	21.2	38.9	35.3, 42.7
≥200 - <300	846	15.7	37.9	33.2, 42.5
≥300 - <400	628	13.8	37.6	32.6, 42.7
≥400	1470	36.5	33.4	30.4, 36.4
Smoking				
Current smoker	1239	24.4	35.4	32.3, 38.5
Previous smoker	1552	26.1	37.1	33.5, 40.6
Never smoked	2822	49.5	36.3	33.3, 39.4
Alcohol				
Above moderation drinker	381	8.3	31.5	27.2, 36.0
Moderate drinker	3088	62.0	34.5	32.3, 36.8
Non-drinker	1859	29.7	42.4	38.9, 45.9
Family history of heart disease				
Yes	449	6.8	51.2	43.0, 59.4
No	5171	93.2	35.5	33.7, 37.4
Family history of diabetes				
Yes	451	5.7	52.6	42.3, 63.0
No	5169	94.3	35.5	33.6, 37.3

NHANES= National Health and Nutrition Examination Survey. AHA/NHLBI= American Heart Association/National Heart, Lung, and Blood Institute. CV= Cardiovascular. CI= Confidence interval.

were found to have the lowest overall prevalence of the metabolic syndrome (30.8%; 95% CI 27.9, 33.7) while Mexican-Americans were found to have the greatest prevalence (41.2%; 95% CI 37.9%, 44.4%). In addition, level of educational attainment, lifestyle habits, and having family history of heart disease or diabetes were also associated with metabolic syndrome prevalence in U.S. adults (See Table 1).

Metabolic syndrome prevalence by LTPA MET·minutes and the CDC/ACSM recommendation

Table 2 illustrates the prevalence of the metabolic syndrome among U.S. adults by weekly LTPA MET·minutes and according to the current CDC/ACSM public health PA recommendation. When examining metabolic syndrome prevalence by the LTPA quintiles of weekly MET·minutes found in Table 2, there was an inverse relationship found between LTPA weekly MET·minutes and the prevalence of the metabolic syndrome. The lowest metabolic syndrome prevalence (27.2%; 95% CI 22.7-31.7) was found among those reporting the greatest volume of LTPA and was significantly different than from those reporting no LTPA and those reporting weekly LTPA MET·minutes falling within the first three quintiles of activity (See Table 2).

When focusing on the CDC/ACSM public health PA recommendation, a significant difference was found for metabolic syndrome prevalence between those meeting the current public health PA recommendation, 29.0% (95% CI 25.5-32.6) and those reporting no LTPA, 40.0% (95% CI 37.5-42.6). The

Table 2. Metabolic Syndrome Prevalence by Weekly LTPA and the CDC/ACSM Public Health PA Recommendation† Among U.S. Adults ≥20 Years - NHANES 1999-2004.

	Age-adjusted prevalence	
Weekly LTPA MET minutes	%	95% CI
0.0	40.0	37.5, 42.6
>0.0 - ≤156.24	41.2	36.8, 45.7
>156.24 - ≤393.10	37.2	32.9, 41.4
>393.10 - ≤736.55	36.3	31.8, 40.8
>736.55 - ≤1360.15	29.5	24.5, 34.6
>1360.15	27.2	22.7, 31.7

Weekly LTPA MET minutes	%	95% CI
Inactive	40.0	37.5, 42.6
Insufficiently active*	37.6	35.1, 40.0
Meets Recommendation†	29.0	25.5, 32.6

AHA/NHLBI=American Heart Association/National Heart, Lung, Blood Institute.

CDC/ACSM=Centers for Disease Control and Prevention / American College of Sports Medicine.

LTPA= Leisure-time physical activity; CV= Cardiovascular disease. PA=Physical activity.

†Every US adult should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week and/or 20 minutes of vigorous physical activity on three days of the week (24).

*Physically active but insufficient to meet CDC/ACSM recommendation (24).

metabolic syndrome prevalences for those reporting some LTPA 37.6% (95% CI 35.1-40.0) and no LTPA, 40.0% (95% CI 37.5-42.6) were found to be quite similar (See Table 2).

Metabolic syndrome and LTPA MET·minutes per week

Table 3 illustrates the OR for a metabolic syndrome diagnosis and the OR for adding one additional CV risk factor inherent within the MSRS by LTPA weekly MET·minute volume. Adults who acquired between 736.55 and 1360.15 MET·min·wk^{-1} of LTPA were found to be 35% (OR 0.65; 95% CI 0.48-0.88) less likely to meet the AHA/NHLBI metabolic syndrome diagnosis criteria compared to those reporting no LTPA; and those reporting >1360.15 MET·min·wk^{-1} were found to be 45% (OR 0.55; 95% CI 0.42-0.71) less likely to have the metabolic syndrome compared to those reporting no LTPA (0 MET·min·wk^{-1}).

When examining the risk of increasing the metabolic syndrome risk score (MSRS), decreased CV risk was also found beginning at the fourth quintile of LTPA (See Table 3). Adults who acquired between 736.55 and 1360.15 MET·min·wk^{-1} of LTPA were found to be 31% (OR 0.69; 95% CI 0.56-0.85) less likely to accumulate one additional CV risk factor compared to those reporting no LTPA. Furthermore, those reporting >1360.15 MET·min·wk^{-1} were found to be 42% (OR 0.58; 95% CI 0.48-0.70) less likely to add an additional CV risk factor.

Table 3. Odds Ratios of Metabolic Syndrome diagnosis and Increasing Metabolic Syndrome Risk Score (MSRS) by LTPA* Weekly MET-minutes - NHANES 1999-2004.

	Metabolic syndrome risk by LTPA level			Risk of increasing MSRS		
Weekly LTPA MET minutes	Odds ratio	95% CI	P value for trend	Odds ratio	95% CI	P value for trend
0.0	1.00		0.0001		1.00	<0.0001
>0.0 - ≤156.24	1.17	0.94, 1.45		1.06	0.86, 1.32	
>156.24 - ≤393.10	0.99	0.81, 1.23		0.97	0.79, 1.20	
>393.10 - ≤736.55	0.86	0.66, 1.12		0.79	0.62, 1.01	
>736.55 - ≤1360.15	0.65	0.48, 0.88		0.69	0.56, 0.85	
>1360.15	0.55	0.42, 0.71		0.58	0.48, 0.70	

Covariates adjusted for in the model include gender, age, race/ethnicity, education, income, smoking status, alcohol intake, family history of heart disease, and family history of diabetes.

*LTPA= Leisure-time physical activity. MET=Metabolic equivalent (1 MET= 3.5 ml/kg/min^{-1})

Metabolic syndrome and the CDC/ACSM public health PA recommendation

Table 4 illustrates the OR of metabolic syndrome diagnosis and the OR for adding one additional CV risk factor in the MSRS by the CDC/ACSM public health PA recommendation examining LTPA. Compared to those who reported being inactive (no LTPA), participants who reported a volume of LTPA meeting or exceeding the current CDC/ACSM public health PA recommendation were found to be 39% (0.61; 95% CI 0.48-0.77) less likely to have the metabolic syndrome compared to those reporting no LTPA. When examining the risk of accumulating one additional CV risk factor (MSRS), those meeting or exceeding the current CDC/ACSM PA recommendation with LTPA were found to be 36% (OR 0.64; 95% CI 0.53-0.77) less likely to accumulate an additional risk.

Note: Alternate findings from examining total PA from all three domains and a brief discussion can be found in Appendix C.

Discussion

With the most recent 1999-2004 NHANES data and the metabolic syndrome definition proposed by the AHA/NHLBI (15), this study found that 36.3% of the U.S. adult population can be classified as having the metabolic syndrome. This study represents the first national prevalence estimate of the metabolic syndrome in the U.S. adult population using the AHA/NHLBI definition and is similar to metabolic syndrome prevalence estimates found by Ford (11) utilizing the International Diabetes Federation and World Health Organization definitions in 1999-2002 NHANES. These findings also illustrated a strong

Table 4. Odds Ratios of Metabolic Syndrome diagnosis and Increasing Metabolic Syndrome Risk Score (MSRS) by CDC/ACSM public health PA recommendation* (LTPA) -NHANES 1999-2004

	Metabolic syndrome risk by LTPA level			Risk of increasing MSRS		
LTPA Level	Odds ratio	95% CI	P value for trend	Odds ratio	95% CI	P value for trend
Inactive	1.00	--	0.0003	1.00	--	0.0001
Insufficiently active†	0.99	0.86, 1.15		0.93	0.81, 1.07	
Meets PA recommendation*	0.61	0.48, 0.77		0.64	0.53, 0.77	

Covariates adjusted for in the model include gender, age, race/ethnicity, education, income, smoking status, alcohol intake, family history of heart disease, and family history of diabetes.

CDC/ACSM=Centers for Disease Control and Prevention / American College of Sports Medicine.

LTPA= Leisure-time physical activity; CV= Cardiovascular disease.

*Every US adult should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week and/or 20 minutes of vigorous physical activity on three days of the week (24).

†Physically active but insufficient to meet CDC/ACSM recommendation (24).

inverse association between LTPA and the metabolic syndrome. Beginning with a LTPA volume of 736.55 weekly MET·minutes, adults that met or surpassed this level of LTPA were 35% less likely to be classified as having the metabolic syndrome. A similar inverse association (OR 0.61; 95% CI 0.48-0.77) was observed when PA was coded to represent the CDC/ACSM public health PA recommendation. Furthermore, a similar inverse association (OR 0.64; 95% CI 0.53-0.77) for meeting the CDC/ACSM public health PA recommendation was found when examining the metabolic syndrome risk score (MSRS). It appears that in order to reduce the risk of the metabolic syndrome through LTPA, an adult needs, at a minimum, to meet the current CDC/ACSM public health PA recommendation (24).

Our findings concur with previous epidemiological PA studies that have examined the relationship between PA and the metabolic syndrome utilizing the 1988-1994 NHANES III (9, 28). Zhu et al. (28) found that men and women who reported the greatest volume of LTPA were 59% and 75%, respectively, less likely to have the metabolic syndrome. DuBose et al. (9) when examining the potential association between LTPA and metabolic syndrome, with the most active participants being the referent group, found that those adults who reported no LTPA were 45% more likely to have the metabolic syndrome. In the present study, the metabolic syndrome prevalence of 40.0 % in the inactive group translates into this group being 65% (OR 1.65; 95% CI 1.31-2.08) more likely to be classified with the metabolic syndrome when compared to those meeting the CDC/ACSM public health PA recommendation.

Interestingly, in a study utilizing the most recent NHANES data, Ford et al. (13), found no significant association between PA and the metabolic syndrome. However, Ford et al. only utilized frequency and duration to measure PA in total minutes per week. The current study linked each specific LTPA with a specific MET level from the compendium of PA (1) to create a total MET·minutes per week, a more precise measure of LTPA volume. It appears that using this more precise measure of LTPA allows for a more accurate analysis of the association between LTPA and the metabolic syndrome.

In further examining LTPA volume, as it relates to the metabolic syndrome, the magnitude of the inverse association increased (OR 0.55; 95% CI 0.42-0.71) for adults who accrued >1360.15 weekly MET·minutes of LTPA. This volume of LTPA (*i.e.* 60 minutes per day of moderately intense PA) coincides with the AHA and ADA PA recommendation (16) for the clinical management of the metabolic syndrome. This additional benefit was not only observed for being diagnosed with the metabolic syndrome, but also when examining the odds of an increasing metabolic syndrome risk score (MSRS) that ranged from 0 (no risk) to 5 (all five CV risk factors present). This recommended volume of LTPA may be preferable by physicians and other health care professionals working with populations at risk for developing the metabolic syndrome. Greater volumes of LTPA may increase the likelihood that these populations will be able to lose or maintain a healthy weight, thus reducing the risk of the metabolic syndrome. However, motivating people to become physically active is a difficult task and with the findings in this study suggesting the current CDC/ACSM public health

PA recommendation for health translate over to a possible reduction in the risk of the metabolic syndrome, recommending 30 minutes per day of moderately intense PA may be prudent.

To date, no randomized control trials (RCTs) examining the role of the CDC/ACSM public health PA recommendation with the prevention of the metabolic syndrome as the primary outcome have been conducted. The closest smaller prospective studies toward this end were conducted by Laaksnen et al.(21) and Ekelund et al. (10). Laaksnen et al.(21), in a prospective study found that middle-aged men who met the current CDC/ACSM PA recommendation, through structured or other lifestyle PA, were half as likely to develop the metabolic syndrome compared to men engaging in no more than 60 minutes of moderate exercise per week. In another prospective study, Ekelund et al. (10) reported that middle-aged men who had a physical activity energy expenditure (PAEE) equivalent to one hour per day of brisk walking were found to have a significantly lower risk of developing the metabolic syndrome. Perhaps there is enough evidence from this and other studies (2, 9, 10, 19) to warrant RCTs that focus on identifying the precise volume of PA that coincide with the current CDC/ACSM public health PA recommendation (24) and the PA recommendation issued by the AHA and ADA (16).

One of the weaknesses of physical activity epidemiology studies related to the metabolic syndrome is the lack of a standardized measure. Unlike NHANES III, the current NHANES assessed frequency, intensity, and duration of PA, thus allowing investigators to more precisely examine association between LTPA and

metabolic syndrome risk. Unfortunately, despite the precision of our LTPA measure of weekly MET·minutes, it is not possible to directly compare our findings to those from previous studies (9, 13, 28) examining PA and metabolic syndrome risk in NHANES.

Study limitations

These findings must be interpreted in light of the potential limitations. First, the cross-sectional nature of the study design does not allow causality to be inferred. Second, recall bias was possible due to LTPA being assessed by a self-report interview from a frame of reference of the previous 30 days. Third, LTPA, smoking, and alcohol responses may have been subjected to the social desirability effect (*i.e.* providing answers to impress or please interviewer). Lastly, dietary factors (*i.e.* caloric intake) were not controlled due to the complex nature of this data inherent to 1999-2004 NHANES.

Conclusion

Our findings estimate one in three U.S. adults have a Metabolic Syndrome Risk Score (MSRS) classifying them as having the metabolic syndrome. Metabolic syndrome risk and the risk associated with MSRS were found to be inversely associated with increasing LTPA volume. This is consistent with the majority of metabolic syndrome studies examining the association with PA (14). In addition, the magnitude of the inverse association between LTPA and the metabolic syndrome becomes greater when LTPA volume increases. However,

longitudinal studies and RCTs using population-based methodology are needed to reaffirm this study and previous smaller prospective studies (3, 10, 18-21).

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APPENDICES

APPENDIX A

The Metabolic Syndrome: How Definition Impacts Prevalence and Risk in U.S. Adults NHANES 1999-2002

Abstract

Purpose: To examine the relationships various definitions have on MetS prevalence and risk estimates among a national sample of adults. **Methods:** The sample for this study-included adults, 20 years and older, (N=3745) who completed the mobile examination center (MEC) examination in the 1999-2002 National Health and Nutrition Examination Survey (NHANES). SUDAAN statistical software was used to estimate age-adjusted prevalence and odds risk ratios. **Results:** The overall age-adjusted MetS prevalence ranged from a high of 39.5% (ACE/AACE), to a low of 22.0% (WHO). For most MetS definitions, males, people in the seventh decade of life (60-69 years of age), Mexican-Americans, those without a high school education, and those living in poverty were found to have the greatest prevalence. Corresponding to prevalence estimates, females were 23% to 30% less likely to be diagnosed with the MetS. People in the seventh decade of life, Mexican-Americans, those with less than a high school education and those living in poverty were found to have the greatest risk for being diagnosed with the MetS. **Conclusion:** MetS prevalence and risk estimates within populations are highly dependent on the requisite criteria and definition used.

Introduction

The aggregation of multiple cardiovascular risk factors was first observed by Kylin early in the twentieth century (50), when he reported a syndrome that included the clustering of hypertension (HTN), hyperglycemia, and hyperuricemia. Subsequently, Kylin's syndrome was expanded through the work by Vague (70) who proposed adding central adiposity and diabetes, and Avogaro (7) who added obesity, both of which strengthened the relationship between the clustering of risk factors and cardiovascular disease (CVD). In a landmark paper, Reaven (62) described a series of abnormalities called "Syndrome X", which included insulin resistance (IR), glucose intolerance, HTN, hyperinsulinemia, elevated very low-density lipoprotein (VLDL) triglycerides, and low high-density lipoprotein cholesterol (HDL-C). This clustering of metabolic abnormalities, or the metabolic syndrome (MetS) as it is most commonly known today, has had many labels over the past four decades, including special metabolic syndrome (47), syndrome X (62), the deadly quartet (48), insulin resistance syndrome (43), and the plurimetabolic syndrome (28).

This abundance of syndrome names is congruent with the competing criteria for defining the MetS. These competing criteria and their associated prevalence estimates often lead to confusion for the clinician and researcher alike (10). Previous MetS prevalence estimates in United States (U.S.) adults range from a low of 7% in persons aged 20-29 years to a high of 44% to those in the seventh decade of life (38). MetS prevalence has been shown to vary depending on which medical society definition is adopted (9). To date, there is no

consensus for a definition between the five most commonly used medical society definitions that measure the MetS (See Table 1). Several investigators have attempted to identify the best working definition by comparing multiple definitions (9, 27, 30, 51, 71). However, only 11 studies have been conducted utilizing national surveillance data (4, 6, 14, 16, 17, 35-38, 42, 49).

Cameron et al. (16), summarized two studies that have reported using a nationally representative sample (17, 31). Overall prevalence estimates from the Australian Diabetes, Obesity and Lifestyle Study (AusDiab) (31) were reported to be 15.9% for the European Group for the Study of Insulin Resistance (EGIR) definition (8), 18.3% for the National Cholesterol Education Program (NCEP) definition (55), and 20.9% for the World Health Organization (WHO) definition (72). The other prevalence estimate in this review originated from a national sample of Mauritians in which prevalence estimates ranged from a high of 19.1% (WHO) to a low of 13.8% (NCEP) (17).

Since the MetS has become a focal point of metabolic research, several researchers have used national representative samples in reporting prevalences (4, 6, 14, 35, 37, 39, 42, 49), but most investigators utilized only one definition. Ford (36, 37), using data from the National Health and Nutrition Examination Survey (NHANES) has taken the lead in contrasting prevalences of the MetS using various published definitions. Ford (2003) initially reported national prevalences of the MetS using the WHO (1999) and the NCEP (2001) definitions. The age-adjusted prevalence of the MetS in U.S. adults $\geq$ 20 years in NHANES

Table 1. Metabolic syndrome definitions from various medical societies.

	WHO [1999]	EGIR [1999]	ACE/AACE [2003]	IDF [2005]	AHA/NHLBI [2005]
Requisite criteria	IGT, IFG, type 2 diabetes, insulin in top quartile of population	Insulin in top quartile of population	High risk [a]; BMI >25 or waist >102 cm (men) or >88cm (women)	Waist ≥94 cm (men) and ≥80 cm (women), population specific for ethnic groups [b]	N/A
Other Criteria	Plus ≥ 2 of:	Plus ≥ 2 of:	Plus ≥ 2 of:	Plus ≥ 2 of:	≥ 3 of:
Glucose	N/A	≥100 mg/dL, 2-hour post OGTT ≥140 mg/dL but not diabetes	≥100 mg/dL, 2-hour post OGTT ≥140 mg/dL but not diabetes	≥100 mg/dL, diabetes	≥100 mg/dL, diabetes
Obesity	W:H ratio >0.9 in men or >0.85 in women; BMI >30	Waist ≥ 94 cm in men or ≥80 cm in women	N/A	N/A	Waist ≥102 cm in men or ≥88 cm in women
Lipids	TG ≥150 mg/dL	TG >180 mg/dL	TG >150 mg/dL	TG ≥150 mg/dL	TG ≥150 mg/dL or

Table 1. Metabolic syndrome definitions from various medical societies (continued).

	and/or HDL-C <35 mg/dL in men or <39 mg/dL in women	and/ or HDL-C<39 mg/dL in men or women or RX	or HDL-C <40 mg/dL in men or <50 mg/dL in women	or Rx or HDL-C <40 mg/dL in men or <50 mg/d/L in women or Rx	HDL-C <40 mg/dL in men or <50 mg/dL in women or Rx
Hypertension	≥140/90 mm Hg or Rx	≥140/90 mm Hg or Rx	>130/85 mm Hg or Rx	≥130/85 mm Hg or Rx	≥130/85 mm Hg or Rx
Other	Microalbuminuria ACR ≥30mg/g				

WC, waist circumference; W:H, waist hip; TG, triglycerides; OGTT, oral glucose tolerance test; Rx, medication; ACR, albumin: creatinine ratio; others designated in text. WHO=World Health Organization EGIR=European Group for the study of Insulin Resistance AHA/NHLBI=American Heart Association/National Heart, Lung, and Blood Institute ACE/AACE=American College of Endocrinology/American Association of Clinical Endocrinologists IDF=International Diabetes Federation.

[a] Family history of type 2 or gestational diabetes, known CVD, polycystic ovary syndrome, physically inactive lifestyle, >40 years of age, and ethnic populations at high risk for a type 2 diabetes.

[b] Mexican-American men waist circumference cut-off point is ≥ 90 cm.

III was 25.1% (WHO) and 23.9% (NCEP). In a follow-up study using data from the most recent NHANES 1999-2002, Ford (36) contrasted the NCEP and International Diabetes Federation (46) criteria for the MetS, reporting prevalences of 34.6% and 39.1%, respectively.

To date, no one study has compared prevalence estimates of all five commonly used medical society definitions described in Table 1. This study examines the prevalence estimates for all of these definitions using the NHANES (1999-2002) national database, thus extending the previous work of Ford by three definitions. In addition, risk profiles for being diagnosed with the MetS specific to each definition will be examined.

Methods

This study utilized data from NHANES, a continuous survey conducted by the National Center for Health Statistics (21). In 1999, the National Center for Health Statistics (NCHS) began releasing public use data files continuously as smaller component-specific data files on an annual basis. The most recent survey was conducted from 1999 through 2004 and represents the eighth series of surveys. These surveys were designed to provide national estimates of the health and nutritional status of noninstitutionalized U.S. civilians over the age of two months.

Sample

The 1999-2002 NHANES databases contain information on 21,004 individuals over two months of age. Complete data assuring full fidelity for all five MetS definitions in this study was not released at the time of our analysis, therefore only the first four years of data was utilized in our investigation. The sample for this study-included non-Hispanic White, non-Hispanic Black, Mexican-American, and the Other race/ethnicity category, aged 20 years and older (N=9,688). Eligible participants for this study attended the mobile examination center (MEC) following an overnight fast (minimum 8 hours) and received a clinical exam up. Women who reported being pregnant were excluded. Complete data, for the final sample in our study, included 3,745 adults.

Measures

The five demographic variables utilized in our analysis included gender, age, race/ethnicity, and two markers of socioeconomic status (SES), *i.e.* education and income. Education was categorized as completing less than 12^{th} grade, completing 12^{th} grade, or education beyond 12^{th} grade. Income was categorized as a percent of the poverty threshold (< 100, 100 to 199, 200 to 299, 300 to 399, > 400). The standardized poverty thresholds represent dollar amounts that define poverty status while accounting for family size (22). Falling below a poverty threshold of 100% demarcates living in poverty.

The collection of blood and urine was performed in the MEC during the clinical examination. These samples were obtained in order to measure specific

variables, allowing researchers to examine risk profiles. The data utilized from blood samples in this study were fasting plasma insulin values to verify meeting the top population quartile, demarcating IR, HDL-C and triglyceride values to classify dyslipidemia, and blood glucose values in order to classify IFG. The data utilized from the urinanalyis was for the classification of microalbuminuria (high-protein levels in the urine. Detailed specimen collection and processing instructions are discussed in the NHANES Laboratory/Medical Technologists Procedures Manual (LPM) (20). Three or four blood pressure (BP) readings were taken in the MEC and the average was reported for analysis (60). In addition, participants were asked as part of the home interview process if they have ever been told by a doctor or health care professional that they had diabetes.

Metabolic syndrome definitions

This study utilized five working medical society definitions proposed for the diagnosis of the MetS. Table 1 summarizes the various definitions published by the World Health Organization (WHO) (72), EGIR (8), American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI) definition (41) which refers to the updated NCEP (2001) definition, the joint American College of Endocrinology (ACE) and American Association of Clinical Endocrinologists (AACE) consensus definition for epidemiological research (33), and the IDF (46). The ACE/AACE definition represents the official position of an ACE/AACE task force appointed by the AACE president (33). To facilitate comparisons, all five definitions reflect the change adopted by Grundy and others

(41, 46) put forth by the American Diabetes Association (1) for lowering the diagnosing of IFG, lowering the cut-point from 110 mg/dL to 100 mg/dL. In addition, we considered the current use of antihypertensive medication an indication of high BP.

The majority of research that has been done on the MetS involved the use of the NCEP, WHO, and EGIR definitions (See Table 1). The NCEP definition requires that three of the following five criteria be present for a diagnosis of the MetS: impaired fasting glucose (IFG), low HDL-C, elevated triglycerides, an increased waist circumference (WC), or HTN. The NCEP definition is unique in the respect that it precludes specific inclusion criteria of any one condition (e.g. IFG) in order for MetS to be diagnosed. The most recent definition put forth by the AHA and NHLBI (41) mirrors the NCEP (55) definition with the following modifications: medication use for those with dyslipidemia, HTN, and IFG maintains the diagnosis, and the cut-off point for IFG was lowered from 110 mg/dL to 100 mg/dL to reflect the recent changes put forth by the American Diabetes Association (ADA) for IFG (1).

The WHO definition includes at least one of the following requisite conditions: impaired glucose tolerance (IGT), IFG, type 2 diabetes (T2D), or insulin levels in the top quartile of the population plus two of the following: low HDL-C or elevated triglycerides, a waist/hip (W/H) ratio >0.9 for men or >0.85 for women or body mass index (BMI) > 30 kg/m^2, HTN, or microalbuminuria. The WHO definition recommends a hyperinsulinemic-euglycemic clamp technique and an oral glucose tolerance test be used for estimating IR. Because these

techniques were not employed in NHANES, fasting insulin concentrations were utilized to estimate IR and IFG was utilized in place of IGT, which has been previously recommended by EGIR (8). The EGIR definition requires insulin in the upper quartile plus two or more of the following: low HDL-C or elevated triglycerides, WC of ≥94 centimeters (cm) for men and ≥80 cm for women, HTN, or IGT or IFG but not diabetes. The EGIR feels diabetes should be treated as a separate entity (8). A key factor in T2D is beta-cell function, as this diminishes, ability in estimating insulin sensitivity is abated (75).

In addition, the IDF and ACE/AACE definitions have been proposed. The ACE/AACE definition requires one of the following: an individual to be classified as high risk for IR, BMI >25 kg/m^2 or WC of >102cm in men or >88cm in women plus at least two of the following: IFG or IGT but not diabetes, low HDL-C, elevated triglycerides, or a diagnosis of HTN. The recent definition put forth by the IDF mirrors the AHA/NHLBI criteria except for the WC cut-points being lowered and individuals taking medication(s) for hyperglycemia being included in the IFG or diabetes category (See Table 1).

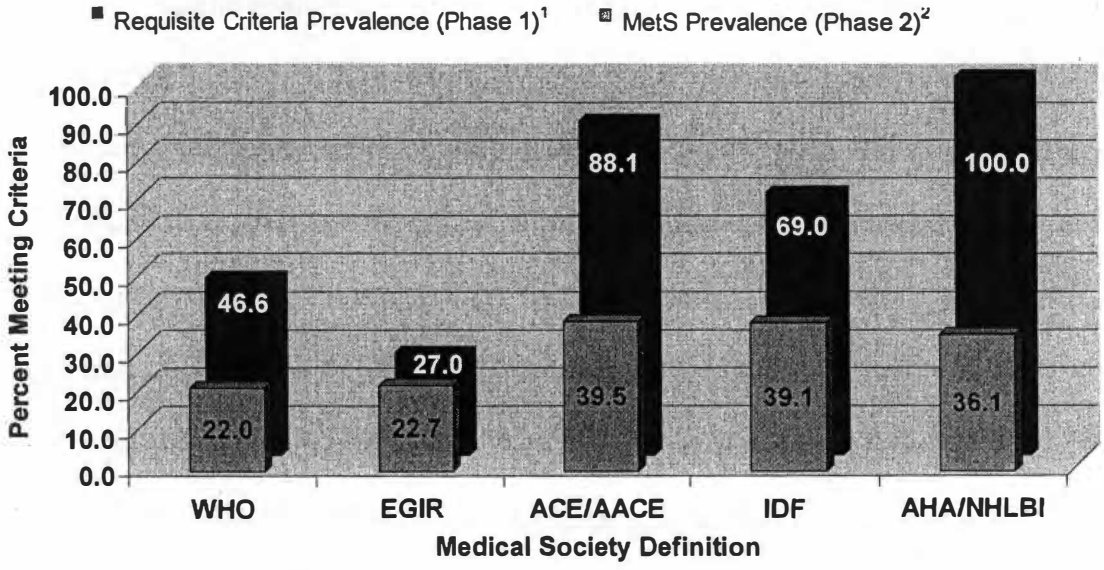
Statistics

SAS (65) was used to recode the variables of interest, and SUDAAN (63) was used to conduct the analysis. SUDAAN incorporates sampling weights within the context of the complex sampling design inherent to NHANES (21). Age-adjusted prevalences for the MetS were computed using PROC DESCRIPT with the direct method based on the 2000 U.S. population. Logistic regression using

PROC RLOGIST was used to estimate odds risk-ratios for being diagnosed with the MetS (MetS yes versus MetS no). With logistic regression we controlled for gender, age, race/ethnicity, education, and income.

Results

Figure 1 displays two distinct phases of the MetS diagnosis process. Phase 1 reflects the proportion of the US adult population who meet the requisite condition(s) for each of the medical society definitions found in Table 1. The requisite condition prevalences range from 27% (EGIR) to the entire eligible sample (AHA/NHLBI). Subjects who met the requisite condition specific to each definition were then subjected to the phase two diagnostic criteria indicative of the MetS diagnosis. Figure 1, phase two, presents the MetS prevalence specific to each of the five medical society definitions. The two medical society definitions resulting in the lowest prevalence rates (EGIR, 22.7%; and WHO, 22.0%) were found to have the lowest eligible pools for MetS diagnosis. Approximately half of those meeting the requisite criteria for WHO were found to have the MetS, while more than 80% of those identified with the requisite condition for EGIR met the diagnostic criteria for the MetS. The IDF and ACE/AACE definitions were associated with the highest prevalence rates (39.5% and 39.1% respectively). Similar to the WHO definition, the ACE/AACE and IDF prevalence estimates are approximately half of their respective eligible pools (See Figure 1). The AHA/NHLBI definition, which allows more flexibility, requires no requisite condition(s) and classifies one out of every three U.S. adults as having the MetS.



[1] Requisite criteria prevalence specific to medical society definition
[2] MetS prevalence for each medical society definition

Figure 1. Prevalence of the MetS in US adults by diagnostic phase specific to medical society definition.

The overall age-adjusted and demographic-specific MetS prevalences across the various MetS definitions are shown in Table 2. The overall age-adjusted MetS prevalence was highest (39.5%) within the ACE/AACE definition, while the lowest overall prevalence (22.0%) was found in the WHO definition. In two of the five definitions, males were found to have greater prevalences than females. The exception was found with the AHA/NHLBI definition, where gender-related prevalences were identical. The greatest difference between male and female MetS prevalence was found within the ACE/AACE definition with males at 42.7% and females at 36.0%. Prevalences varied for gender between definitions, ranging from a low of 19.9% (EGIR) to a high of 36.8% (IDF) in females, and a low of 22.6% (WHO) to a high of 42.7% (ACE/AACE) in males.

Specific to age, delineated by 10-year age groups, there was a consistent increase in MetS prevalence through the seventh decade (60-69 years of age) of life. MetS prevalence begins to decline or level off in the eighth decade (70-79 years of age) of life; this is consistent across the various definitions except ACE/AACE, where the drop in prevalence is not seen until the ninth decade ($\geq$ 80 years of age). Across definitions, MetS prevalence values ranged from a low of 9.4%, (WHO) in the 20-29 year old age group, to a high of 60.3%, (ACE/AACE) in the 70-79 year old age group.

MetS prevalences specific to race/ethnicity, found Mexican-Americans to have the highest overall age-adjusted prevalence across all definitions, with the greatest prevalence rate being associated with the ACE/AACE definition at 48.5%. The lowest race/ethnic prevalence rates were associated with non-

Table 2. Metabolic Syndrome prevalence specific to medical society definitions by demographic characteristics among U.S adults aged ≥ 20 years, NHANES 1999-2002.

		WHO[1999]		EGIR[1999]		ACE/AACE[2003]		IDF[2005]		AHA/NHLBI[2005]	
	N	%*	95% CI†	%*	95% CI†	%*	95% CI†	%*	95% CI†	%*	95% CI†
Total Age-Adjusted Prevalence	3745	22.0	(20.3, 23.8)	22.7	(20.7, 24.6)	39.5	(37.2, 41.8)	39.1	(37.4, 40.1)	36.1	(34.3, 37.8)
Gender											
Male	1893	22.6	(19.8, 25.3)	25.5	(22.7, 28.3)	42.7	(39.0, 46.4)	41.2	(38.3, 44.1)	36.3	(33.3, 39.3)
Female	1852	21.4	(19.2, 23.5)	19.9	(17.4, 22.3)	36.0	(34.0, 38.0)	36.8	(34.6, 39.0)	35.6	(33.2, 37.9)
Age											
20-29	574	9.4	(5.8, 13.0)	12.3	(8.7, 15.9)	20.3	(16.3, 24.3)	18.5	(14.4, 22.6)	14.2	(10.4, 18.0)
30-39	623	14.8	(12.0, 17.6)	19.3	(16.2, 22.4)	26.2	(22.9, 29.6)	24.7	(21.3, 28.1)	23.9	(20.1, 27.7)
40-49	692	20.6	(15.9, 25.3)	25.0	(20.2, 29.9)	40.4	(34.4, 46.4)	38.7	(33.3, 44.1)	35.4	(30.5, 40.3)
50-59	523	28.0	(22.5, 33.4)	27.4	(21.5, 33.3)	50.3	(44.4, 56.2)	51.9	(47.2, 56.5)	47.3	(43.5, 51.2)
60-69	625	37.6	(32.2, 43.0)	34.8	(30.3, 39.3)	57.7	(52.1, 63.3)	63.2	(59.1, 67.2)	59.0	(55.3, 62.7)
70-79	416	35.6	(30.5, 40.8)	23.9	(19.3, 28.4)	60.3	(54.0, 66.7)	60.1	(54.7, 67.0)	58.7	(52.8, 64.7)
> 80	292	31.5	(24.2, 38.9)	19.5	(12.3, 26.6)	57.6	(51.4, 63.8)	50.9	(43.6, 58.2)	49.4	(42.7, 56.0)
Race/Ethnicity											
Non-Hispanic White	1898	21.7	(19.6, 23.9)	21.8	(19.4, 24.2)	38.9	(35.6, 41.9)	38.9	(36.6, 41.1)	35.7	(33.5, 37.8)

Table 2. Metabolic Syndrome prevalence specific to medical society definitions by demographic characteristics among U.S adults aged ≥ 20 years, NHANES 1999-2002 (continued).

Non-Hispanic Black	663	23.8 (20.2, 27.3)	24.8 (21.7, 27.9)	31.4 (27.7, 35.2)	33.2 (29.6, 36.8)	31.5 (27.7, 35.3)
Mexican-American	916	27.9 (24.7, 31.0)	30.3 (27.8, 32.8)	48.5 (45.4, 51.6)	48.4 (45.3, 51.5)	42.7 (39.4, 46.1)
Other	268	19.9 (16.0, 23.8)	22.6 (17.0, 28.1)	44.5 (36.5, 52.5)	41.9 (37.0, 46.9)	40.9 (34.7, 47.2)
Education						
< High school	1251	24.0 (21.2, 26.7)	26.2 (22.5, 29.9)	46.3 (42.2, 50.3)	45.8 (41.9, 49.8)	42.1 (37.6, 46.6)
High school	839	25.1 (21.3, 29.0)	24.4 (19.5, 29.4)	43.1 (37.9, 48.3)	42.8 (38.1, 47.6)	41.1 (36.1, 46.0)
> High school	1647	19.8 (17.1, 22.6)	20.4 (17.5, 23.4)	35.3 (32.4, 38.3)	34.9 (32.3, 37.5)	31.3 (28.7, 33.9)
Income (% of poverty level)						
< 0 -<100	579	25.4 (21.3, 29.4)	26.8 (22.7, 30.8)	45.2 (38.6, 51.8)	40.3 (35.0, 45.6)	40.8 (34.0, 47.7)
≥100 -<200	851	24.3 (20.1, 28.4)	24.3 (20.3, 28.4)	41.3 (37.0, 45.7)	42.7 (38.4, 47.0)	38.4 (33.5, 43.3)
≥200 -<300	544	23.8 (18.2, 29.5)	21.0 (14.9, 27.2)	40.6 (34.3, 46.9)	37.2 (31.4, 43.0)	37.6 (31.2, 44.0)
≥300 -<400	419	22.4 (16.9, 28.0)	21.7 (15.7, 27.7)	42.3 (36.0, 48.5)	41.8 (35.3, 48.4)	39.4 (32.5, 46.3)
≥400	999	19.1 (16.1, 22.1)	21.2 (18.2, 24.1)	35.0 (31.4, 38.5)	36.5 (34.0, 39.0)	31.6 (28.9, 34.3)

*Percent prevalence. †95 percent confidence interval. **WHO**=World Health Organization **EGIR**=European Group for the study of Insulin Resistance **AHA/NHLBI**=American Heart Association/National Heart, Lung, and Blood Institute **ACE/AACE**=American College of Endocrinology/American Association of Clinical Endocrinologists **IDF**=International Diabetes Federation.

Hispanic Blacks in three out of the five definitions (AHA/NHLBI, ACE/AACE, and IDF). Non-Hispanic Whites had the lowest prevalence rate (21.8%) according to the EGIR definition, and the "other" race/ethnicity category had the lowest prevalence (19.9%) specific to the WHO definition.

A focus on educational attainment found that the lowest MetS prevalence, across all five medical society definitions, occurred in the group with the highest level of educational attainment (> high school). For four of the five definitions, the highest MetS prevalences were found in those who did not complete high school. In addition, Table 2 shows while there is no consistent trend either between or within definitions as reflected by poverty levels, those people below the 100% poverty threshold for four of the five definitions were found to have the highest prevalence of the MetS.

After controlling for gender (not stratified by gender), age, race/ethnicity, education, and poverty level in multivariate logistic regression, several consistent risk factors were identified across the definitions (See Table 3). For three of the five definitions, females were found to have a decreased likelihood of being diagnosed with the MetS. This reduced risk for females ranged from 23% to 30%. These findings closely mirrored the difference in prevalences between males and females found in Table 2.

After controlling for all other factors, our data indicate the risk of being diagnosed with the MetS to be highly age-dependent, with risk increasing each decade through the seventh decade of life. For four of the five definitions, people in the seventh decade of life (60-69 years of age) were four to eight times more

Table 3. Odds ratios for being diagnosed with the metabolic syndrome specific to medical society definitions: U.S adults aged ≥ 20 years, NHANES 1999-2002.

	WHO[1999]	EGIR[1999]	ACE/AACE[2003]	IDF[2005]	AHA/NHLBI[2005]
Independent variables and effects	Adjusted Odds ratio 95% CI†	Adjusted Odds ratio 95% CI†	Adjusted Odds ratio 95% CI†	Adjusted Odds ratio 95% CI†	Adjusted Odds ratio 95% CI†
Gender					
Male*	1.00	1.00	1.00	1.00	1.00
Female	0.93 (0.75, 1.15)	0.70 (0.56, 0.87)	0.70 (0.59, 0.83)	0.77 (0.64, 0.93)	0.94 (0.77, 1.14)
Age					
20-29*	1.00	1.00	1.00	1.00	1.00
30-39	1.78 (1.08, 2.91)	1.79 (1.22, 2.64)	1.50 (1.08, 2.08)	1.51 (1.05, 2.19)	1.94 (1.27, 2.97)
40-49	2.72 (1.53, 4.83)	2.55 (1.77, 3.69)	3.09 (2.02, 4.74)	3.26 (2.14, 4.97)	3.69 (2.46, 5.52)
50-59	4.42 (2.59, 7.56)	3.13 (1.98, 4.93)	4.82 (3.32, 7.00)	5.66 (4.07, 7.88)	6.56 (4.59, 9.39)
60-69	6.19 (3.96, 9.68)	4.03 (2.76, 5.87)	5.96 (4.16, 8.53)	8.45 (6.25, 11.41)	8.93 (6.10, 13.05)
70-79	5.53 (3.05, 10.03)	2.42 (1.41, 4.15)	6.43 (4.11, 10.05)	8.10 (5.12, 12.79)	8.95 (5.68, 14.10)
> 80	4.88 (2.56, 9.32)	2.00 (0.97, 4.14)	6.06 (3.83, 9.58)	5.75 (3.80, 8.72)	5.90 (3.85, 9.05)

Table 3. Odds ratios for being diagnosed with the metabolic syndrome specific to medical society definitions: U.S adults aged ≥ 20 years, NHANES 1999-2002 (continued).

Race/Ethnicity										
Non-Hispanic White*	1.00		1.00		1.00		1.00		1.00	
Non-Hispanic Black	1.09	(0.83, 1.45)	1.09	(0.84, 1.42)	0.67	(0.52, 0.85)	0.71	(0.55, 0.93)	0.74	(0.57, 0.97)
Mexican-American	1.31	(0.94, 1.84)	1.44	(1.08, 1.92)	1.34	(1.03, 1.74)	1.35	(1.04, 1.76)	1.17	(0.86, 1.58)
Other	0.81	(0.58, 1.13)	0.99	(0.69, 1.44)	1.26	(0.87, 1.82)	1.15	(0.86, 1.54)	1.15	(0.83, 1.57)
Education										
< High school*	1.00		1.00		1.00		1.00		1.00	
High school	1.13	(0.81, 1.56)	1.01	(0.66, 1.55)	0.96	(0.72, 1.27)	0.89	(0.64, 1.24)	1.02	(0.72, 1.43)
> High school	0.92	(0.69, 1.21)	0.86	(0.61, 1.21)	0.69	(0.48, 0.99)	0.64	(0.47, 0.88)	0.67	(0.48, 0.92)
Income (% of poverty level)										
< 0 -<100*	1.00		1.00		1.00		1.00		1.00	
≥100 -<200	0.90	(0.68, 1.20)	0.87	(0.64, 1.18)	0.83	(0.58, 1.19)	1.03	(0.72, 1.47)	0.88	(0.59, 1.31)
≥200 -<300	0.88	(0.62, 1.26)	0.67	(0.43, 1.05)	0.85	(0.59, 1.24)	0.87	(0.61, 1.23)	0.88	(0.58, 1.33)
≥300 -<400	0.80	(0.51, 1.23)	0.70	(0.44, 1.09)	0.93	(0.64, 1.33)	1.02	(0.72, 1.46)	0.98	(0.66, 1.45)
≥400	0.65	(0.47, 0.89)	0.70	(0.50, 0.96)	0.70	(0.48, 1.02)	0.84	(0.62, 1.13)	0.70	(0.48, 1.02)

*Referent group. †95 percent confidence interval. **WHO**=World Health Organization **EGIR**=European Group for the study of Insulin Resistance **AHA/NHLBI**=American Heart Association/National Heart, Lung, and Blood Institute **ACE/AACE**=American College of Endocrinology/American Association of Clinical Endocrinologists **IDF**=International Diabetes Federation.

likely to be diagnosed with the MetS compared to adults in the third decade of life (See Table 3).

According to three of the five definitions, Mexican-Americans had the greatest risk for being diagnosed with the MetS compared to non-Hispanic Whites. This increased risk ranged from 34% (ACE/AACE) to 44% (EGIR). Conversely, a significantly lower risk for being diagnosed with the MetS was noted for non-Hispanic Blacks in three of the five definitions. Non-Hispanic Blacks were 29% to 33% less likely to be diagnosed with the MetS compared to their non-Hispanic Whites counterparts (See Table 3).

For three of the five definitions (AHA/NHLBI, ACE/AACE, and IDF), MetS risk was significantly lower in people with greater than a high school education. After controlling for other factors, adults with this level of education were found to have a 31% to 36% reduction in risk of being diagnosed with the MetS. In addition, reduced risk ranging from 30% to 35% was found among adults in the $\geq$ 400% poverty category, compared to those below the 100% poverty demarcation (See Table 3). This risk reduction was only found in this most affluent group within the WHO and EGIR definitions.

Discussion

To date, nationally representative MetS prevalence studies in the U.S. comparing prevalences across definitions have only simultaneously employed a maximum of two definitions (36, 37). Our study extends this earlier research by simultaneously comparing the MetS prevalences for all five medical society

definitions using a nationally representative sample of the U.S. adult population within 1999-2002 NHANES.

When examining the trends seen across the five working medical society definitions, there appears to be two levels of prevalence - low (WHO and EGIR), and high (ACE/AACE, IDF and AHA/NHLBI). The lower prevalence estimates found with the WHO and EGIR definitions appear to be due to the restrictive nature of the requisite criteria (See Table 1). The eligible pools for each definition as defined by the percentage of people from our background population meeting the requisite criteria are displayed in Figure 1. When examining the four definitions with requisite criteria, the WHO, ACE/AACE and IDF definitions estimate prevalence to be approximately half of their eligible pool. However, the EGIR definition captures 84% of its eligible pool, thus suggesting insulin resistance and/or hyperinsulinemia may be a more sensitive filter for MetS than other criteria. Previous research examining prevalence estimates of the MetS and the individual components defining the syndrome has found there to be a strong link between insulin resistance and hyperinsulinemia with the clustering of risk factors that designate the MetS (26, 34, 43, 48, 61, 62, 74).

Excluding the AHA/NHLBI criteria, for which a requisite condition is not applicable, the specific requisite condition prevalence (phase 1) appears to serve as a filter in the remaining definitions, thus impacting the risk pool eligible for MetS diagnosis based on other criteria specific to each definition (See Figure 1). In addition to the restrictive requisition criteria found in these low prevalence definitions, additional restrictions are imposed through HTN and triglycerides.

The moderate-level prevalence estimate of MetS associated with the AHA/NHLBI definition is likely due to the liberal nature of the definition in that no requirements or requisite conditions are imposed. In the absence of requisite criteria within the AHA/NHLBI definition, any combination of three of the five defining criteria for MetS diagnosis is plausible. The reason for this approach in defining the MetS was that the AHA/NHLBI definition was developed to enable the clinician to easily ascertain values and make a MetS diagnosis in the office. The more recently developed IDF definition mirrors the AHA/NHLBI definition in order to maintain clinical utility. However, since the lower WC cut-off points demarcating obesity found in the IDF definition are a requisite condition, this directly impacts MetS prevalence (36).

The high-level prevalence estimates were observed for the ACE/AACE and IDF definitions. A plausible reason for this is that requisite criteria of the ACE/AACE and IDF are related to a high-level estimate of prevalence (phase 1) and their focus emphasizing BMI or WC. With 66.3% of the US adult population estimated to be overweight or obese (57), the eligibility pools for either of these two definitions is quite large. A closer examination of body size the obesity requisite criteria identifies three possible reasons for the large eligibility pools. First, the requisite criterion for the ACE/AACE definition includes a BMI > 25 kg/m^2, thus capturing those who are both overweight and obese. Second, the ACE/AACE requisite criteria classify everyone > 40 years of age a high-risk. A closer look at Table 2 illustrates this would include two-thirds of the U.S. population. And thirdly, the IDF requisite criterion for WC is ethnic specific, which

not only enlarges the eligibility pool, but allows for more accurate, ethnically sensitive prevalence estimates. Until recently, epidemiological research utilized National Institutes of Health (NIH) WC cut-off points for all ethnic groups in the US (56). Ethnic-specific WC cut-off points (which are often lower) are now recommended due to the fact recent research has shown the co-morbidities associated with body size or central obesity vary among populations (46, 75).

MetS and gender

When focusing on demographic MetS prevalence estimates, males were found to have a greater overall prevalence in two of the five working definitions. Males were also found to have a greater overall prevalence of the MetS in NHANES III (37). One explanation for this may be the higher prevalences of HTN and hypertriglyceridemia found in males in NHANES III. Furthermore, in the CARDIA study (18), a prospective study examining demographic characteristics and modifiable cardiovascular risk profiles with the likelihood of developing the MetS in adult males and females, males were found to be two to four times more likely to have the MetS without abdominal adiposity, thus suggesting the remaining MetS risk factors may cluster more in males.

The lower prevalence estimates found among females in two of the five definitions correspond to our findings of females being 23% to 30% less likely to be diagnosed with the MetS. In NHANES III, Tong et al. (68) found men aged 35-54 years to be more then twice as likely (OR 2.22, 95% CI, 1.03-4.81) to have the MetS when compared to women in the same age category (OR 1.05, 95% CI,

0.40-2.79). The transition from pre-to postmenopause is accompanied by many characteristics defining the MetS, including increases in central adiposity, increases in both glucose and insulin levels, and often a shift to a more atherogenic lipid profile (19). The decreased risk of being diagnosed with the MetS found in our study may be explained by the protective effects of endogenous estrogen found in pre-menopausal females (69), however, this is still an unanswered question (68).

Nevertheless, the clustering of cardiovascular risk factors is prevalent in both males and females and leads to an increase in CVD risk in both genders (73).

MetS and age

There is a strong positive association between the prevalence of the MetS and age. Our study found males and females 60-69 years of age to be four to eight times more likely to be diagnosed with MetS than those 20-29 years of age. Males and females age 35-64 in NHANES III were found to be two to three times more likely to be diagnosed with the MetS than those age 20-34 (59). This likely occurs because of the increase in MetS risk factors (e.g. insulin resistance, obesity) that accompanies the normal aging process (13, 33).

MetS and ethnicity

Specific to race/ethnicity, Mexican-Americans were found to have the highest prevalence estimates and risk of the MetS across all five medical society definitions. Mexican-Americans have been found to have greater prevalences of

abdominal obesity and hypertriglyceridemia (38), and greater prevalences of fasting hyperglycemia (25), compared to their non-Hispanic black and non-Hispanic white counterparts. All of these conditions represent either requisite (phase 1) or threshold (phase 2) conditions for MetS diagnosis. Additionally, the clustering of cardiovascular risk factors associated with the MetS has been found to be more common in Mexican-Americans (25, 38, 59), thus leading to the higher prevalence rates found in this population.

Conversely, non-Hispanic blacks were found to have the lowest MetS prevalence estimates and risk in three of the five medical society definitions (See Tables 2 and 3). The differences in metabolic alterations associated with central obesity may hold some the explanation for this racial disparity found between racial/ethnic groups. Despres (29) found blacks to have higher HDL-C levels and a more cardioprotective lipoprotein profile for similar levels of abdominal adiposity compared to whites. In NHANES III, non-Hispanic blacks were found to have a lower prevalence of dyslipidemia than their non-Hispanic white and Hispanic counterparts (58). This may be one reason non-Hispanic blacks were found to have lower overall MetS prevalences in three of the five definitions. This metabolic protection carried by non-Hispanic blacks has been shown to be the result of carrying lower amounts of visceral fat for the same level of adiposity compared to other populations (24, 45).

The non-Hispanic white (EGIR) and other racial/ethnic (WHO) category are found to have the lowest prevalence estimates when HTN diagnostic criteria are raised from 130/85 mmHg to 140/90 mmHg in the WHO and EGIR definitions

(See Table 2). This was not surprising knowing that non-Hispanic blacks have greater prevalences of HTN (44, 58, 66). Interestingly, approximately 50% of people with essential HTN have been found to be insulin resistant and hyperinsulinemic (61). Insulin resistance has been postulated by many to be the core component of the MetS (2, 3, 5, 11, 32, 34, 40, 62, 67). The coexistence of insulin resistance and HTN would identify approximately half of the eligibility pools for the WHO and EGIR definitions as being one condition away from MetS diagnosis, thus greatly increasing the likelihood of diagnosis in a smaller at risk eligibility pool. This relationship between insulin resistance and HTN warrants continued investigation.

MetS and SES

Socioeconomic status is a well established marker commonly used by epidemiologists (52). Outside of gender and race/ethnic background which are genetically determined, in this study environmental and societal markers of affluence were found to have the greatest relationship with risk and prevalence of the MetS. Our study utilized the two most common surrogates of SES, education and income. The relationship between SES and the core components of the MetS has been previously examined (12, 15, 23, 53, 54). In NHANES III, Loucks et al. (54) found socioeconomic position (SEP) to be associated with the MetS in non-Hispanic whites, non-Hispanic blacks, and Mexican-Americans, with the association being greater in women. People with diabetes from a low SES have been found to be at a greater risk for developing the MetS because they are

more likely to be obese and hypertensive (23). Brunner et al. (15) found central obesity, triglycerides, and high waist to hip ratios to be inversely associated with SES. Additionally, in a landmark paper by Rose and Marmot (64) looking at risk factors for CVD, overweight, obesity, and HTN, all conditions contributing to a diagnosis of the MetS across all five medical society definitions, were reported to be associated with a lower SES.

Study limitations

Our findings must be interpreted in light of the potential limitations. Among the total number of criteria identified in all five definitions of the MetS, we were unable to measure four criteria due to them not being available in the most recent NHANES. First, oral glucose tolerance test (OGTT) values were not available. We utilized three markers of insulin resistance or diabetes included in the WHO definition. These included IFG, T2D, and insulin in the top quartile of the background population. Insulin in the top quartile of the background population and IFG but not diabetes was utilized in the EGIR definition, and IFG and diabetes in the AHA/NHLBI (NCEP) definition (See Table 1). Second, the most recent NHANES did not collect data on hip measurements. We utilized only the BMI data for our obesity value in the WHO definition. Third, gestational diabetes data, and lastly, data on polycystic ovary syndrome were not available for women who may have had a history of these two conditions. Thus, in the ACE/AACE high-risk requisite criteria we only included 1) family history of CVD, 2) known CVD, 3) inactive lifestyle, 4) over 40 years of age, and 5) ethnic populations at

high-risk for T2D. Another limitation is the cross-sectional nature of our study, precluding causation from being inferred.

Conclusion

In conclusion, the magnitude of MetS prevalence is highly dependent on the medical society definition used. Thus, direct comparisons of prevalence values across MetS studies may be severely limited. Future studies should carefully consider which medical society definition to adopt in order to maximize their ability to relate to findings from other studies. In addition, our study may also assist researchers to anticipate the magnitude of the expected prevalence they will encounter in study populations based on the definition adopted, thus allowing them to refine project methodologies (i.e. power analysis). Furthermore, this study will allow practitioners and researchers to continue dialogue which may lead to a consensus on which definition would be the best to employ in both clinical and research environments.

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APPENDIX B

Metabolic Syndrome and its Relationship to Total Physical Activity: NHANES 1999-2002.

Abstract

In the past, the examination of the relationship between physical activity (PA) and the metabolic syndrome (MetS) has been restricted to leisure-time physical activity. The 1999-2002 National Health and Nutrition Examination Survey (NHANES IV) currently assesses PA across all domains (leisure-time, destinational, and domestic), allowing the MetS to be examined from a global perspective. **Purpose:** To explore the relationship between total PA (leisure-time, destinational, and domestic) and the MetS among a national sample of adults. **Methods:** This study included 4059 adults, 20 years and older who completed the mobile examination center (MEC) examination in NHANES IV. MetS was defined based on the current National Cholesterol Education Program-Adult Treatment Program III criteria. Each subject completed a PA interview that measured all domains of PA, and included the assessment of intensity, frequency, and duration. **Results:** The national age-adjusted prevalence for the MetS was 32.4%. Prevalence of the MetS among adults meeting the ACSM/CDC recommendation was 21.8% (met recommendation), 30.2% (insufficient), and 36.9% (physically inactive), demonstrating an inverse relationship. Adults with the MetS performed significantly less PA (827 MET-minutes per week) compared to those without the MetS (1076 MET-minutes per week). However, there was not a significant difference between frequency of PA (per week) and PA duration (daily minutes), suggesting that exercise intensity may be the best explanation for explaining the difference adults with and without the MetS relative to the ACSM/CDC

recommendation. **Conclusion:** Those with MetS are less likely to meet ACSM/CDC recommendations for PA. Those with the MetS achieve less PA than their counterparts due to the difference in intensity of the PA.

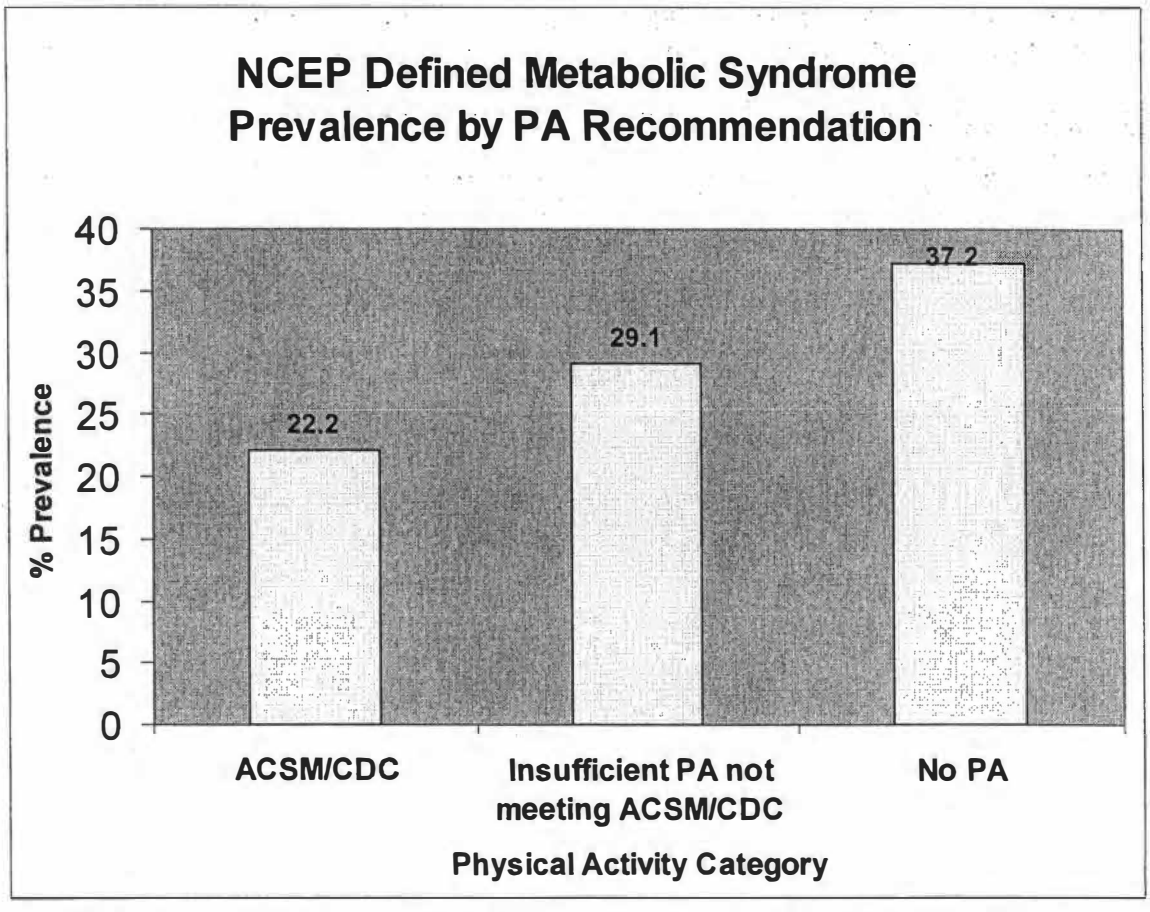

Figure B-1. Inverse association of physical activity and the metabolic syndrome when measuring physical activity from the parameters of the CDC/ACSM physical activity public health recommendation, NHANES 1999-2002.

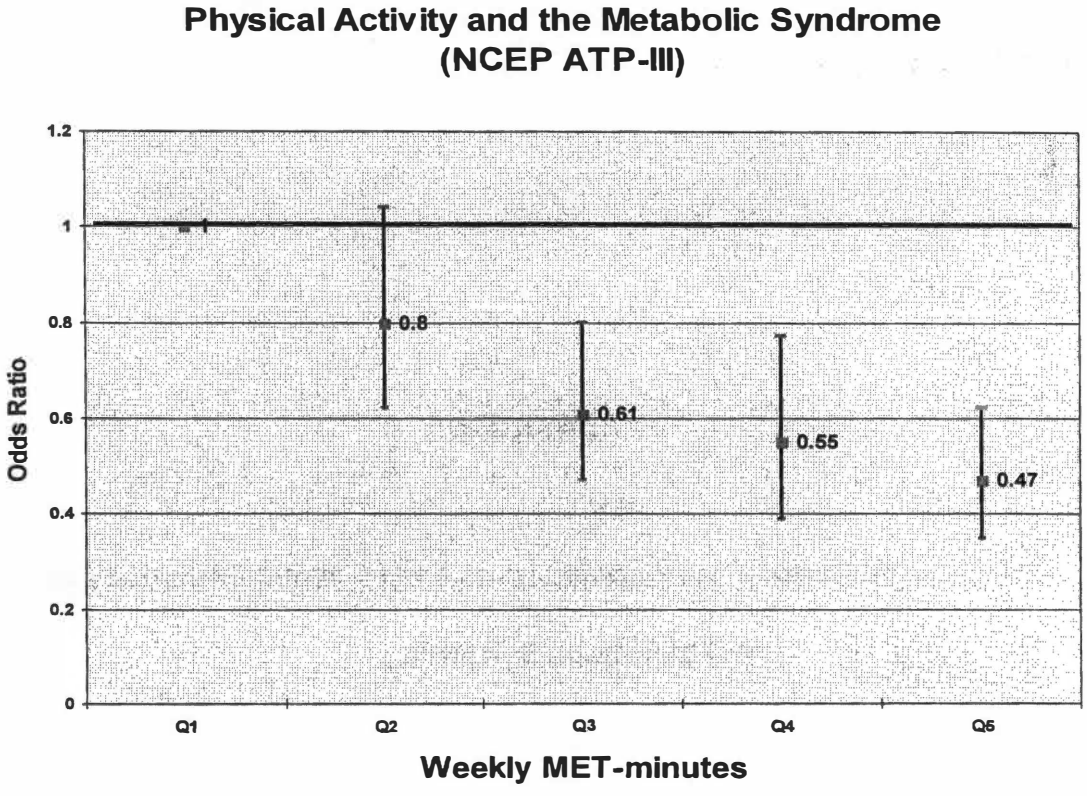

Figure B-2. Inverse association of physical activity when examining MET·min·wk^{-1} and the risk of the metabolic syndrome in the United States adult population aged ≥20 years in NHANES 1999-2002.

APPENDIX C

Alternate Findings: The Association of Total Physical Activity with the Metabolic Syndrome

Abstract

This study also took a preliminary look at a more global physical activity (PA) measure utilizing information on PA from three domains (LTPA, domestic, and transportation). Data utilized to measure total PA was accessed from two distinct NHANES questionnaire data files - the 'Physical activity' data file (PAQ_C) and the 'physical activities individual activities file' (PAQIAF) (1). The PAQ_C asked questions related to the frequency, intensity, and duration specific to transportational and domestic PA performed over the past 30 days (*e.g.* Over the last 30 days, how often did you walk or cycle as a part of getting to or from work, or school, or to do errands?). The PAQIAF is the second of the two files on PA and includes more detailed information regarding 43-specific types of moderate and vigorous LTPA. The combination of information from the two PA files allowed us to create a global measure of PA to examine the possible inverse association with metabolic syndrome risk. Appendix C includes replicate tables also found in Part IV.

Table C-1 illustrates the prevalence of the metabolic syndrome according to the American Heart Association and National Heart, Lung, and Blood Institute (AHA/NHLBI) definition by the Centers for Disease Control and Prevention and the American College of Sports Medicine (CDC/ACSM) public health PA recommendation and total weekly MET·minutes from all three domains of PA. The prevalence of the metabolic syndrome among those meeting the current CDC/ACSM PA recommendation (3) was 33.0% (95% CI 30.0-36.0). The prevalence among those reporting no PA (inactive) from any of the three

domains was 41.6% (95% CI 38.0-45.3), significantly greater than those meeting the current public health recommendation.

Table C-2 depicts the relative risk odds ratio (OR) of a metabolic syndrome diagnosis and the accumulation of increasing the metabolic risk score (MSRS) by total weekly MET·minutes. Interestingly, we found an inverse association (OR 0.76; 95% CI 0.58-0.98) beginning at a volume of 1261.18 weekly MET·minutes, a much greater level than that found when examining the results of Part IV which solely focused on LTPA (OR 0.65; 95% CI 0.48-0.88) (736.55 weekly MET·minutes). A similar inverse association was found for increasing the MSRS (OR 0.79; 95% CI 0.64-0.96).

Table C-3 depicts the OR of a metabolic syndrome diagnosis and the increasing metabolic risk score MSRS by the CDC/ACSM public health PA recommendation when focusing on total weekly MET·minutes. Those meeting the current public health PA recommendation were found to be 31% (OR 0.69; 95% CI .057-0.84) less likely to have the metabolic syndrome and 25% less likely (OR 0.75; 95% CI 0.64-0.88) to add an additional risk factor to the MSRS compared to those reporting no PA (inactive) from any of the three domains. These associations were similar to those found in Part IV when examining LTPA; however, the inverse relationships were not as strong. This too warrants future study.

One possible explanation for these conflicting results between LTPA and Total PA resides with intensity of PA. Table C-4 compares the proportion of vigorous MET·minutes among those who reported strictly LTPA and those

reporting PA from up to all three domains. When examining the first two levels of PA, approximately 10%-15% of the weekly MET·minutes come from vigorous activities for LTPA and total PA. However, as the volume of LTPA MET·minutes increases, the proportion of those MET·minutes coming from vigorous PA also increases. Those accumulating the greatest volume of LTPA (>1360.15 MET·minutes) acquired 45.7% of their MET·minutes from vigorous PA. Those accumulating the greatest volume of total PA (2298.66 MET·minutes) only acquired 27.6% of their MET·minutes from vigorous PA.

The level and appearance of protection associated with PA and the metabolic syndrome clearly differs when examining multiple domains (LTPA, domestic, and transportation), versus one domain, in this case LTPA. Perhaps the reason Ford et al. in an earlier NHANES metabolic syndrome and PA study (2) did not find protection associated with PA was because he utilized multiple domains (LTPA and domestic). These data suggest intensity, one of the parameters of PA volume, may play an important role in the relationship between PA and the metabolic syndrome. Future studies need to examine all these parameters to elucidate which of these components may be related to these conflicting outcomes. This type of information may assist health care professionals to understand how to prescribe PA to people for prevention and disease control specific to the metabolic syndrome.

Table C-1. Metabolic Syndrome Prevalence According to the AHA/NHLBI Definition by CDC/ACSM Public Health PA Recommendation* and Total PA MET·Minutes from All Three Domains† Among U.S. Adults ≥20 Years - NHANES 1999-2004.

	Age-adjusted prevalence	
Weekly LTPA MET minutes	%	95% CI
0.0	41.1	37.6, 44.6
>0.0 - ≤283.43	41.4	37.3, 45.5
>283.43 - ≤675.48	36.2	32.6, 39.8
>675.48 - ≤1261.18	35.3	31.3, 39.3
>1261.18 - ≤2298.66	34.3	30.5, 38.1
>2298.66	31.0	27.1, 35.0

	%	95% CI
Inactive	41.6	38.0, 45.3
Insufficiently active‡	38.2	35.9, 40.4
Meets Recommendation*	33.0	30.0, 36.0

CDC/ACSM=Centers for Disease Control and Prevention / American College of Sports Medicine.

MET=Metabolic equivalent (1 MET= 3.5 ml/kg/min^{-1})

*Every US adult should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week (3).

†PA from LTPA, domestic PA, and transportational PA.

‡Physically active but insufficient to meet CDC/ACSM recommendation (3).

Table C-2. Odds ratios of Metabolic Syndrome diagnosis and Increasing Metabolic Syndrome Risk Score (MSRS) by Weekly MET·minutes from All Three Domains of PA*: NHANES 1999-2004.

	Metabolic syndrome risk by total PA level			Risk of increasing MSRS		
Weekly MET minutes	Odds ratio	95% CI	P value for trend	Odds ratio	95% CI	P value for trend
0.0	1.00		0.0006	1.00		0.0003
>0.0 - ≤283.43	1.15	0.88, 1.51		1.27	1.00, 1.61	
>283.43 - ≤675.48	0.84	0.66, 1.08		0.92	0.73, 1.15	
>675.48 - ≤1261.18	0.85	0.66, 1.10		0.91	0.73, 1.14	
>1261.18 - ≤2298.66	0.76	0.58, 0.98		0.79	0.64, 0.96	
>2298.66	0.64	0.49, 0.83		0.69	0.57, 0.84	

Covariates adjusted for in the model include gender, age, race/ethnicity, education, income, smoking status, alcohol intake, family history of heart disease, and family history of diabetes.

MET=Metabolic equivalent (1 MET= 3.5 ml/kg/min^{-1})

*PA from LTPA, domestic, and transportation.

Table C-3. Odds ratios of Metabolic Syndrome diagnosis and Increasing Metabolic Syndrome Risk Score (MSRS) by CDC/ACSM public health PA recommendation* and Total PA from All Three Domains†: NHANES 1999-2004

	Metabolic syndrome risk by total PA level			Risk of increasing MSRS		
LTPA Level	Odds ratio	95% CI	P value for trend	Odds ratio	95% CI	P value for trend
Inactive	1.00	--	0.0010	1.00	--	0.0015
Insufficiently active‡	0.88	0.71, 1.09		0.98	0.81, 1.18	
Meets PA recommendation*	0.69	0.57, 0.84		0.75	0.64, 0.88	

Covariates adjusted for in the model include gender, age, race/ethnicity, education, income, smoking status, alcohol intake, family history of heart disease, and family history of diabetes.

CDC/ACSM=Centers for Disease Control and Prevention / American College of Sports Medicine.

CV= Cardiovascular disease.

*Every US adult should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week (3).

†PA from LTPA, domestic PA, and transportational PA.

‡Physically active but insufficient to meet CDC/ACSM recommendation (3).

Table C-4. Proportion of Vigorous Intensity PA Comparing Total PA from All Three Domains* and PA from those Reporting Only LTPA†: NHANES 1999-2004.

LTPA MET·minutes			Total MET·minutes*
	% from vigorous PA	% from vigorous PA	Weekly MET minutes
0.0	-	-	0.0
>0.0 - ≤156.24	10.0	9.4	>0.0 - ≤283.43
>156.24 - ≤393.10	15.8	15.7	>283.43 - ≤675.48
>393.10 - ≤736.55	24.8	21.4	>675.48 - ≤1261.18
>736.55 - ≤1360.15	34.5	25.9	>1261.18 - ≤2298.66
>1360.15	45.7	27.6	>2298.66

*PA from LTPA, domestic PA, and transportational PA.

†LTPA= leisure-time physical activity

References

1. CDC. Codebook for data collection (1999-2000); Physical Activity Section of the SP and MEC CAPI Questionnaire. 2006.
2. Ford, E. S., H. W. Kohl, 3rd, A. H. Mokdad, and U. A. Ajani. Sedentary behavior, physical activity, and the metabolic syndrome among U.S. adults. *Obes Res*. 13:608-614, 2005.
3. Pate, R. R., M. Pratt, S. N. Blair, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *Jama*. 273:402-407, 1995.

VITA

James Richard Churilla was born in Lackawanna, New York on September 20, 1966. He grew up on Long Island, where he attended school and graduated from Brentwood Ross High School in 1984. He completed a Bachelor of Science in Physical Education from Towson State University in 1989. He then worked as an exercise professional from 1989 to 2004 in South Florida. He attended Florida International University where he completed a Masters of Science in Exercise Physiology in 1998 while working as an Exercise Physiologist in the Neurological Rehabilitation Center in Tamarac, Florida. Following his graduation he accepted a position as a Clinical Exercise Physiologist working in cardiopulmonary rehabilitation at Broward General Medical Center in Fort Lauderdale, Florida. While continuing to work as a Clinical Exercise Physiologist, he returned to graduate school, once again attending Florida International University and completed a Masters of Public Health with a concentration in epidemiology, graduating in 2003. He graduated with a Doctor of Philosophy degree in Education-Exercise Physiology from the University of Tennessee in May 2007. He accepted a position as an Assistant Professor in the Brooks College of Health at the University of North Florida in Jacksonville, Florida.