Classes of Physical Activity: Associations with Sociodemographic Characteristics and Risk Factors for the Metabolic Syndrome

Jesse S. Metzger

A dissertation submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Epidemiology

Chapel Hill
2007

Approved by:

Advisor: Anna Maria Siega-Riz

Reader: Diane J. Catellier

Reader: Kelly R. Evenson

Reader: Wayne D. Rosamond

Reader: Margarita S. Treuth

ABSTRACT

JESSE METZGER: Classes of Physical Activity: Associations with Sociodemographic Characteristics and Risk Factors for the Metabolic Syndrome
(Under the direction of Anna Maria Siega-Riz)

The last several decades have produced a substantial body of literature indicating the health benefits of physical activity, including reduced risk of all-cause mortality, coronary heart disease (CHD), and CHD risk factors. Nevertheless, the prevalence of physical activity in the United States (US) continues to be suboptimal for most as work and daily activities become more and more sedentary. Concurrently, in 2004, 32.2% of adults were classified as obese as defined by a body mass index ≥ 30 kg/m^2. These two factors (obesity and physical inactivity) along with genetic factors are the primary root causes of the metabolic syndrome.

Associations are well established between physical activity and hypertension, diabetes, obesity, triglycerides and high-density lipoproteins, all components of the metabolic syndrome. However, many of these associations may be somewhat transient in nature. Given this, those who demonstrate regular activity patterns across a seven day week would be associated cross-sectionally with fewer diagnoses of the metabolic syndrome compared with irregular activity. Therefore, the purpose of this analysis is to employ latent class analysis (LCA) to determine which activity patterns exist in the US, which sociodemographic characteristics are associated with these patterns, and finally whether

certain patterns are disproportionately associated with any of the risk factors for the metabolic syndrome.

The results indicate that a very large portion of the US population may be classified into patterns of physical activity that represent low levels of physical activity throughout the week. A weekend warrior class emerged for approximately 1% of the population. Both gender and age emerged as significant predictors of class membership. Mexicans, other Hispanics, and blacks all had higher odds of being in the most active class.

Accumulating the recommended amount of physical activity for a week was consistently associated with positive profiles of the risk factors related to the metabolic syndrome, and accumulating substantially more physical activity was even better. However, the manner in which you accumulate this activity, either spread over many days of the week or compressed into just a couple, may have similar associations with the risk factors for the metabolic syndrome as well as the syndrome itself.

Acknowledgements

I would like to acknowledge all of the hard work and assistance offered by my committee. Their guidance made the development of this research much more pleasant than I had initially anticipated and, more importantly, made the dissertation phase of my education by far the most educational.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ACSM	American College of Sports Medicine
ADA	American Diabetes Association
ATP III	Adult Treatment Panel III Report
BLRT	Bootstrap Likelihood Ratio Test
BMI	Body Mass Index
BP	Blood Pressure
BRFSS	Behavior Risk Factor Surveillance System
CDC	The Centers for Disease Control and Prevention
CHD	Coronary Heart Disease
CI	Confidence Interval
CV	Co-Efficient of Variation
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
EM	Expectation Maximization Algolrithm
FITT	Frequency, Intensity, Time and Type
GMM	Growth Mixture Model
HDL	High-density Lipoprotein
IGT	Impaired Glucose Tolerance
JNC 7	Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
LCA	Latent Class Analysis
LCAT	Lecithin-Cholesterol Acyltransferase
LCGA	Latent Class Growth Analysis

LDL	Low-density Lipoprotein
LMR	Lo-Mendell-Rubin Likelihood Ratio Test
LPL	Lipoprotein Lipase
LRT	Likelihood Ratio Test
MET	Metabolic Equivalents of Task
MSSE	Medicine and Science in Sports and Exercise
MVPA	Moderate-to-Vigorous Physical Activity
NCEP	National Cholesterol Education Program
NCHS	The National Center for Health Statistics
NH	Non-Hispanic
NHANES	The National Health and Nutrition Examination Survey
NHES	The National Health Examination Survey
NHIS	National Health Interview Survey
NHLBI	The National Heart, Blood and Lung Institute
OR	Odds Ratio
PA	Physical Activity
PAEE	Physical Activity Energy Expenditure
PDF	Probability Density Function
PIR	Poverty Income Ratio
RCT	Randomized Controlled Trial
RMR	Resting Metabolic Rate
RR	Relative Risk
SBP	Systolic Blood Pressure
US	United States
VPA	Vigorous Physical Activity

Chapter One

Background and Significance

1.1. Rates of Obesity in the United States

Beginning in the early 1960's, rates of obesity in the US have been tracked in several cross-sectional national surveys, including the earliest survey from 1960-62, referred to as the National Health Examination Survey (NHES). Then, several successive surveys entitled the National Health and Nutrition Examination Survey (NHANES) were conducted in 1971-74 (referred to as NHANES I), 1976-80 (NHANES II), and 1988-94 (NHANES III). Later NHANES are simply referred to by the years in which they were conducted. The surveys are designed to sample around 5,000 adults and children each year from throughout the non-institutionalized civilian US population.[1] A questionnaire component of the survey includes information on demographics, socio-economic status, dietary habits and other health related questions, while an examination component includes a medical and dental exam, physiological measurements and laboratory tests.

Based on data from these surveys, between 1960 and 1994 there was little change in the prevalence of pre-obesity (defined by a body mass index (BMI) of 25.0-29.9 kg/m^2),increasing only slightly from an age-adjusted prevalence of 30.5% in 1960-2 to 32.0% in 1988-1994 for those aged 20-74 years old.[2] However, the increase in obesity, as defined by a BMI ≥ 30 kg/m^2, increased markedly from a prevalence of

12.8% in 1960-2 to 22.5% in 1988-1994. Extreme obesity, as defined by a BMI ≥ 40 kg/m^2, also increased, from an age-adjusted prevalence of 0.8% in 1960-2 to 2.9% in 1988-94.

In more recent years, the increasing trends have continued. The Centers for Disease Control and Prevention (CDC) reported that in the 2003-2004 NHANES assessment, 32.2% of US adults (≥20 years old) were obese.[2] This was almost 2% higher than the 1999-2000 NHANES survey, in which 30.5% of adults were classified as obese. The increase originated primarily from a disproportionate increase in male obesity. In the 1999-2000 survey, 27.5% of males and 33.4% of females were obese, whereas in 2003-2004, 31.1% of males and 33.2% of females were obese.

During the same time period, extreme obesity rates (defined by a BMI ≥ 40 kg/m^2), while higher than the 1988-94 rates, have remained relatively constant.[2] The earlier 1999-2000 survey reported 3.1% and 6.3% for men and women, respectively, and 2.8% and 6.9% in 2003-2004.

Mexican Americans and non-Hispanic blacks have higher overall obesity rates than non-Hispanic whites, but this difference is due mostly to high rates found in females.[2] While non-Hispanic white females had a 30.2% obesity rate in 2003-2004, 42.3% of Mexican-American females were obese and 53.9% of non-Hispanic black females were obese. Clearly, obesity rates are influenced by race.

1.2. National Guidelines and Recommendations for PA

Due to the unprecedented recent rise in obesity rates and low levels of PA in the United States, several government organizations have produced guidelines regarding the quality and quantity of PA a person should accumulate during each week.[3] The urgency of the guidelines is based on the ideas that 1) obesity is an independent risk factor for disease, 2) a low-level of PA is an independent risk factor for disease, 3) increased PA can help reduce obesity rates, and 4) PA is a modifiable behavior.

1.2.1. Key Concepts for Defining Physical Activity and the PA Recommendations

The development of PA as a field of epidemiologic research has led to several conventions necessary to interpret the current recommendations and guidelines. These conventions will also be adopted in the current research proposal.

1.2.1.1. Measuring Physical Activity: FITT

The frequency, intensity, time and type of each activity (or FITT principle) is commonly used to categorize PA. Frequency is used to indicate how often PA is performed, Intensity indicates how vigorous it is, Time measures for how long the activity is sustained, and Type indicates the mode of activity, such as running, cycling, etc.. All of these criteria are used in defining the current PA recommendations.

1.2.1.2. Definition of the Metabolic Equivalents of Tasks (METs)

Intensity of activity is typically measured in Metabolic Equivalents of Task, or METs. One MET is intended to represent the body's energy requirements while at rest, referred to as the Resting Metabolic Rate (RMR). Typically, this quantity is assumed to be 3.5 ml O_2*kg^{-1}*min^{-1}, or 1 Kcal* kg^{-1}*hr^{-1}. The intensities of various activities are then measured as multiples of this reference value. Even though there is some disagreement about the applicability of this reference value to all populations, as it was originally obtained from a 70kg, 40-year-old male, and studies have shown that body composition and age both affect the RMR, it has typically been used in modern PA research as the benchmark average RMR.[4]

1.2.1.3. Defining Sedentary, Light, Moderate and Vigorous PA based on METs

Some modern epidemiologic research categorizes PA based on METs, labeling sedentary behavior as 1 MET (the RMR), light activity as 1 to 2.9 METs, moderate levels of PA range between 3.0 and 6.0 METs, and vigorous activity is 6.1 METs or above.[3] A compendium published by Ainsworth et. al.[5] has classified a large variety of physical activities according to previously published MET levels in order to facilitate comparability between research studies. According to the compendium, walking 2.5 mph on a firm surface requires 3.0 METs of exertion, on average, which provides a reference for the lower range of moderate physical activity. Walking 4.5 mph on a level, firm surface "very, very briskly" was classified as 6.3 METs, or in the lower range of vigorous. This compendium allows researchers to identify activities by MET level and gives the ability to compare across studies by this MET standard.

1.2.2. Recommendations in the US

Recommendations encouraging participation in vigorous physical activity have existed for decades, but only in 1995 did the government produce official recommendations as part of a joint statement from the CDC and the American College of Sports Medicine (ACSM). The recommendation stated that "Every US adult should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week."[3] [page 404] The novel part of this recommendation was the acceptance of moderate-intensity activity, again defined as PA intensity equivalent to 3-6 METs, as sufficient for disease prevention and cardiac health. The type of PA classified as moderate-intensity in this recommendation included examples such as brisk walks, canoeing, cycling ≥ 10 mph as well as activities around the home such as mowing the lawn and painting. Another novel part of the recommendation was that the 30 minutes of PA could be accumulated in short bouts such as "walking up the stairs instead of taking the elevator" and "walking instead of driving short distances".

In 1996, the Surgeon General's report on Physical Activity[6] also called for at least 30 minutes of moderate-intensity PA on most days, and also supported the accumulation of 8-10 minute bouts of PA.[6] This report, however, while acknowledging the benefits of moderate-intensity PA and the plateau effect after 30 minutes per day, still indicated that "additional health and functional benefits of physical activity can be achieved by adding more time in moderate-intensity activity, or by substituting more vigorous activity". Many other recommendations have been produced by various organizations, often focusing on specific health benefits, such as cancer prevention from the American Cancer Society. This proposal will focus, however, on the previous guidelines, since they represent the primary general government recommendations for PA.

1.2.2.1. US population meeting PA recommendations

Based on a recent report by the CDC using data from the 2001 and 2003 Behavior Risk Factor Surveillance System (BRFSS), a population-based, random-digit-dialed survey of over 214,000 respondents, the age-adjusted prevalence of adult participation in at least the minimum recommended level of PA was 45.9% in 2003, similar to the 45.3% reported in 2001.[7] These results are based on the self-report of whether, during a usual week, the respondent participated in any of three varieties of PA: household work, transportation, or discretionary/leisure time PA. Recommended levels of PA could be achieved by either performing moderate-intensity activities, as defined by "brisk walking, bicycling, vacuuming, gardening or any activity that causes small increases in breathing and heart rate", for at least 30 minutes 5 or more days per week, or by vigorous-intensity activities, defined by "running, aerobics, heavy yard work, or any activity that causes large increases in breathing and heart rate", for at least 20 minutes 3 or more days per week. In 2001, 16.0% of respondents reported no moderate or vigorous PA of at least 10 minutes in a usual week, similar to the 15.6% reported in 2003.[7]

In another recent CDC report, also using data from the BRFSS, the trends in leisure-time physical inactivity from 1994 to 2004 showed steady improvement.[8] Physical inactivity was defined as a response of "no" to the following question – "During the past month, other than your regular job, did you participate in any physical activities or exercise, such as running, calisthenics, golf, gardening, or walking for exercise?" The report indicated that the rates of inactivity declined from 29.8% in 1994, to 23.7% in 2004. While women responded "no" more frequently then men, both groups showed similar reductions in physical inactivity (men, 27.9% - women, 31.5% in 1994; men, 21.4% - women, 25.9% in 2004).

1.3. Socio-Demographic correlations with PA: Gender, Race, Age, Income, Education.

The low PA participation rates in the United States have led many researchers to investigate what characteristics are associated with higher levels of PA, and, conversely, what characteristics are associated with low-levels of PA in order to target interventions. Several recent review papers, reflecting over 300 articles on the correlates of PA, have indicated numerous strong associations. In the review by Bauman et. al.[9], they emphasize, however, that most of the associations do not necessarily reflect causal relationships. Distinguishing between determinants of PA and simple correlations is important both for the interpretation of results as well as for the targeting of interventions, particularly in considering how other psycho-social factors may act as mediators or moderators of observed associations.[10]

Many cognitive or emotional factors have been shown to be associated with PA such as social support from family and friends, expectation of benefits, and enjoyment of exercise. [9] Environmental factors have also been identified, such as neighborhood safety and the frequency of seeing others exercising. [9] Behavioral attributes such as dietary habits and Type A personality are also highly correlated with PA. [9]

Importantly for this proposal, several demographic characteristics have also been identified as correlates. Higher education is consistently associated with higher levels of PA, as is male gender. Increasing age is consistently associated with decreasing levels of PA. Higher income and socioeconomic status correlates with higher PA levels. Non-white race/ethnicity is associated with lower levels of PA compared to whites.[9]

1.4. Current research methodology for measuring PA

In order to assess PA levels, either for large national surveys or for specific research, many methods are available. However, developing valid and reliable measures of PA has proved challenging and has become an active area of research in itself. Numerous methods have been utilized in past research, ranging from direct observation of PA, biological markers of PA (such as heart rate monitors and cardiorespiratory fitness), direct and indirect calorimetry, self-report and motion sensors. Each of the measures has their own strengths and weaknesses, which affects their use in certain types of studies. Only self-report and motion sensors will be discussed further as these were the two measures implemented in NHANES 2003-2004.

1.4.1. Self-Report Questionnaires

Self-report questionnaires have been the primary assessment tool for the research upon which the US PA recommendations were based. The two primary concerns regarding self-report that would influence the interpretation of the epidemiological data are that 1) correlations between self-report and other objective measures of PA are generally low, ranging of r=0.17 to r=0.53,[11] and 2) self-report tends to over-report PA, especially in the area of time and intensity.[12, 13] These two issues together would tend to under-estimate the health benefits of PA while over-estimating the amount of PA necessary for health benefits. For these reasons, more objective measures of PA have been developed, including accelerometers.

1.4.2. Accelerometers

Accelerometers are small, electronic devices that record the intensity of the change in bodily motion either in one dimension (usually the vertical plane), three dimensions, or omni-directional and can be worn on the hip, wrist or ankle. Measurements can be made in time units ranging from one second to many minutes over the course of many days, leading to hundreds or thousands of data points per day. Time units are referred to as "epochs" and every epoch is assigned a count value, which is a measure of the changes in moment that occur during the epoch period. The total counts can provide a proxy estimate of total activity. In addition, for research purposes, individual count values can be converted into an estimated measure of METs for that epoch. This can be accomplished in various ways, such as using ROC curves to determine a cut-point with the most preferable sensitivity and specificity, or by creating specific count value cut-points using one of many prediction equations that have been developed by PA researchers.

In the 2003-2004 NHANES survey, accelerometers were added to the battery of questionnaires and physical exams. The chosen accelerometer for the NHANES survey was the MTI Actigraph, a uni-axial monitor that records count values which range from 0-32767. Eligibility for this component of the survey consisted of being over 5 years old and ambulatory. Whereas in the past, most estimates of PA in the US population were based on self-report, the new inclusion of accelerometers to this large nationally representative sample of the US population now provides an objective measure of PA.

1.4.2.1. Methods for calibrating accelerometer values to levels of PA

Many issues have arisen with the increasing usage of accelerometers in research studies. The important questions that have arisen about accelerometers that relate to the current proposal are 1) how well do measurements correlate with actual PA energy expenditure (PAEE) and 2) which prediction equation best predicts the actual MET level of the measurement period. Differences in device placement and the choice of a comparison measure (such as questionnaire or direct calorimetry, for example) can both create discrepant results, but the types of activity selected for assessment, and specifically whether the activity is dynamic or static, appears to be the major consideration for correlations as well as prediction equations and MET-level cut-points.

1.4.2.2. Correlation with PAEE

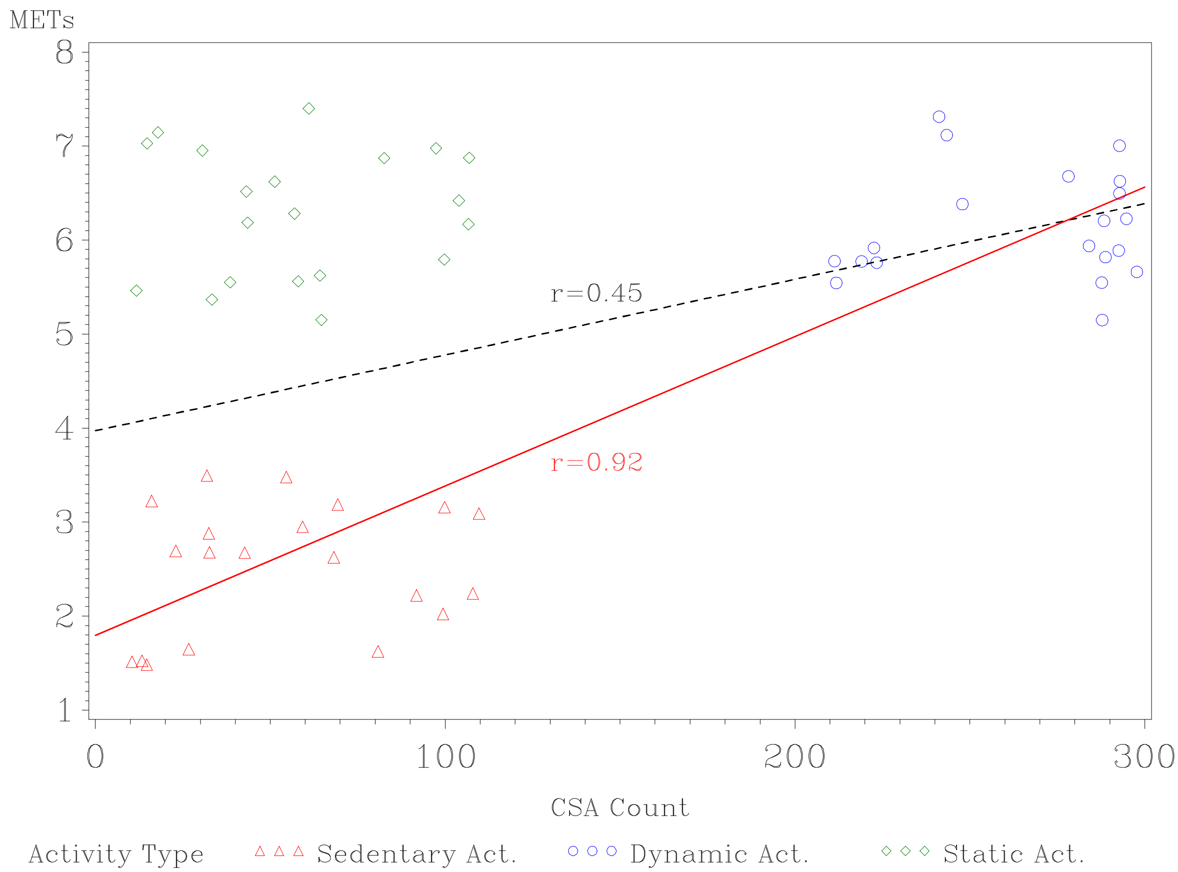
Due to the many methodological issues, the correlations between Actigraph measurements and EE have been inconsistent across studies, ranging from $r = 0.48$ to $r = 0.90$.[14] For example, Leenders et al.[15, 16] compared the uniaxial Actigraph as well as the triaxial Tritrac-R3D to PA assessment using 7-day recall. Correlations for both accelerometer types was r = 0.90. However, when compared to PAEE measured using doubly-labeled water, the correlations dropped to 0.45 and 0.54 for the uniaxial and the triaxial, respectively.

In a study by Hendelman et al.[17], the validity of the Actigraph was assessed based on a variety of activities including overland walking as well as various household and recreational activities. When only the overland walking was included, the correlation with EE in METs based on indirect calorimetry was r = 0.77. However, when additional indoor and outdoor activities were included, the correlation dropped to r = 0.59. This was due primarily to the static nature of the non-walking activities.

The same effect was also seen in an analysis by Welk et al..[18] When the Actigraph was compared with oxygen uptake (VO_2) during laboratory-based treadmill exercise, the correlation was fairly strong (r = 0.85), but when lifestyle activities such as sweeping, vacuuming and shoveling were added, the correlation dropped to r = 0.48.

The impact that different types of activities can have on the estimated correlations is demonstrated in figure 1.1.[19] When only dynamic or sedentary activities are included in the model, the resulting predicted MET values for a given Actigraph count are indicated by the solid red line. The associated correlation coefficient is r = 0.92, indicating a close correspondence between predicted and actual energy expenditure for dynamic activities. However, when the static lifestyle activities, which require a significant amount of energy expenditure but record low Actigraph counts, are added to the analysis, the resulting predicted MET values now have a much lower correlation coefficient of r = 0.45 (indicated by the dashed black line). So, depending on which types of activities are intended to be captured by the Actigraph, the correlations with their true EE may vary greatly. This then would influence the ability to estimate the EE of individuals or groups using accelerometer data.

Figure 1. 1. Predicted Regression Equations – with and without Static Activities



Modified from 'Calibration of Accelerometer for Adults', Matthews, 2005

1.4.2.3. Predictions Equations

Prediction equations attempt to translate counts from an accelerometer into an estimated measure of EE, and then these estimates can be converted into estimates of MET levels. Typically, moderate PA is defined as 3.0-6.0 METs, and vigorous PA is greater than 6.0.[19] Actigraph count thresholds can be determined in order to classify activity periods as above or below the moderate or vigorous EE. Thus far, the equations developed for adults have had widely varying results, especially for the moderate activity cut-points.

In a review paper concerning the calibration of accelerometers for adults, several studies used walking and running as calibration activities. [19] These provided fairly consistent moderate activity cut-points ranging from 1,952 to 2,743 counts. When two other studies[17, 20] used only walking and mixed dynamic-static activities for calibration, however, the moderate cut-points fell to 574 and 191.

The reason for this can again be seen in Figure 1.1. When static lifestyle activities are included in the model (which, again, record very low counts), the intercept for the prediction equation is pulled very high. This would indicate that counts very near zero actually reflect moderate levels of EE. But this is just an averaging effect, between low counts that are truly sedentary, and low counts that reflect moderate or vigorous exertion.

The final choice of cut-point can be based on considerations of sensitivity and specificity. Using a low cut-point for moderate PA, for example, increases sensitivity, ensuring that the majority of moderate PA is classified as such. However, many periods of sedentary activity will be misclassified. Conversely, a high cut-point will ensure that the majority of activity classified as moderately active will truly be so, but will miss many periods of moderate activity with low counts. Thus, the choice of a cut-point can influence the interpretation of one's research findings.

1.4.2.4. Data reduction using an accelerometer

Due to the vast amount of information collected by an accelerometer over the course of a week, it is clearly necessary to summarize the data in some way. Based on a review by Masse et. al. [21] of previously employed data reduction techniques., there are five major considerations for summarizing the data.

The first consideration is identifying a wearing period. This is done by determining if the chosen epoch periods contain consecutive zero counts for some specified period of time. Previous research has used time periods ranging from 10 to 60 minutes. If the period is determined to be a non-wearing period, this data is considered missing.

The next issue is identifying minimal wearing requirements for a day. Based on whether or not a period is considered a wearing period, previous studies have required anywhere from 1 to 16.67 hours of valid wear time in order to count a day as a valid wearing day. If not, the day is discarded.

Third is to identify spurious data, which occur when the accelerometers record inappropriate values, either due to technical issues or operator error such as dropping the device on a hard surface. Researchers have used maximum cut-points, such as any value above 20,000 or any consecutive series of identical count values greater than 0 for 10 minutes, in order to classify invalid data. Such data is also considered missing.

The final two considerations concern how to compute outcome variables such as counts per minute/counts per day, or bouts of activity, such as a bout of MVPA. Mean counts per minute will differ, for example, if the protocol indicates that the monitor should be worn for 24 hours/day compared to protocols that only indicate that the Actigraph should be worn during waking hours. Comparisons between studies will need to consider how the summary outcome variables were derived.

Measuring total minutes of MVPA requires using previously defined calibration cut-points to determine if an epoch is above the moderate threshold; additionally, since the recommendations call for bouts of MVPA of 8-10 minutes, some studies have chosen to only count time in MVPA if it is part a bout of MVPA lasting 10 minutes or more. Given that there are likely to be short lapses in the intensity of activity, even in the course of an overall highly vigorous period of activity, most studies requiring bouts of MVPA have allowed from 1 to 2 minutes of the total 10 minutes to drop below the MVPA cut-point to still classify a 10 minute period as bout.

Obviously, all of these issues can create differences in the final variables. Masse et. al.[21] tested four different data reduction techniques and found statistically significant differences between their total wearing time, average counts per minute and per day, average minutes in MVPA, and average bouts of MVPA per day.

1.4.2.5. Imputation of missing data

The NHANES protocol asked participants in the accelerometry portion of the survey to wear the monitor for a seven day period during their normal waking hours, except when engaging in water activities. However, consistently remembering to wear the monitor over such an extended period of time may be difficult even for the most diligent. When the monitor is not worn, the sensors will continue recording zero counts, indicating no activity. If it could be assumed that there is nothing different between those who forget to wear the monitor and those who didn't, and that at least some minutes of MVPA were being accumulated during these non-wearing, active periods, then a calculation of their total minutes of MVPA will be lower, on average, than for those who wore it during their entire waking hours.

Different methods have been suggested for dealing with this issue. The first is to create a minimum time in the course of a day that a participant must wear the monitor (and thus record non-zero counts) in order for the day to be considered a valid day for analysis. As mentioned previously, the required wear time has ranged from 1 to 16.67 hours. The problems with excluding the days that do not meet the criteria are that there will still likely be a large range of valid wear time above the cut-point and that there may be bias due to the differences between wear days and non-wear days. Additionally, a significant amount of information is lost in the analysis if days are simply discarded.

In order to better handle missing data, some researchers have suggested imputing the minutes of MVPA for invalid days.[22] This procedure uses information from the participant's other valid days, as well as the correlations between the minutes of MVPA between the different days of week from the overall study population, to assign an expected value for that day's MVPA. In a paper by Catellier et. al.[22], this method, at least among middle-school girls, provided estimates that were less biased than using only valid days, while at the same time producing more precise estimates.

1.4.2.6. Age specific considerations for accelerometry calibrations for adolescents and adults

Research using accelerometry typically separates adults and adolescents. There are many reasons for this, but the most practical consideration is that the calibration of the accelerometers simply differs between adults and adolescents. The prediction equations that have been developed thus far for adolescents vary as widely as previously mentioned for adults and the cut-points for various activity levels span similar ranges; nevertheless, physiological and biomechanical differences in the age groups makes using similar cut-points inappropriate.

A fundamental reason for this is that adults have a lower average resting metabolic rate (RMR) of 3.5 $ml*Kg^{-1}*min^{-1}$, than children. In contrast, children have a higher average resting metabolic rate. In a review article by Freedson et al.[23], RMRs for children were based on 1 MET = 3.8 $ml*Kg^{-1}*min^{-1}$ in order to determine predicted counts. Using one age group's RMR to assign MET levels for the other age group would lead to a systematic error in the prediction equations. A similar concern is that energy expenditure from activity, measured per kilogram of body mass, decreases as children age, leading to an analogous bias. A final concern is that the sensitivity of the accelerometer counts is affected by stride length and frequency leading to lower monitor counts at a similar speed when the step frequency is higher.

In order to account for these differences, EE prediction equations for adolescents have included additional information such as age in years or weight in kilograms. For example, Eston et al.[24] scaled the oxygen uptake per $kg^{0.75}$ so that the EE among children age 8.2-10.8 was measured in $mL*Kg^{-0.75}*min^{-1}$. Using the mean body weight of 29.8 kg, the Actigraph cut-point count for moderate activity (MET = 3) was 500. Two other studies by Treuth et al.[25] and Puyau et al.[26] found very different moderate activity cut-points of 3,000 and 3,200, respectively. These differences may be explained by the differences in the age ranges, the types of activities that the participants were asked to perform in each study, or the methods for measuring energy expenditure.[23]

Due to these concerns of non-comparability, the use of the same calibration equation for adults and adolescents has thus far been avoided in modern PA research.

1.5. Physical Activity (PA) and Health

The last several decades have produced a substantial body of literature indicating the health benefits of PA, including reduced risk of all-cause mortality, CHD and CHD risk factors. Many of the reviews also separate their assessments into primary, secondary and tertiary prevention of disease outcomes. The importance of this distinction lies in the fact that PA has been shown to have both a preventive as well as a palliative effect on disease and disease progression. The importance of these findings led the US Surgeon General to produce the 1996 report on physical activity, highlighting the benefits along with providing recommendations. Nevertheless, the rates of PA in the US continue to decline as work and daily activities become more and more sedentary.[7, 8]

1.5.1. PA's association with disease specific outcomes related to the Metabolic Syndrome

The physiological issues surrounding the Metabolic Syndrome were first articulated by Reaven in 1988 as a complex set of inter-related factors that typically cluster together and significantly increase the risk of CHD, a condition he called Syndrome X.[25] The factors he identified at the time included dyslipidemia, hypertension, hyperglycemia. He and others postulated that the underlying disorder linking the conditions was insulin resistance (the condition is sometimes referred to as *insulin resistance syndrome*). [26]

The National Cholesterol Education Program's (NCEP) Adult Treatment Panel III report (ATP III) in 2002 included 6 different components which comprise the metabolic syndrome.[27] The first component is obesity, and particularly abdominal obesity which is most closely associated with the metabolic syndrome. The second component is atherogenic dyslipidemia, which the ATP III defines as high triglyceride levels and low levels of high-density lipoproteins. Elevated blood pressure is the third component, commonly associated with insulin resistance. Insulin resistance itself is considered a fourth component of the Metabolic Syndrome. A proinflammatory state, indicated by elevated levels of C-reactive protein, is also common among those with Metabolic syndrome, possibly due to the co-occurrence of obesity and excess adipose tissue which releases inflammatory cytokines, thus raising the C-reactive protein levels. The final component of the Metabolic syndrome is a prothrombotic state, due to increased plasma plasminogen activator inhibitor-1 and fibrinogen.

While the NCEP executive summary in 2001 considered the control of low-density lipoproteins (LDL) as the primary goal of clinical treatment for dyslipidemia due to its' strong associations with CHD, they emphasized the importance of a secondary goal of treating the Metabolic Syndrome to reduce the risk of CHD.[28] In this summary, they described the clinical assessment of the Metabolic Syndrome as comprising at least three of the following:

Waist circumference in men of > 102 cm (>40 in), and in women > 88 cm (35 in)
Triglycerides of ≥ 150 mg/dl
High-density lipoprotein of < 40 mg/dl in men, and < 50 mg/dl in women
Blood pressure of ≥ 130/ ≥ 85 mm Hg
Fasting glucose of ≥ 110 mg/dl

And importantly for this proposal, the 2002 report by the NCEP indicated that the first strategy for the treatment of the Metabolic Syndrome is the modification of its' root causes, those being overweight/obesity and physical inactivity.[27]

Congruent with this last statement, the reviews and position papers related to disease specific associations with physical activity provide convincing evidence to support the position that positive associations exist between a lack of PA and hypertension, diabetes, obesity, triglycerides and high-density lipoproteins, all of which are components of the clinical definition of the metabolic syndrome.

Nevertheless, all of the review papers also indicate caution regarding these findings due to the difficultly of drawing summary conclusions given the diversity of study designs, study sizes, and definitions of the respective outcomes and of what constitutes PA.

1.5.1.1. Physical Activity and Hypertension

1.5.1.1.1. Biological Plausibility

The mechanisms by which PA affects blood pressure are complicated, but a basic description of these factors will be provided here.

Blood pressure is directly proportional to total cardiac output and total peripheral resistance to this output.[29] This has an intuitive interpretation, in that blood pressure depends on the volume of blood in the circulatory system, the rate at which this blood is flowing, and the diameter of the vessels through which it is flowing. Thus, blood pressure may be elevated by either increasing the volume of blood in the system, increasing the flow rate or by constricting the blood vessels.

The primary way that PA is believed to lower blood pressure is through activity of the autonomic nervous system. When norepinephrine, a neurotransmitter released by sympathetic nerves, along with the hormone epinephrine, bind with adrenergic receptors of the heart, both the pulse rate and the force of contraction are increased. In addition, when they bind with smooth muscle cells of the blood vessels, the diameter of the vessels constrict.[29] In a study by Cleroux et. al., among mild hypertensives who exercised for 30 minutes at an intensity of 50% of VO_2max, blood plasma has been shown to experience a 20% reduction in norepinephrine, leading to period of hypotension lasting up to 90 minutes post-exercise.[30] Many other studies have indicated a similar reduction in norepinephrine in blood plasma after bouts of exercise. Due to the activity of norepinephrine on the circulatory system, this reduction leads to a decrease in both flow rate and TPR, which will tend to lower blood pressure all other things being equal.

Another mechanism by which PA is believed to reduce blood pressure is through weight loss and increased insulin sensitivity. Those who experience weight loss also typically experience increased insulin sensitivity along with a corresponding decrease in plasma insulin levels. High levels of plasma insulin has been hypothesized to promote sodium reabsorption by the kidneys which leads to increased plasma volume.[6] Consistent with this theory, blood pressure and plasma insulin concentrations have been shown to be directly proportional.[29] Thus, this mechanism by which PA lowers blood pressure appears to be mediated by the affect of PA on plasma insulin, which then leads to changes in blood pressure.

Interestingly, changes in cardiac output, and thus blood pressure, do not appear to be affected by PA. While PA does appear to lower the resting heart rate, the stroke volume also increases due to increased venous return to the heart, thereby leaving total cardiac output unchanged.[29]

1.5.1.1.2. Epidemiological Evidence

The 1996 NIH consensus statement on PA and cardivascular health states "Most studies of endurance exercise training of individuals with normal blood pressure and those with hypertension have shown decreases in systolic and diastolic blood pressure."[31] The Surgeon General's report also states that prospective observational studies as wells as several randomized controlled trials (RCTs) confirm that both higher PA and cardiorespiratory fitness are associated with decreased blood pressure.

Two later review articles provided quantitative summaries of the literature. In a review of 44 RCTs, Grundy et. al.[32] reported a 3.4 mm Hg and 2.4 mm Hg reduction in systolic and diastolic blood pressure, respectively, from PA. Among hypertensives, this effect was more pronounced (7.4 / 5.8 mm Hg reduction), while normotensives showed lesser improvement (2.6 / 1.8 mm Hg reduction). In a separate meta-analysis by Whelton et. al. of 53 RCTs, they indicate slightly larger improvement overall (3.8 / 2.6 mm Hg reduction). Among studies that separated results by hypertensive status, Whelton also found differences in improvement, with hypertensive blood pressure dropping 4.9 / 3.7 mm Hg and normotensive blood pressure only falling 4.0 / 2.3 mm Hg.[33]

1.5.1.2. Physical Activity and Diabetes

1.5.1.2.1. Biological Plausability

While diabetes can affect individuals in different ways, the commonality between clinical symptoms is an elevated level of blood glucose along with other related metabolic disorders.[6] The two main types of diabetes are Type 1 diabetes, or insulin-dependent diabetes, and Type 2 diabetes, or non-insulin-dependent diabetes. Insulin is responsible for the regulation of blood glucose levels as well as the transport of glucose from the blood into the cells for use as energy. In Type 1 diabetes, the pancreas produces an insufficient amount of insulin, thought to be caused by an auto-immune response. Without a sufficient level of insulin due the insufficient production by the pancreas, glucose lingers in the blood leading to hyperglycemia. Prolonged hyperglycemia eventually leads to ketosis, an acidotic condition that, over time, causes damage to the small blood vessels and nerves. This explains the common clinical symptoms of diabetes related to neuropathy, retinopathy, and poor circulation to the extremities. Only about 20% of diabetes cases in the United States are of the Type 1 form.[29]

Type 2 diabetes is caused by two concurrent conditions: 1) a peripheral insulin resistance, meaning that the body has developed an insensitivity to circulating insulin, primarily in the skeletal muscles, and 2) an insulin-secretory defect, such that the body is unable to increase the beta-cell production of insulin. The two factors together again lead to hyperglycemia and ketosis.[34] Type 2 diabetes is far more common than Type 1 diabetes and, because many of the causes are related to lifestyle, Type 2 diabetes is more likely to be affected by PA levels.

PA is hypothesized to reduce the risk of diabetes through several synergistic mechanisms. First, PA increases the blood flow into the skeletal muscles, which enhances the transport of glucose into the muscle cells. This increased glucose transport appears to be due to increased insulin sensitivity, and this effect has been shown to persist for up to 24 hours or more after a prolonged bout of exercise while glycogen levels are being replenished in the cells. Studies suggest that improvements in glucose tolerance due to PA are more effective when the impairment is due to reduced insulin sensitivity than when the impairment is due to insufficient amounts of circulating insulin.

An additional mechanism through which PA is believed to improve insulin sensitivity is through weight loss, and specifically intra-abdominal weight loss. Excess fat mass, and particularly intra-abdominal fat, is a known risk factor for insulin resistance, and roughly 80% of Type 2 diabetes cases occur among the obese.[29] So, again, this mechanism through which PA decreases the risk of diabetes appears to be mediated by the effect of PA on reducing total fat mass, and thus increasing insulin sensitivity.

1.5.1.2.2. Epidemiological Evidence

According to a joint statement by the American Diabetes Association (ADA) and the American College of Sports Medicine (ACSM), exercise has been found to be effective and appropriate for both pre-diabetics as well as for those with Type I or II diabetes. "Several long term studies have demonstrated a consistent beneficial effect of regular exercise training on carbohydrate metabolism and insulin sensitivity which can be maintained for at least five years."[35] A later consensus paper in 2006 by the ADA which focused only on type 2 diabetes, stated "there is firm and consistent evidence that programs of increased physical activity and modest weight loss reduce the incidence of type 2 diabetes in individuals with Impaired Glucose Tolerance (IGT)."[36]

A representative example of the longitudinal studies comes from the Finnish Diabetes Prevention Study. Five hundred and twenty-two overweight subjects, aged 40-65, with impaired glucose tolerance (IGT) were randomized to a control or intervention group, the latter of which consisted of moderate exercise for at least 30 minutes per day, along with losing at least 5 percent of body weight, limiting saturated and total fat to 10 and 30 percent of total energy consumed, respectively, and increasing fiber intake to at least 15g per 1000 kcals. The follow-up time period averaged 3.2 years. Cumulative incidence of type 2 diabetes was 11% in the intervention group, while 23% in the control group, or a 58% reduction in the risk of diabetes.[40]

1.5.1.3. Physical Activity and Obesity

1.5.1.3.1. Biological Plausibility

Obesity occurs when energy intake exceeds energy expenditure over a prolonged period of time. Three sources account for total energy expenditure: 1) the resting metabolic rate, 2) the thermic effect of food, and 3) non-resting energy expenditure such as PA. Among those who are at risk for or who are already obese, increasing the non-resting energy expenditure can favorably shift the balance of energy toward weight maintenance or weight loss. It also does not appear that increasing PA leads to a compensatory increase in energy intake.[6]

Several additional factors aid in weight loss beyond just the additional energy expended during a bout of PA. After a bout, the resting metabolic rate may remain elevated for up to 24 hours, depending on the intensity and duration of the bout.[29] Also, increasing PA appears to reduce the decline in the resting energy expenditure that accompanies weight loss by preserving lean muscle mass. This is in contrast to the effects of caloric restriction through dieting.[6] Finally, because resistance training produces larger increases in fat-free mass than aerobic exercise, resistance training has been shown to be more effective in raising the resting metabolic rate, which may provide additional benefits in terms of weight loss or weight maintenance.

1.5.1.3.2. Epidemiological Evidence

Two lines of argument are often provided for why the current obesity epidemic is likely due to an insufficient amount of energy expenditure, and specifically physical activity. First, several national surveys indicate that total energy intake has only very modestly increased or decreased in the last decades during a time when obesity increased. The other argument is that, while twin and family studies have indicated that the inheritability of body fatness accounts for between 25%-70% of the overall variation in body fatness, and even though there is a significant amount of variation in individual resting metabolic rate (RMR), it is unlikely that there has been such a dramatic change in the genetic profile of western populations which could account for the steep rise in obesity during the last 50 years.[37]

Given this, a significant amount of research has focused on how a sedentary lifestyle contributes to obesity and whether moderate physical activity can prevent or reduce obesity. In a review in a 1999 supplement of Medicine and Science in Sports and Exercise (MSSE) dedicated entirely to issues of obesity, Dipietro et al. [38] concluded that PA can positively affect body composition by promoting fat loss while maintaining lean mass; in addition, the frequency and duration of PA is directly associated with weight loss, even if the rate of weight loss is relatively slow. Another review article in the same supplement summarized the results of eight prospective studies of the effects of sedentary behavior on obesity and, although the analyses were highly variable, most studies showed a link between sedentary behavior and the risk of obesity.[39]

1.5.1.4. Physical Activity and Cholesterol

1.5.1.4.1. Biological Plausability

Only the mechanisms involved in the decrease of triglycerides and the increase in high-density lipoproteins (HDL) will be discussed here as only these two types of cholesterol have been consistently shown to be affected by PA.

Triglycerides are the primary form of fat in the body. During exercise, triglycerides are hydrolyzed by lipoprotein lipase (LPL) into glycerol and fatty acids which are used as energy for muscle contractions. LPL activity has been shown to increase during bouts of PA, and increased activity may last for up to 48 hours after acute endurance exercise.[29] This is the primary mechanism by which PA is believed to reduce levels of triglycerides.

Several mechanisms are believed to be involved in the increase of HDL due to PA. First, PA has been shown to increase the activity of an enzyme called lecithin-cholesterol acyltransferase (LCAT). This enzyme is responsible for transporting free fatty-acids as well as the esterification of cholesterol to produce HDL2, a form of HDL.[29] Because only the activity, and not the levels, of LCAT have been demonstrated following bouts of PA, it is not known whether the increase in LCAT activity is due to PA itself, or whether the increased activity is simply due to increased LPL activity which provides additional fatty acids upon which the LCAT can act.

Another mechanism thought to increase the levels of HDL is the decrease in the activity of hepatic lipase following PA. Hepatic lipase is an enzyme found in the liver responsible for HDL2 catabolism. By reducing the activity of this enzyme through bouts of PA, less HDL2 is catabolized, thus leaving more HDL in the blood.[29]

Other mechanisms are believed to be involved in the increase of HDL after PA, but a complete understanding of the biological mechanism are as yet not fully understood.

1.5.1.5. Epidemiological Evidence

The epidemiological evidence that physical activity can lead to pronounced improvements in CHD risk has become quite clear; however, the study of dyslipidemia as a risk factor for CHD and its' association with PA has been less frequent and has lead to less consistent results. The literature, though, does support that PA can improve certain aspects of lipoprotein profiles, specifically HDL and triglycerides.

A dose-response relationship has been shown between an increasing intensity and frequency of PA and an increasing level of HDL as well as a decreasing level of triglycerides.[40] However, in a review by an independent panel for the ACSM of 11 randomized controlled trials, this effect may occur only with the concurrent weight loss of at least 2.5 kg among overweight men and women, and with a weight loss of 4.5 kg among normal weight men and post-menopausal women. PA has not been shown to affect low-density lipoprotein (LDL) levels, high levels of which, at least in overweight individuals, appear to be more associated with dietary intake of cholesterol and saturated/trans fatty acids.[32]

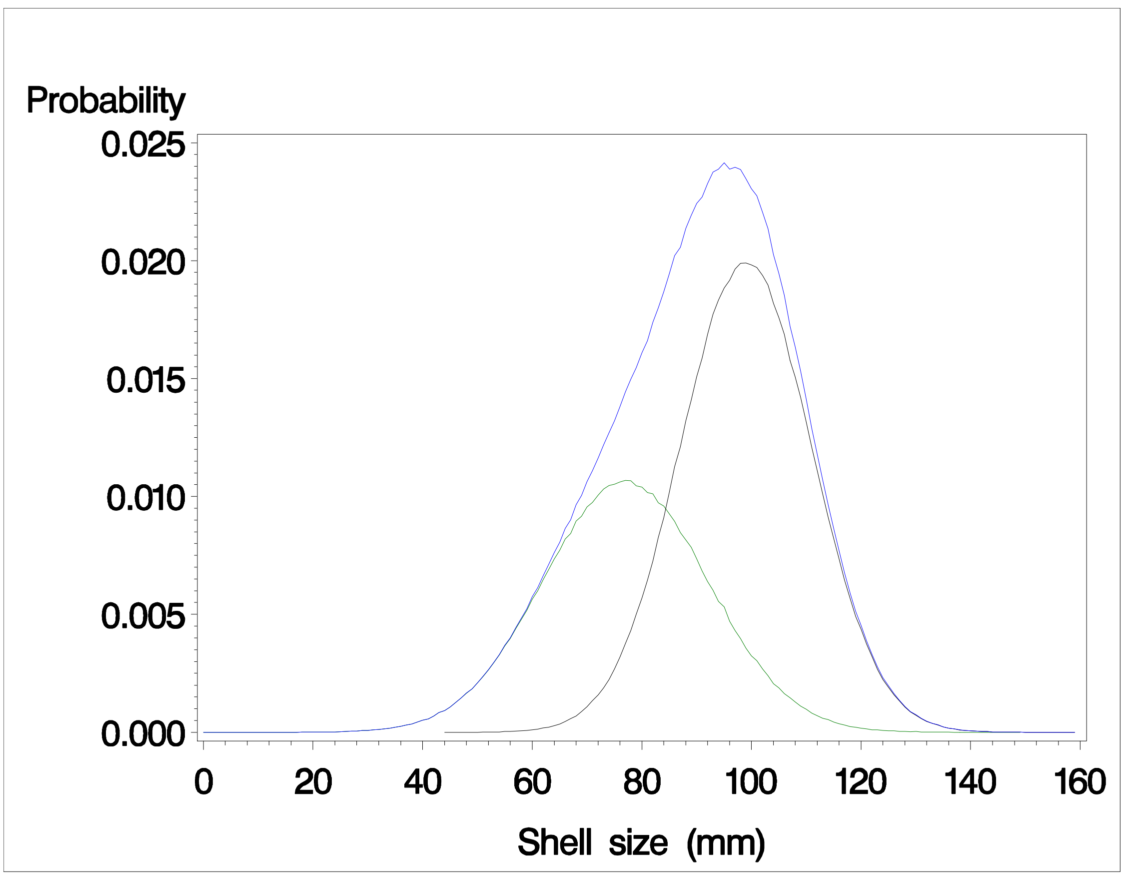
1.6. Conceptualizing Growth Mixture Models

The first use of a simple mixture model dates back to 1894 when Pearson was approached with a mathematical challenge that had thus far proved too difficult to answer.[41] The question revolved around the nature of the distribution of crab shell sizes, which was bell shaped but skewed to the left. The theory to be tested was whether this long tail was actually the result of the mixing of two separating species of crabs, one growing larger and the other smaller, each with a different mean size and variance. If it were assumed that there were actually two groups, then the question was what two underlying normal distributions best fit the observed distribution.

The theoretical mixture distribution is demonstrated in Figure 1. 2. Pearson was able to fit the non-normality of the overall distribution very closely with two normal distributions, each with a different mixture of population percent, variance, and mean – hence the name.

Later, a debate arose in the 1950's about the nature of the distribution of blood pressure, which is skewed to the right with a very long tail.[41] Some believed that there was a recessive gene for high blood pressure, leading to a mixture of people, one group in the lower, normal range with a high degree of variation, and another, smaller group of genetically predisposed individuals who make up a significant portion of those in the higher levels.

Figure 1. 2. Mixture model of crab shell sizes with two underlying normal distributions



More recently, the social sciences have explored the uses of mixture models with an interest in following groups of individuals' changes over time or developmental periods.

This has led to a rapid increase in statistical tools for this purpose, one of which is the intended analytical tool for the current project – Growth Mixture Modeling.

This technique extends the mixture model concept, but adds the possibility of finding underlying normal distributions from continuous data collected at several different points in time. This theoretical model is demonstrated in Figure 1. 3 and Figure 1. 4. These graphs represent the hypothetical distributions of accumulated minutes of moderate to vigorous PA for, in this case, three distinct groups (or classes) with measurements recorded over a three day period (Monday through Wednesday). In Figure 1. 3, only the overall, observed distribution of values are presented. Notice that the distributions are irregular and non-normally distributed. Figure 1. 4 presents the same distribution, but overlaid in the graph are the three underlying distributions in each of the three days. Membership is consistent over the three days in each of the red, green and blue groups. The task of Growth Mixture Modeling is to find these three groups when they are unknown to us. By using iterative techniques, a maximum-likelihood estimate is used in order to classify participants into the underlying distributions.

Previous studies have used a wide variety of other outcomes to develop their classes. One study looked at the average number of beers drunk per week by college freshman over the course of an academic year. Students were then placed into several classes, such as early academic year drinkers, late academic year drinkers, light drinkers but heavy on holidays, non-drinkers, and continuous binge drinkers.[42] Another study looked at the frequency of bed wetting during the developmental years from age 4 to 15. The classes reported included transient, relapsing, persistent, chronic and normal bed-wetters over the 12 year period.[43]

Figure 1. 3.   Hypothetical Distribution of Minutes of MVPA per Day

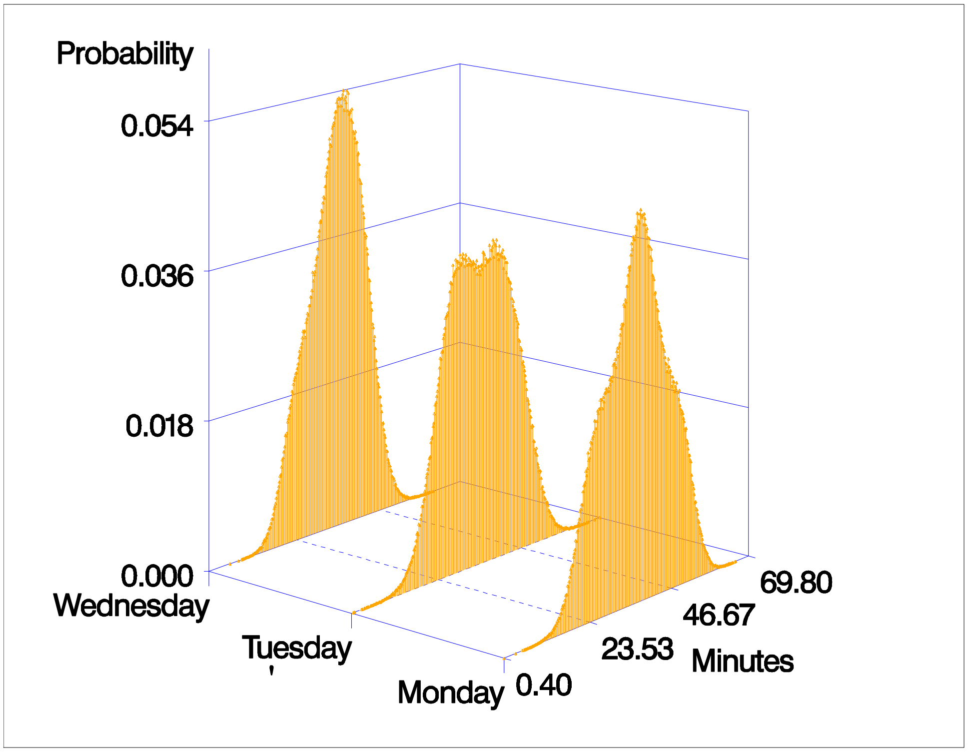
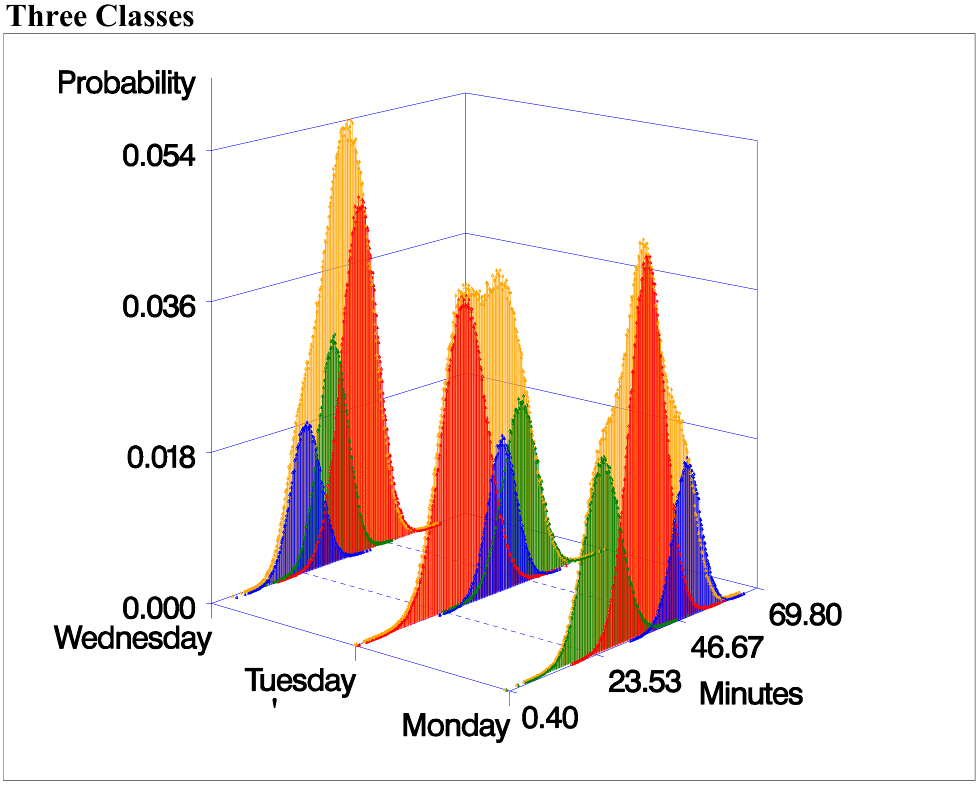


Figure 1. 4. Underlying Normal Distributions - Minutes of MVPA per Day with Three Classes



Using the NHANES data, we intend to classify each person according to their total minutes of moderate-to-vigorous physical activity (MVPA) on each of the seven days in a week. Growth Mixture Modeling will then attempt to determine if there exist groups, or classes, of people who tend to accumulate their minutes in a similar pattern over the seven days. For example, one group may have a very low mean number of minutes from Monday to Friday, with a high average number of minutes on Saturday, and then a slightly lower, but still high, average minutes of MVPA on Sunday. Another group, possibly active workers, will have a large mean number of minutes during the work week but very low mean minutes on the weekend.

1.6.1. Testing the Mixture Model with M-Plus

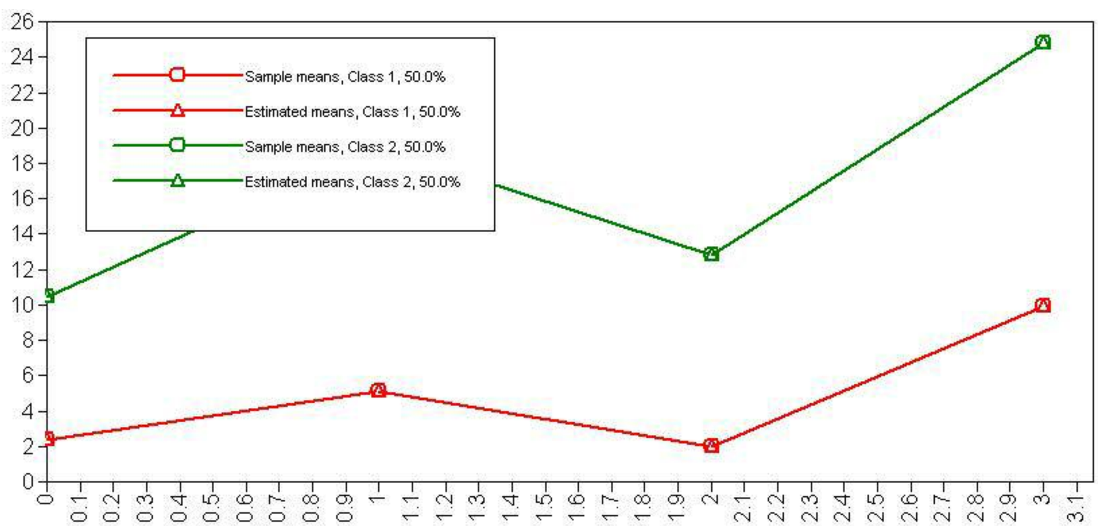
In order to test whether unique underlying classes can be discovered with the mixture model analytical technique, a hypothetical dataset was created with longitudinal data collected over, in this hypothetical case, a four day period. For simplicity, only two classes were created with 100 observations in each class for each day. The two classes were created with very different mean minutes of MVPA, hopefully allowing M-plus to successfully classify all 100 observations of each group into its' correct class. The means for each day in each class are shown in Table 1. 1.

Table 1. 1. Means for the Two Classes over the four days

	Mean Minutes of MVPA for Class 1 (N = 100)	Mean Minutes of MVPA for Class 2 (N = 100)
Day 1	2.34	10.47
Day 2	5.12	18.95
Day 3	1.96	12.83
Day 4	9.88	24.77

When M-plus analyzes the data, no indication of the classes is provided, only the minutes of MVPA per person per day. A priori, the number of desired classes is provided to M-plus, in this case two. Mixture modeling then finds the best fit to this number of classes, and performs a statistical test of whether one less class would have been sufficient. Results of the M-plus analysis for two classes are presented in Figure 1. 5. The estimated means match the true means presented in Table 1. 1. The percentages listed in the graph represent the proportion of the total population in the given class. The statistical test for whether one fewer classes would have been sufficient was significant at the <0.001 level, indicating that two classes helps explain a significant portion of the variation compared to only one class.

Figure 1. 5. Results of the M-Plus analysis with two classes



Additional results from M-Plus are presented in Figure 1. 6 and Figure 1. 7 below, each representing a separate plot for each class. In Figure 1.6, the plot of the class with the higher mean number of minutes of MVPA is shown with each individual’s minutes of MVPA over-layed. Figure 1. 7 represents the same information for the class with the lower mean minutes of MVPA. These plots help visualize how much variation exists around each specified class.

Figure 1. 6. Observed values for each observation in underlying Class 1, distributed around the mean for each day

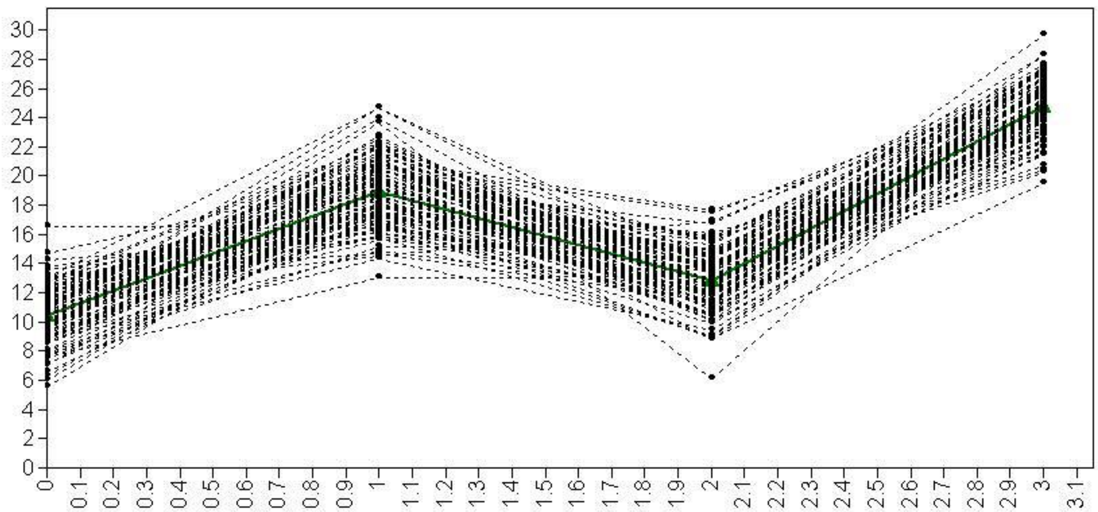
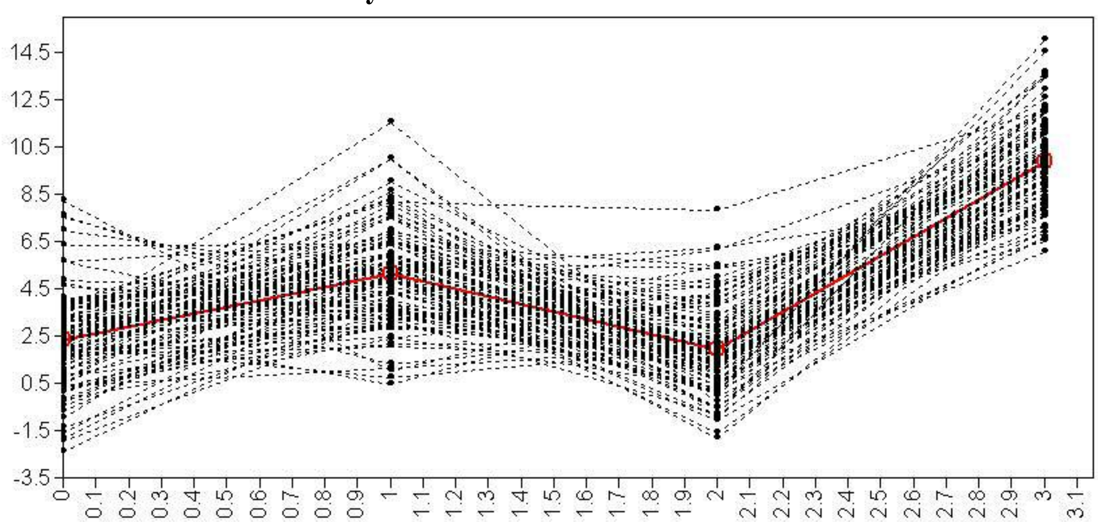


Figure 1. 7. Observed values for each observation in underlying Class 2, distributed around the mean for each day



1.7. Analytical considerations for cross-sectional data

The NHANES data represent a cross-sectional sample of over 10,000 participants. The primary concern with this type of analysis is that, without knowing the temporal sequence of the exposures and outcomes, it is possible to make inaccurate inferences and misconstrue the meaning of significant associations. This, however, should not limit the importance of the proposed work.

First, we do not intend to infer causation with this analysis. Associations between classes of PA and health outcomes will be investigated without drawing any conclusions with regards to their temporal sequence. Given this caveat, cross-sectional studies are considered a valid tool for developing hypotheses, even if inappropriate for testing hypotheses. Since growth mixture modeling has never been used before with physical activity data, our analysis is, by nature, exploratory. Therefore, the NHANES data represent the ideal dataset with which to conduct this analysis. It is a very large dataset which has already been collected, the sampling methodology is sound and will provide national estimates, and there is a fair amount of covariate information collected as part of the primary NHANES survey. If findings from this study generate enough interest, future studies with longitudinal designs may build on this research to help clarify any of the observed associations.

Secondly, NHANES has a long history of influencing additional research leading to significant public health findings. For example, results from the first NHANES survey in the 1960's alerted researchers to the possible connection between high levels of cholesterol and risk of heart disease.[44] Later longitudinal research, such as the very influential Lipids Research Clinics (LRC) series of studies begun in 1971, confirmed this association.

Given the previous considerations, the NHANES data should provide an excellent resource to achieve the stated research goals.

1.8. Conclusion

The health surveillance mechanisms that have been in place over the last several decades, including the NHANES and the BRFSS surveillance systems, helped detect and characterize the growing obesity epidemic as well as the extent to which inactivity has become commonplace. These findings led to a significant amount of research into how much PA is necessary to achieve positive health benefits, and ultimately to the issuing of numerous PA recommendations. Concurrently, a large body or research investigated what characteristics are associated with PA.

However, the majority of the studies of the health benefits of PA were based on self-report and tended to aggregate PA into average kilocalories per day or per week. In terms of the FITT model for PA assessment, the sub-components of Frequency and Time were combined in this overall summary of total kilocalories. This was an effective strategy for determining how much PA, on average, was necessary for health benefits. However, determining the effects of different patterns of Frequency of PA and Time engaged in PA might also be important in establishing appropriate PA recommendations.

To our knowledge, only one recent study has so far attempted to distinguish whether different patterns of PA accumulation affect mortality risk.[45] In this study, four groups were compared: those who accumulated less than 500 kcal/week ("sedentary"), those with 500-99 kcal/week ("insufficiently active"), those who accumulated ≥1000 kcal/week in 1 or 2 days (“weekend warrior”), and those who accumulated ≥1000 kcal/week in any other way (“regularly active”). This study found that, among low risk men, the risk of mortality for the “weekend warriors” was even lower than for those who were “regularly active” (Relative Risk of 0.41 for “weekend warriors” and 0.58 for “regularly active”, compared to “sedentary”). Among high risk men, the “weekend warrior” group showed no improvement over the “sedentary” group, whereas the “regularly active” still showed a lowered relative risk of mortality (RR of 1.02 for “weekend warriors” and 0.61 for “regularly active”, compared to “sedentary”).

By establishing activity classes in the NHANES sample using the Growth Mixture Model, the question of whether different classes lead to better health profiles can be similarly addressed. While the recommendations call for 30 minutes of MVPA on most, and preferably, all days of the week, it may be that accumulating all of these minutes during shorter periods of time, for example on only non-work days, lead to similar benefits as more regular PA. A finding such as this may then encourage those who can’t find time for PA otherwise to find time on free days. It is this issue that will be explored in the current proposal, as well as what characteristics are associated with the given classes.

Chapter Two

Statement of the Problem and Specific Aims

Physical activity (PA) has been recognized throughout history as an important part of a healthy lifestyle[46], and recent research has shown that adequate PA can help reduce the risk of cardiovascular disease[6], osteoporosis[51], high blood pressure[33], as well as diabetes[49]. Nevertheless, modern society and technology have made it possible for a large portion of the population, at least in the developed world, to greatly reduce their physical activity to minimal levels. As the Centers for Disease Control and Prevention reported, "in 2003, the majority (54.1%) of US adults did not engage in physical activity at the minimum recommended level."[7]

Concurrently, during the last several decades we have witnessed a large increase in obesity in the United States (US). In 2004, The National Center for Health Statistics (NCHS) reported that 17.1% of adolescents were overweight (as defined by $\geq 95^{th}$ percentile of the sex-specific body mass index or BMI for age growth charts) and 32.2% of adults were obese (as defined by a BMI ≥ 30 kg/m^2). Extreme obesity (BMI ≥ 40 kg/m^2), which in 1990 only affected 0.5% of men and 1.2% of women, presently affects 2.8% of men and 6.9% of women.[2, 47] Several recent studies have shown that weight gain leading to obesity is strongly associated with sedentary behavior, and weight loss or weight maintenance is associated with being physically active and fit.[48, 49]

Participation rates in PA vary greatly across different socio-demographic groups. Females, African-Americans, Hispanics, older adults, as well as those with less education and income have been shown to engage in less leisure time PA.[10, 53] Several questions still remain about these socio-demographic correlates of PA. First, most studies use self-report which has been shown to over-report PA[12, 13]; in addition, inaccurate reporting may vary by demographic characteristics. Secondly, these cross-sectional associations do not indicate in what way PA is accumulated. Additionally, little research using objective measures of PA has been done to determine how the quantity and intensity of physical activity over time is distributed in the general population or in selected sub-populations. Finally, the associations between different patterns of PA and health outcomes are also not known. Determining how PA is accumulated during the course of a week and its association with health outcomes would help target interventions for those who do not achieve an adequate level of PA. For example, while the current recommendations are to be active at least 30 minutes on most, and preferably all days of the week[3], a large portion of the population has employment which requires them to be sedentary for the majority of the day throughout the week. This would potentially allow for greater time for activity during the weekend. If this pattern of physically activity is insufficient, then interventions incorporating activity during the typical work-week would be important. Conversely, it may be that a significant amount of vigorous PA only on the weekend is sufficient for desired health benefits. At present, this is not known.

Accelerometry has become an increasingly popular method to measure PA, primarily because these devices have been shown to be valid and reliable, acceptable for large studies and for all ages while providing specific information about activity over the entire course of a day for many days[50]. Because of these positive features, accelerometry was added to the 2003-2004 National Health and Nutrition Examination Survey's (NHANES) battery of assessments. These data now provide the first US sample of participants' physical activity with which to estimate the distribution of PA over time. The purpose of this study is to determine the level and patterns of PA in the US population, examine the socio-demographic characteristics associated with these patterns, and finally establish which combination of activity patterns are associated with positive profiles of biological markers of health.

The specific aims include:

Aim 1

Model patterns of PA and develop a set of descriptive classes, or activity groups, into which study participants fall based on their daily minutes of moderate-to-vigorous PA (MVPA) and vigorous PA (VPA) across a seven day week.

Hypothesis 1

Activity classes will consist of:

Class 1) Little MVPA/VPA during the week with more activity on the weekend,
Class 2) MVPA/VPA during the weekdays with additional PA on the weekends,
Class 3) MVPA/VPA during the weekdays with little activity on the weekends,
Class 4) Those with little MVPA/VPA on all days.

Aim 2

Determine the distribution of socio-demographic characteristics in each of the established activity classes, including race, gender, age, household income and education.

Hypothesis 2a

Women, African-Americans and those with less education are more highly associated with activity class 4 than males, non-African-Americans and those with more education, respectively.

Hypothesis 2b

Hispanics are more consistently associated with activity classes 2 and 3 due to the nature of work such as construction and agriculture.

Hypothesis 2c

Older age is associated with less active classes (classes 1 and 4).

Hypothesis 2d

Higher household income is more highly associated with classes 1 and 2 than lower household income.

Aim 3

Determine which classes and relevant socio-demographic characteristics are associated with positive health outcomes. Fasting glucose, blood pressure, high-density lipoprotien (HDL), triglycerides and BMI (all clinical components of the metabolic syndrome), as well as the metabolic syndrome itself, will be used as the relevant biological markers of health.

Hypothesis 3a

Higher overall activity is positively associated with all of the previously mentioned biological markers of health, i.e. lower blood pressure, fasting glucose, BMI, triglycerides, higher HDL, and a lower occurrence of the metabolic syndrome.

Hypothesis 3b

Certain patterns of PA are associated with positive profiles, regardless of overall activity.

These aims will be accomplished by using the accelerometry data from the 2003-2004 NHANES. This data source includes 10,122 participants, 7,176 of which wore an accelerometer over a seven day period. Activity classes will be established by using the recent advances in Latent Growth Curve Analysis (LGCA). To our knowledge this will be the first time that LGCA will be applied to this type of PA data. Such a large study size, randomly sampled from the entire non-institutionalized US population, provides an excellent data source with which to determine the classes of PA in the general US population.

Chapter Three

Methods

3.1. Data Source

The three aims of this proposal will be accomplished by analyzing data from the 2003-2004 data release from the National Health and Nutrition Examination Survey (NHANES). The survey consists of two principle components. The first is an interview, which includes a wide array of topics ranging from tobacco use, sexual behavior, weight history, health insurance and hospital utilization in addition to basic demographics. The second component is a physical examination, which also collects a wealth of information such as anthropometric measurements, blood pressure, audiometry, as well as various laboratory analyses ranging from measles, sexually transmitted diseases, blood lipids and glucose. In addition, in the most recent release of NHANES, seven consecutive days of accelerometry measurements were collected for participatants. Interviews are usually conducted in the participant's home while the physical examinations take place in mobile examination centers (MECs), which travel to the regions of the country where the interviews will take place. The target population is civilian, non-institutionalized US citizens randomly sampled from 15 US counties. NHANES 2003-2004 over-sampled certain populations, including low-income persons, Mexican-Americans, African-Americans, and those age 12-19 and 60 or over, in order to have a sufficient amount of data on these special populations. Each year, roughly 7,000 participants complete the interview portion of the survey, while only approximately 5,000 complete the physical examination.

3.1.1. Sampling procedures

NHANES is a multistage, stratified random sample of the civilian, noninstitutionalized U.S. population. Fifteen Primary Sampling Units (PSUs) are initially selected for visitation in the 12 month data collection period. The PSUs are either single counties or a small group of contiguous counties. Segments of the PSUs are then selected, which can be blocks or groups of blocks with clusters of households. Households within segments are selected for randomization, at which time a sample is randomly drawn. As mentioned previously, low-income persons, Mexican-Americans, African-Americans, and those age 12-19 and 60 or over were assigned a higher probability of selection. Finally, one or more participants within a household are selected based on an age, sex, and race/ethnicity screening criteria. On average, 1.6 participants are selected per household.

3.1.2. Analytical issues related to sampling

In order to achieve national estimates with appropriate variance estimation, it is necessary to use analytical techniques that incorporate multistage sampling. For analytic purposes, each of the previously mentioned 15 PSUs are grouped into strata, and each strata contains two PSUs. In addition, each participant is assigned a weight reflecting the number of people from the nation as a whole that this sampled person represents. The weight is based on the unequal probability of selection as well as non-response adjustment.

Software such as SUDAAN and SAS are both equipped to analyze sampled data. The stratas and PSUs represent the needed variance units, and along with the weights, either software package will arrive at national estimates with appropriate variances. Analysis for this proposal will use the SAS survey procedures. Below is a sample of the code for assessing the mean age (RIDAGEYR) of the NHANES population. The STRATUM line incorporates the strata variable, while the CLUSTER line uses the information for the PSUs. The WEIGHT line uses the weight for the entire 2 year interview. There is a separate weight for analyzing the examination data (**WTMEC2YR**), which had a smaller sample size. Additional weights are also provided for items that were only collected on a subset of the sampled population, such as for blood glucose levels.

Table 3. 1. Sample SAS Survey Procedure Code

```
PROC SURVEYMEANS DATA= DEMO_C;
STRATUM SDMVSTRA;
CLUSTER SDMVPSU;
WEIGHT WTINT2YR;
VAR RIDAGEYR;
RUN;
```

3.1.3. Re-weighting sample weights due to missing data

Using individual sample weights generates results that are generalizable to the entire US population as well as adjusts for any over- or under-sampling that may have occurred during the data collection phase. If, however, respondents did not answer certain questions or did not take part in the accelerometer portion of the examination, then these missing data will lead to estimates that no longer reflect a proper sample of the entire United States.

This problem can be dealt with by re-weighting the data to reflect non-response. When the original sample is drawn based on unequal probabilities of selection, then the weight for an individual is based on the inverse of the sampling probability, or $w_i = 1/p_i$, where w_i is the individual weight and p_i is the sampling probability. If r_i is the probability the subject I responded to a particular question, then the probability that a subject will be sampled and provide a response to a particular question is thus p_i*r_i, and thus the weight for this individual is $w_i = 1/(p_i*r_i)$.

This process can also be performed based on a class adjustment basis, so that the weights of all members of a class will be increased based on an overall probability of non-response within a class. The estimate of the non-response probability for a given class is:

$$p_i = \frac{\text{sum of weights for all members in the given class}}{\text{sum of weights for actual respondents in the given class}}$$

Then the sampling weight for each member of the given class is multiplied by $1/p_i$. In this way, the sum of all of the weights among respondents will still equal the weights of the unadjusted original population.[51]

Within the NHANES data, different sampling weights were assigned based on race, age, and gender. Using the sampling categories, weights will be adjusted based on a race of black, Mexican-American, or others, by gender, and by age categories of 20-34, 35-49, 50-65, and 65+. Starting with the total population 20 years of age and older, we will apply sampling weight adjustment factors based on the pattern of missing data and the sum of weights in each category. Missing data was generated by not providing valid accelerometer data, not reporting family income, and not reporting educational attainment. See Table 3. 2 for the sampling weight adjustments that will be applied to the appropriate strata.

3.1.5. Data Collection

Once individuals have been selected, an advance letter is sent to each household indicating that the interviewers will visit their home. The interview portion of the survey is usually conducted at individuals' homes, at which time household members are asked to sign an Interview Consent form and respond to an initial Screener questionnaire, used to determine eligibility for the study. If selected for the survey, the participants are interviewed by the NHANES representative.

At the end of the Interview portion of the survey, participants are provided with an informed consent brochure regarding the Health Examination. All participants are asked to participate in the Health Examination portion of the survey and, if they agree, will sign additional informed consent forms. At the MECs, a battery of physical examinations are administered. Participants provide blood samples and those over 5 years old are asked to provide a urine sample.   At the end of the exam, participants are given remuneration for their time.

3.1.6. Measuring Physical Activity with Accelerometry

NHANES 2003-2004 used the ActiGraph Model 7164 accelerometer manufactured by Actigraph (formely MTI/CSA) of Ft. Walton Beach, FL to collect information on participant's physical activity.   Those who took part in the physical exam were asked to wear a monitor if they meet the eligibility criteria, which consisted of being over 5 years old and ambulatory. Because not all participants opt to wear the monitor, the total number of subjects who took part in the examination and wore a monitor was 7,176.

Table 3. 2. Sum of category weights, sum of weights with no missing data, and the weight adjustment factor for sampling categories in the NHANES.

Race	Age Categor y	Gender	Sum of all weights	Sum of weights with data	Weight Adjustment
Mexican American	20-34	Female	3456684.8	3054331.9	1.13
		Male	4167809.5	3340888.9	1.25
	35-49	Female	2504901.6	2303235.5	1.09
		Male	2719173.6	2525081.6	1.08
	50-64	Female	978709.12	915572.33	1.07
		Male	992140.6	940472.59	1.05
	65+	Female	608449.45	502884.35	1.21
		Male	512367.87	457372.21	1.12
Non-Hispanic Black	20-34	Female	4319197.8	3460070.6	1.25
		Male	3634014.6	2960404.6	1.23
	35-49	Female	4422020.2	3906823.1	1.13
		Male	3185212	2609530.2	1.22
	50-64	Female	2420091.6	2109787.5	1.15
		Male	2184334.6	1878088.3	1.16
	65+	Female	1746295.6	1209267.1	1.44
		Male	1123562.7	947499.61	1.19
All others	20-34	Female	22163032	19162842	1.16
		Male	22202779	18447233	1.20
	35-49	Female	26249155	22816651	1.15
		Male	25234924	22177739	1.14
	50-64	Female	20544160	17962925	1.14
		Male	18720711	16630790	1.13
	65+	Female	17442472	14082066	1.24
		Male	13752468	11589155	1.19

The protocol asked the participants to wear the monitor for 7 days during normal waking hours. Because the monitors are not water proof, participants were to remove them during swimming or bathing. A flexible, easily removable, waist belt was provided to which the monitor could be attached. After 7 days, the participant's mailed the monitor back, at which time they were issued a $40 payment for returning the monitors.

3.2. Cleaning the data

The NHANES accelerometry data is very complete in terms of the total number of participant's with all seven days of collected data. However, within each day, there may be extended periods of zeros, which indicate a non-wearing period. Researchers currently analyzing the NHANES data have indicated that using a period of one hour for consecutive zeros is necessary to capture true wearing periods for certain populations, such as the elderly who may remain very sedentary for extended periods of time (personal communication - Troiano). For this reason, data will be treated as missing if at least one hour of consecutive zeros have been recorded.

3.3. Analysis Strategy

The details of the statistical models will be explored in the following chapters. In general, the modeling will be conducted using latent class analysis (LCA) in which unobserved, or "latent", classes of activity patterns are ascertained from the observed levels of physical activity across the seven days of accelerometer data. Once the classes are established and members are assigned to these classes, the associations between the sociodemographic characteristics and class membership may be assessed. New developments in LCA methods then allow for the simultaneous assessment of the associations between these derived patterns of physical activity and the risk factors for the metabolic syndrome.

Chapter Four

Patterns of Objectively Measured Physical Activity in the United States

Introduction

Due to the increased concern about the lack of physical activity in the United States (US), many annual national health surveys such as the Behavioral Risk Factor Surveillance System (BRFSS) and the National Health Interview Survey (NHIS) collect information on physical activity levels. Reports and research from these surveys cover various aspects of the nation's levels of physical activity (or inactivity), such as general physical activity trends,[52] trends among certain subpopulations such as Hispanics,[58] percent of the US population meeting the Healthy People 2010 leisure-time physical activity goals,[53] or associations between physical activity and healthcare expenditures.[63] These reports, however, have in the past relied on self-report, which, when compared to objectively measured physical activity, have been shown to have low correlations in the range of 0.14 to 0.53.[11] In addition, participants are generally categorized into activity levels based on overall descriptions of activity frequency and intensity, without attempting to categorize the potential differences in the pattern of accumulated physical activity over time.

In the 2003-2004 National Health and Nutrition Examination Survey (NHANES), physical activity as measured by accelerometry was added to the battery of assessments among those participants 6 years old and older who were ambulatory, providing the first nationally representative sample of objectively measured physical activity in the United States (US). In addition, the accelerometry was collected over a seven day period, allowing for an assessment of the number of minutes of physical activity accumulated by each participant on each day of a seven day week.

Using latent class analysis (LCA), we assessed whether patterns, or classes, of physical activity exist among adults in this sample over the seven day period. In this type of analysis, a specified number of classes are requested a priori. Then, LCA finds the requested number of best fitting underlying normal distributions for the indicators of these classes (in this case, the daily minutes of physical activity across the seven days of a week). For example, one class may have a very low mean number of minutes of physical activity from Monday to Friday, with a high average number of minutes of physical activity on Saturday and Sunday (i.e., a "weekend warrior"). Another group, possibly active workers, may have a large mean number of minutes of physical activity during the work week but low mean minutes of physical activity on the weekend.

A recent study attempted to assess the effect of the weekend warrior activity pattern on the risk of mortality.[45] In this study, the mortality outcomes of the weekend warrior, defined as those who accumulate a large quantity of physical activity (≥1000 kcal/week) over a short period of time (1-2 days/week), were compared to those who accumulate a similar amount of activity (≥1000 kcal/week) over a longer period of time (3+ days/week), along with those who are insufficiently active (500-999 kcal/week) or sedentary (<500 kcal/week). Among low risk men, weekend warriors demonstrated the lowest relative risk of mortality, indicating that as long as the accumulated physical activity is sufficient then the benefits will be accrued. Among high risk men, however, only the regularly active showed improved mortality risks as compared to the most sedentary group.

Much is now known about the overall levels of activity in the US, but few studies have attempted to define patterns of physical activity. Using LCA may help clarify strategies for how inactive people may accumulate additional physical activity, as well as allow future analysis to assess whether different patterns of physical activity are associated with improved health outcomes.

Materials and Methods

We analyzed the 2003-2004 NHANES, an ongoing health survey with a target population of civilian, non-institutionalized citizens from throughout the entire US. Certain populations were over-sampled, including low-income persons, Mexican-Americans, African-Americans, and those age 12-19 and 60 years or older. The survey consists of an interview, from which sociodemographic information is collected, and a physical examination, from which various biological markers of health are ascertained. In addition, the 2003-2004 NHANES collected seven consecutive days of accelerometry measurements among all ambulatory participants 6 years old and older who agreed to wear the monitor for a week. Written informed consent was obtained from all participants.

Measuring physical activity with accelerometry

Accelerometers are small, electronic devices that record the acceleration of change in bodily motion either in one plane or multi-dimensions. They are particularly useful in measuring physical activity because they eliminate the potential for recall bias, social desirability bias, and are not dependent on literacy. NHANES 2003-2004 used the

ActiGraph Model 7164 accelerometer manufactured by Actigraph (formerly MTI/CSA) to collect information on participant's physical activity. This lightweight uniaxial monitor is a technically reliable instrument, both within and across monitors.[54] Most participants (98.2%) wore the monitor for 7 days during normal waking hours. NHANES used one minute epochs to assign a "count' value, which is a relative measure of the changes in momentum that occurred during these periods, which may then be translated into an estimate of physical activity intensity.

Moderate and vigorous physical activity cut-points based on calibration studies

The accelerometer cut-point used by this study to translate the count value into an estimate of moderate-to-vigorous physical activity (MVPA) was based on a weighted average of published cut-points for adults.[65-68] following the recommendation of NHANES researchers. Each study listed in Table 1 reported a cut-point for MVPA, which were then weighted by their sample size to arrive at an n-weighted average cut-point of 2,020 counts/min for MVPA. Cut-points for vigorous physical activity (VPA) were also reported in these calibration studies and, using the same n-weighted average as used with the MVPA, the VPA cut-point was 5,999 counts/min.

Accumulating minutes of MVPA and/or VPA

Physical activity accumulated in a given a day was quantified as (1) minutes per day in which the count was higher than the given MVPA cut-point, (2) minutes per day in which the count was higher than the given VPA cut-point, and (3) minutes per day of MVPA accumulated in bouts of 10 minutes or more. The latter classification was motivated by the physical activity recommendations published by the Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine

(ACSM),[3] which call for activity to be accumulated in bouts of 10 minutes or more to achieve health benefits. To allow for brief periods of rest common during activities, for example to pause for a water break while playing basketball, the criteria used to define a bout required a running average of 70% of the counts to be above the cut-point. Once the series of accelerometer minutes fell below 70% of minutes in MVPA, the bout was considered over. Thus, bout minutes of MVPA was a sum of all minutes of MVPA accumulated in these bouts. Those who never achieved a 10 minute bout were assigned their longest bout shorter than 10 minutes in length. Bout minutes of VPA were not assessed because too few participants achieved the required 10 consecutive minutes of VPA.

Imputation of missing daily minutes of MVPA

The NHANES accelerometry data was quite complete in terms of the total number of participants providing all seven days of data (over 99.8%). However, within each day there may be extended periods of zero counts, indicating either a non-wearing period or a period with no detectable movement. Periods consisting of one hour or more of consecutive zeros were treated as missing data. In addition, periods of monitor malfunctioning were also considered missing (e.g., 10 minutes of identical consecutive non-zero count values). Occasional missing accelerometry data within a participant's 7-day record was then imputed using the expectation maximization (EM) algorithm, an iterative imputation technique which uses the values of an individual's other, non-missing data as predictors to estimate the expected value of the total minutes of MVPA for each missing segment of time.[22]

Self-reported variables

Age was recorded at the time of the interview and those over 85 years of age were assigned a truncated value of 85. For descriptive purposes, age was categorized into decades but was left continuous in the final LCA. Gender was recorded at the time of interview. Race, ethnicity and country of origin questions were recoded into the following categories: 1) Mexican-American, 2) other Hispanic, 3) Non-Hispanic (NH) Black, 4) NH-White and 5) Other Race – including Multi-Racial. Education was categorized as less than high school, high school or GED, and more than high school. The poverty income ratio (PIR) was recorded as a ratio of the self-reported family income to the poverty threshold based on family size. The smallest value of 0 indicated no family income while the highest value is truncated at 5, indicating a family income at least 5 times the poverty threshold for family size. For descriptive purposes, the poverty ratio was categorized into integer values but was left continuous in the final class analysis.

Statistical Methods

Descriptive Statistics

To determine if the analysis sample differed from the subgroup excluded due to missing data, we used chi-square tests to compare categorical variables, and t-tests to compare the mean of continuous variables. Using SAS (Cary, NC) survey procedures, sample weighted means, standard deviations, standard errors as well as 25^{th}, 50^{th} and 75^{th} percentiles were computed for overall MVPA, bout minutes of MVPA, and VPA for each day of the week.

Latent Class Analysis

Employing LCA, we used each participant's seven days of total MVPA/VPA to determine whether natural groupings, or classes, of people exist who tend to accumulate their minutes of physical activity in a similar pattern over the seven days. Classes can be thought of as groups of people who share similar means for the various indicators of class, in this case the seven days of accumulated MVPA/VPA. The most general probability density function used to define the LCA model is as follows:

$$f\,[\,\mathbf{y} \mid \boldsymbol{\Sigma}(\boldsymbol{\theta}), \boldsymbol{\mu}(\boldsymbol{\theta})] = \sum_{g=1}^{G} \mathbf{p}_{\mathrm{g}}\, f[\,\mathbf{y} \mid \boldsymbol{\Sigma}_{\mathrm{g}}(\boldsymbol{\theta}), \boldsymbol{\mu}_{\mathrm{g}}(\boldsymbol{\theta})]$$

On the left side of this equation, the probability distribution function defines a distribution for y, the vector of minutes of MVPA/VPA across the seven days, conditioned on $\mu(\theta)$, the vector of mean MVPA across the seven days, and $\Sigma(\theta)$, the covariance matrix for the multivariate normal distribution of the seven days. On the right side, for each underlying class (indexed by G), the probability function for the vector y is weighted by probability of being in the each of these specific classes. $\mu_g(\theta)$ is the vector of predicted means for the gth group, and $\Sigma_g(\theta)$ is the covariance matrix for the gth group. The overall probability distribution for y is thus a probability weighted sum of each class's probability density for the given values of y.[55]

If the distribution f is assumed to be a multivariate normal distribution with G components, then the probability density function of an individual in the Gth class is:

$$f\,(\mathbf{y} \mid \boldsymbol{\Sigma}_{\mathrm{g}}(\boldsymbol{\theta}), \boldsymbol{\mu}_{\mathrm{g}}(\boldsymbol{\theta})) = (2\pi)^{-(p)/2} \mid \boldsymbol{\Sigma}_{\mathrm{g}}(\boldsymbol{\theta})|^{-1/2} \;*$$

$$\exp(-1/2\langle[\,\mathbf{y}_{\mathrm{i}} - \boldsymbol{\mu}_{\mathrm{g}}(\boldsymbol{\theta})]'\,[\boldsymbol{\Sigma}_{\mathrm{g}}(\boldsymbol{\theta})]^{-1}[\mathbf{y}_{\mathrm{i}} - \boldsymbol{\mu}_{\mathrm{g}}(\boldsymbol{\theta})]\rangle)$$

where y_i is the vector of minutes of MVPA/VPA across the seven times for the i^{th} subject, $\mu_g(\theta)$ is the vector of predicted means across the seven times t for the i^{th} subject,

$\Sigma_g(\theta)$ is the covariance matrix for the multivariate normal distribution of the seven days of MVPA/VPA, and $|\Sigma_g(\theta)|$ is the determinant of the covariance matrix.[55]

Thus the likelihood function used to maximize this model for all participants across all class possibilities is:

$$L = \prod_{n=1}^{N}\sum_{g=1}^{G} p_{ig}\,(2\pi)^{-(p)/2}\,|\,\boldsymbol{\Sigma}_g(\boldsymbol{\theta})|^{-1/2}$$
$$* \exp(-1/2\langle[\mathbf{y}_i - \boldsymbol{\mu}_g(\boldsymbol{\theta})]'\,[\boldsymbol{\Sigma}_g(\boldsymbol{\theta})]^{-1}[\mathbf{y}_i - \boldsymbol{\mu}_g(\boldsymbol{\theta})]\rangle)$$

where N indexes the subjects and G indexes the classes, and again the p_i weights the probability function for the gth class. This likelihood function is identical to the multivariate normal distribution with the addition of the probability weighted class memberships.[56]

The probability of being a member of a particular class is assigned to an individual based on Bayesian posterior probabilities, using a prior probability proportional to the size of the particular class relative to the entire population. Thus, the probability of an individual being a member of class g is:

$$P_{g|\mathbf{y_i}} = P_{g|\mathbf{z_i}} * f[\mathbf{y_i}\,|\,\boldsymbol{\Sigma}_g(\boldsymbol{\theta}), \boldsymbol{\mu}_g(\boldsymbol{\theta})] \,/\, \sum_{g=1}^{G} P_{g|\mathbf{z_i}} * f[\mathbf{y_i}\,|\,\boldsymbol{\Sigma}_g(\boldsymbol{\theta}), \boldsymbol{\mu}_g(\boldsymbol{\theta})]$$

where Pg is the prior probability of being in class g, conditioned on the covariates. The numerator in this case is the prior probability that subject i belongs to class g, multiplied by the probability density for the observed seven days of MVPA for y_i, given the predicted means and covariance of the seven days of MVPA in class g. The denominator is the sum of the probability densities for all possible class memberships given the individual's set of indicator values y_i, weighted by each class's specific prior probability.[57] Individuals were assigned to the class with their highest posterior probability of class membership, referred to as modal allocation.

Selecting the Number of Classes

One of the most difficult tasks of LCA is determining the proper number of classes which adequately describe the population without over-specifying the number of class groupings, thereby losing the interpretative value of the classes. Several criteria were used to select the appropriate number of classes. We first used the bootstrap likelihood ratio test (BLRT), which compares the fit of k classes to k-1 classes, as it outperformed the Lo-Mendell-Rubin likelihood ratio [58] in controlling both type I and type II error.[59] Second, we considered a measure referred to as "entropy" that is the average highest predicted probability of class membership.[60] This measure ranges from 0 to 1, lower entropy indicating little confidence that individuals belong in to the class with their highest assigned probability, while an entropy of 1 would indicate certainty that individuals belong in their assigned class. Third, if one or more class sizes were too small to be of any public health relevance, the number of classes was reduced. Finally, substantive knowledge was used to establish the appropriate number of classes.[61] There should be a correspondence between the established classes and some practical interpretation of what the classes indicate. As Muthen (the author of the MPLUS statistical software) concluded, "Substantive theory, auxiliary information, and practical usefulness will continue to have to guide the statistical analysis."[61]

Specifying Variance Estimates

In a completely unrestricted model, LCA will estimate a separate variance-covariance matrix for each class. If the number of latent classes or the number of variables is large, so too are the parameters to be estimated. Thus, a typical strategy is to impose restrictions, such as constraining covariances to be zero or constraining classes to have the same variance-covariance matrix (i.e., $\Sigma_g(\theta) = \Sigma(\theta)$). Constrained models allow for more parsimonious and stable results.[57]

Because the mean minutes of physical activity for the lowest activity class had significantly lower variances than the more active classes, a model which allowed this lowest activity class to have variances that differed from all of the other activity classes was selected. For all but the lowest activity class, we allowed weekend and weekday variances to differ, but constrained them to be equal across classes. In this way, we tried to create a parsimonious and stable model that still captured some of the complexity of the substantive issues of the analysis.

The LCA was performed using MPLUS. The modeling was conducted by requesting a range from 1 to 6 classes a priori as the number of group memberships to predict. Beyond six classes, the sample size of the more active classes became very small and the activity patterns over the seven days become highly unstable. While MPLUS allows for complex survey sampling in conjunction with LCA modeling, the software does not currently account for survey sampling when computing the BLRT statistic. As such, this analysis, designed to establish an appropriate number of activity classes, was performed without sample weights and cluster sampling.

Structural equation modeling perspective

Figure 1 provides a visual representation of the LCA model using the graphical presentation typical of structural equation modeling. In this perspective, the latent classes are derived from the patterns of physical activity across the seven days of the week. Simultaneously, the socio-demographic characteristics are used to predict who falls in to each of the derived activity classes. These socio-demographic variables provide the prior distributions upon which the Bayesian posterior class membership probabilities are based.

This research was approved by the Public Health Institutional Review Board of the University of North Carolina at Chapel Hill.

Results

A total of 10,122 participants completed the 2003-2004 NHANES physical examination. We excluded those under age 20 to more clearly focus this research on an adult population. Of the remaining 5,041 participants, 4,252 provided data for the accelerometer portion of the survey. Finally, an additional 450 participants were excluded because of missing covariate data (e.g., education, household income) or because they had no days of valid accelerometer data with which to impute the other, missing days, leaving a final population of 3,802 participants. Because imputation was not performed on the assessment of bout minutes of MVPA, only the 3,462 participants who provided at least 3 valid days of data were included in the analysis of bout minutes.

The sociodemographic characteristics of the final sample and those excluded due to missing data are presented in Table 2. Statistically significant ($p < 0.05$) differences were found between the categorical distributions of age, education, the poverty index, and race/ethnicity. While the chi-square tests for the categorized age and poverty index ratio were significant, the t-tests for the continuous age (p-value = 0.82) and poverty index ratio (p-value = 0.21) were not. For age, this appears to be due to the missing data being over-represented by the younger and older participants in the various age categories, leading to a similar mean age (50.8 years old for those in the final sample vs. 51.0 years old for those not included in the final sample). Similarly, for the poverty index, the poorest and richest were least likely to provide complete data, again leading to a similar mean (2.6 for those in the final sample vs. 2.5 for those not included in the final sample).

The weighted mean minutes of MVPA/VPA and bout minutes of MVPA for all participants are presented in Table 3 by day of the week. The median number of bout minutes of MVPA was 2.0 for all days, indicating that in half of all days participants accumulated no more than two bout minutes of MVPA. The weighted mean minutes of VPA did not exceed 0.8 minutes for any day. The median values were substantially lower than the mean for all types of physical activity and for all days of the week suggesting non-normally distributed data. Weekends had the lowest mean minutes of MVPA, VPA as well as bout minutes of MVPA.

Table 4 shows the Log-likelihood values for the analyses of the class memberships for the overall minutes of MVPA, ranging from 1 to 6 classes. The BLRT test statistic detected a statistically significant improvement in fit at the <0.0001 level for all number of classes, indicating that separating the population into six classes was justified based on this criteria. While entropy decreased as the number of classes increased, it was still high (0.94) for five and six classes. Because the six class analysis resulted in very small active classes, we settled on a more parsimonious five class model for presentation.

Figure 2 shows the plot of the mean minutes of total accumulated MVPA for five classes. The largest percentage of the population fell in the lowest two classes – roughly 81% of the total population. These two lowest classes encompassed activity averaging less than 25 minutes/day of MVPA. The highest activity class, with a mean of 134 minutes of MVPA per day, only comprised 0.8% of the population. This class also demonstrated a high level of activity Monday through Friday with less activity on the weekend, with a particularly pronounced decrease on Sunday. All classes demonstrated this dip on weekends compared to weekends, to varying degrees.

Table 5 shows the Log-likelihood for the analyses of the MVPA when participants are required to accumulate their minutes in bouts. Even though the BLRT test justified as many as 6 classes at the <0.0001 level, the two most active classes in the 6 class analysis were very sparsely populated (0.1% and 0.5% of the population). Given this, we settled on 5 classes for the bout minutes of MVPA, which also allowed for a direct comparison with the overall minutes of MVPA.

Figure 3 show the class means for the 5 class results for the bout minutes of MVPA. The two most active classes represented 0.5% and 3.9% of the population, just slightly less than the two most active overall MVPA classes which had 0.8% and 4.2% of the population, respectively. Roughly 94.4% of the entire population is now classified into the lowest two groups. In addition, for the bout analysis, the second least active group now has a mean of 10.3 bout minutes of MVPA per day, while the second least active group in the overall MVPA analysis had a mean of 21.0 minutes across all seven days. Thus, when only bout minutes are counted, a much larger percentage of the population was classified into the lowest groups, and these groups are less active.

Even though the number of minutes accumulated in bouts tends to shift the classes into lower levels of mean activity level, the general patterns are very similar to the overall MVPA analysis with one exception. A class emerged with moderate levels of physical activity Monday through Friday but with a much higher level of activity on the weekend, particularly on Sunday. This class, representing 1.2% of the population, will be referred to as the "weekend warrior" class. The six class analysis of the overall minutes of MVPA (data not shown) also demonstrated this weekend warrior class, although with a smaller percentage of the population (0.8%).

The VPA analysis did not produce stable results (very large and very small class sizes) due to the very low number of participants accumulating any vigorous activity. For example, both the 3 and 4 class VPA analyses produced a most active class with only 2 and 1 participants, respectively – a trivial class assignment from both a substantive and analytical perspective.

Discussion

This modeling represents the first time that objectively measured physical activity data have been analyzed using LCA. While a large portion of the population presented little activity, a weekend warrior class did emerge, as well as a highly active class with less activity on the weekend. We are unsure whether these activity patterns were driven by specific types of activity, such as work related activities.

In the analysis of the overall minutes of MVPA, the statistical significance of the BLRT statistic indicated that 6 classes were justified based on the data. However, class size for the more active groups displayed a small sample size and, as such, the reduced model with only 5 classes provided a more parsimonious model.

An inactive class emerged in the overall MVPA which represented nearly 41% of the entire population. This class averaged 5.3 minutes of MVPA per day. The second least active class with a mean of 21.0 minutes of MVPA per day also represents a class of which many, if not most, would not have accumulated 30 minutes of MPVA on most days of the week. Together, these two groups represent a very large proportion of the population with PA levels significantly below the recommended levels.[3] Determining the sociodemographic and behavioral characteristics of these groups in order to target appropriate physical activity interventions could lead to significant improvements in the activity levels in the US, and thus in the overall health of the nation.

The analysis of the bout minutes of MVPA produced patterns similar to those found in the analysis of the overall minutes of MVPA, with the important exception of the weekend warrior class. From Monday through Friday, this class had significantly less activity than the class above it (e.g., the class representing 3.9% of the population), but due to the significant increase in the physical activity of the weekend warrior on Saturday and Sunday and the decrease in the other group during this period, their means were relatively similar. The weekend warrior accumulated a daily mean of 31.5 minutes of MVPA, while the more active group was only slightly more active averaging 37.0 minutes. The health outcomes of these two groups would be interesting to compare as they represent two populations which meet the physical activity recommendations, accumulated their minutes in bouts, and have similar mean minutes of MVPA, while accumulating it in very different manners.

A recent article using self-report data from NHANES and the BRFSS reported a prevalence of the weekend warrior pattern in the US population, defined as accumulating $\geq$ 150 minutes of MVPA during 1 or 2 days in a week, of approximately 3% and 1%, respectively.[62] Our results, while based on objectively measured accelerometer data, found that a similar proportion of the population (1.2%) could be classified as a weekend warrior based on bout minutes of MVPA.

Another important difference between the bout minutes of MVPA and the analysis of the overall MVPA minutes is that the more active groups in the bout minutes analysis had significantly fewer participants than in the overall MVPA analysis. In fact, the two most active classes in the six class analysis of bout minutes of MVPA (data not shown) only contained 0.3% and 0.4% of the population. The utility of class assignments with such small populations is an important consideration in mixture modeling, especially if the analyses include associations between the class assignment and any outcomes. If the six class levels of bout minutes of MVPA were used to simultaneously model health outcomes, the two most active classes would likely not be large enough to generate proper associations with the health outcomes, particularly if the outcomes were rare.

This challenge was made most explicit in the analysis of the VPA. Only 1.4% of all days achieved 10 minutes or more of VPA, and in 91.1% of all days participants accumulated less than one minute of VPA (data not shown). Due to the highly skewed data, the model assumptions generally failed to produce results. When classes were successfully modeled, their sizes were too small to serve any useful analytic purposes.

These low levels of VPA are troubling when considered in light of the Healthy People 2010 goals of increasing to 30 percent “the proportion of the adults who engage in vigorous physical activity that promotes the development and maintenance of cardiorespiratory fitness 3 or more days per week for 20 or more minutes per occasion.”[63] Not only does this analysis reflect a much lower percent of the adult population achieving this goal than desired, it also reflects a much lower percentage than the 27.4% of adults reported to have met this goal in 2005 by the BRFSS.[64] In fact, only 23 participants registered 20 minutes of VPA on at least three days of the week, representing only 0.6% of the total population. Because the BRFSS assessment was based on self-report, this discrepancy could reflect a large amount of over-reporting present in the BRFSS levels. It could also reflect that the cut-point for VPA was too high, thereby missing many minutes of activity in our population that should have been classified as VPA.

Although we chose LCA as our modeling strategy, other possibilities were also considered for the method of modeling classes. Latent class growth analysis (LCGA) and growth mixture modeling (GMM) have recently found wide application in the social sciences as an effective method for modeling growth trajectories with longitudinal data.[44, 45] It was determined, however, that the seven days of PA, while contiguous in time, did not constitute a longitudinal analysis analogous to, for example, the development of childhood obesity according to age in adolescence. This decision was based, in part, on the desire to impose no restrictions on the shape of the classes over seven days. In other words, we did not want to force the physical activity classes to follow a "growth" pattern. With this conceptualization, physical activity is more analogous to multiple continuous measurements of academic ability such as math, verbal, spatial, etc., and as such should be modeled with LCA.

Several limitations of this work are worth noting. The analysis population had a socio-demographic distribution that differed from those who were excluded due to non-response or inappropriate data, which in turn could have affected the overall patterns found. Another weakness was that, due to the small number of participants registering sufficient levels of VPA, this part of the analysis was unsuccessful. This would have been an interesting group to assess and possibly with different analytical techniques or a larger study population, this analysis will be possible in the future. Accelerometers do not capture all types of physical activity, particular static activities such as raking leaves or riding a bike.[19] Therefore, while the current analyses do not rely on self-report, they may still not reflect the true activity levels of the US population. Similarly, the cut-points for what constitutes MVPA and VPA are also sensitive to the types of activities being done. Changing these cut-points would affect the amount of physical activity that participants were credited for, which in turn could have affected the outcomes of the latent class analysis. An analytical weakness worth noting was that the BLRT test statistic was not available with the simultaneous use of the NHANES sample weights and, therefore, the sample weights were not used for this analysis. Adding the sample weights could have affected the final decision for the number of classes as well as the pattern that these classes assumed.

These data represent objectively measured physical activity from a large, nationally representative sample of the US population. Physical activity was assessed in several ways in order to analyze the class membership patterns for different patterns of physical activity. Our results indicated that a very large portion of the US population may be classified into patterns of physical activity that represent low levels of MVPA throughout the week. The levels of VPA were most surprising, indicating that fewer than 1% of the population engaged in VPA for at least 20 minutes on 3 or more days per week. In addition, a weekend warrior class emerged for approximately 1% of the population. The

LCA analysis provides a novel approach for assessing patterns of objectively measured physical activity in epidemiologic studies.

Table 4. 1. N-weighted mean cut-point for moderate-to-vigorous physical activity (MVPA) and vigorous physical activity (VPA) based on previously publish calibration equations.

Author	MVPA Cut-point (counts/min)	VPA Cut-point (counts/min)	N	N-weighted MVPA Value*	N-weighted VPA Value*
Freedson [65]	≥ 1,952	≥ 5,725	50	97,600	286,250
Yngve [67]	≥ 2,743	≥ 6,403	28	76,804	179,284
	≥ 2,260	≥ 5,896	28	63,280	165,088
Brage [66]	≥ 1,810	≥ 5,850	12	21,720	70,200
Leenders [67]	≥ 1,267	≥ 6,252	28	35,476	175,056
			146	294,880	875,878

Moderate weighted mean cut-point: 294,880/146 = **2,020**

Vigorous weighted mean cut-point: 875,878/146 = **5,999**

* N-weighted values were based on the MVPA or VPA cut-point value multiplied by the sample size of the particular study.

Figure 4. 1. Structural Equation Model for the prediction of the latent classes based on the minutes of physical activity across the seven days of the week, with socio-demographic characteristics predicting class membership.

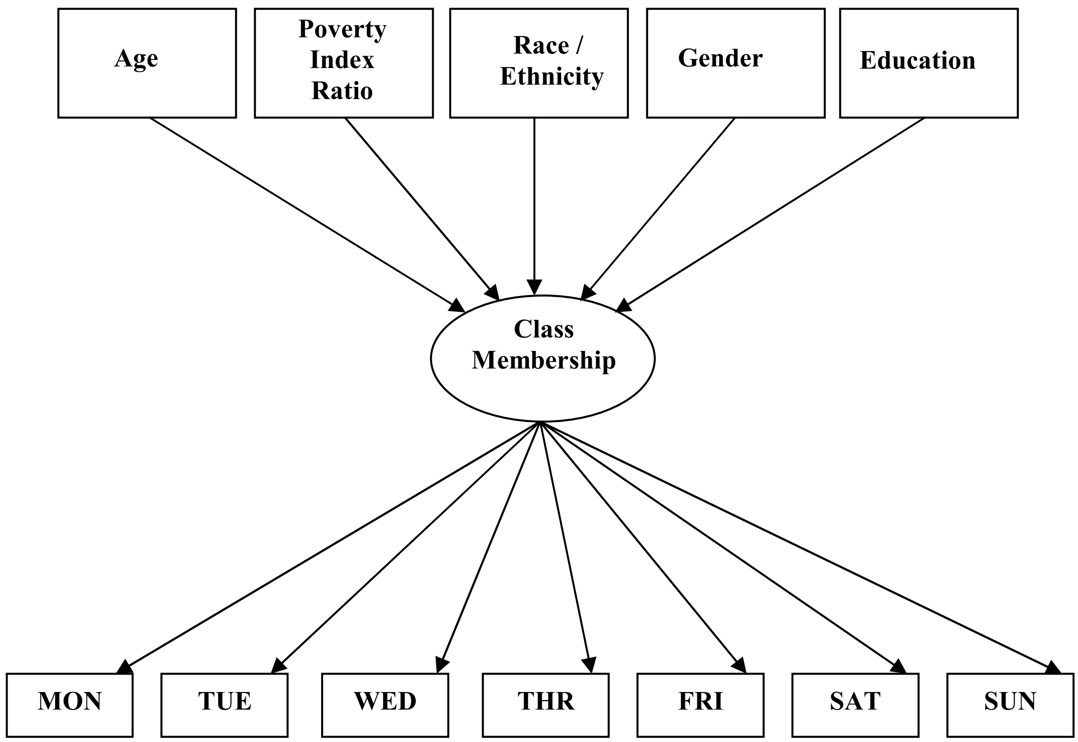


Table 4. 2. Sociodemographic characteristics of the final study sample and the population excluded due to missing data, among those 20 years old and older.

		In Final Sample		Not Included in Sample		
		N	%	N	%	P-value*
Age	**20 to <30**	645	17.0	265	21.4	
	30 to <40	618	16.3	214	17.3	
	40 to <50	637	16.8	152	12.3	
	50 to <60	487	12.8	122	9.8	
	60 to <70	614	16.1	159	12.8	
	70 to <80	484	12.7	127	10.3	
	80+	317	8.3	200	16.1	<.0001
Education	**Less than High School**	1077	28.3	410	33.5	
	High School	940	24.7	329	26.9	
	More than High School	1785	46.9	486	39.7	<.0001
Gender	**Female**	1956	51.4	667	53.8	
	Male	1846	48.6	572	46.2	0.14
Poverty Index	**0 to <1**	678	17.8	180	19.5	
	1 to <2	1032	27.1	257	27.9	
	2 to <3	640	16.8	164	17.8	
	3 to <4	456	12.0	80	8.7	
	4 to <5	368	9.7	73	7.9	
	5+	628	16.5	168	18.2	0.03
Race/Ethnicity	**Mexican**	792	20.8	193	15.6	
	Other Hispanic	106	2.8	46	3.7	
	NH-White	2037	53.6	652	52.6	
	NH-Black	714	18.8	280	22.6	
	Other/Multi-Racial	153	4.0	68	5.5	<.0001

NH = Non-Hispanic
* P-values are based on a chi-square probability distribution.

Table 4. 3. Sample weighted mean, standard deviation, standard error, 25th, 50th and 75th percentile for minutes of moderate-to-vigorous physical activity (MVPA), bout minutes of MVPA, and vigorous physical activity (VPA), by day of the week.

	MVPA Minutes N=3,802						MVPA Bout Minutes* N=3,462						VPA Minutes N=3,802					
Day of week	**Mean**	**Std. Dev.**	**Std. Error**	**25th %ile**	**50th %ile**	**75th %ile**	**Mean**	**Std. Dev.**	**Std. Error**	**25th %ile**	**50th %ile**	**75th %ile**	**Mean**	**Std. Dev.**	**Std. Error**	**25th %ile**	**50th %ile**	**75th %ile**
Monday	25.6	27.3	0.99	7	17.0	36.0	8.2	16.7	0.59	1.0	2.0	5.0	0.8	3.81	0.10	0.0	0.0	0.2
Tuesday	25.4	27.9	0.95	6.5	17.0	34.1	7.9	16.0	0.50	1.0	2.0	6.0	0.8	3.62	0.10	0.0	0.1	0.3
Wednesday	25.1	28.1	1.20	6	16.0	34.0	7.9	17.4	0.57	1.0	2.0	5.0	0.8	5.48	0.15	0.0	0.0	0.2
Thursday	25.5	28.0	1.10	6.7	16.2	35.0	8.0	16.5	0.53	1.0	2.0	6.0	0.8	3.21	0.08	0.0	0.1	0.3
Friday	24.6	26.5	0.94	6.6	16.4	33.5	6.9	14.4	0.52	1.0	2.0	5.0	0.7	3.51	0.09	0.0	0.0	0.2
Saturday	21.4	25.0	0.73	6	13.5	28.0	6.9	16.4	0.41	1.0	2.0	4.0	0.7	4.51	0.12	0.0	0.0	0.2
Sunday	19.4	23.5	0.87	5	12.0	24.0	6.9	16.6	0.58	1.0	2.0	4.0	0.7	4.22	0.08	0.0	0.0	0.2

* A participant was only credited for physical activity that occurred in bouts of 10 minutes or more in length. Bouts were based on a running average of 70% of the counts above the MVPA cut-point of 2,020 counts/min. If no bouts of at least 10 minutes in length were accumulated in a particular day, the participant was credit with their longest bout shorter than 10 minutes in that day.

Table 4. 4. Likelihood ratio (LRT) and bootstrap LRT statistical criteria as well as entropy values for deciding on k versus k-1 number of classes for overall MVPA.

Number of classes	1	2	3	4	5	6
Log Likelihood	-124,179	-107,756	-105,424	-104,380	-103,919	-103,675
Number of Parameters	9	28	45	62	79	96
Bayesian Information Criteria (BIC)	248,433	215,742	211,219	209,271	208,490	208,142
Adjusted BIC	248,404	215,653	211,076	209,074	208,238	207,837
Akaike Information Criteria (AIC)	248,377	215,567	210,938	208,884	207,996	207,543
Bootstrap LRT p-value for k-1 vs. k*	N/A	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Entropy	N/A	0.961	0.956	0.953	0.943	0.947

N/A = not applicable

* P-value is comparing whether the addition of one extra class provides statistically significant improvement in the fit of the class assignments.

Figure 4. 2. Five latent classes - MVPA.

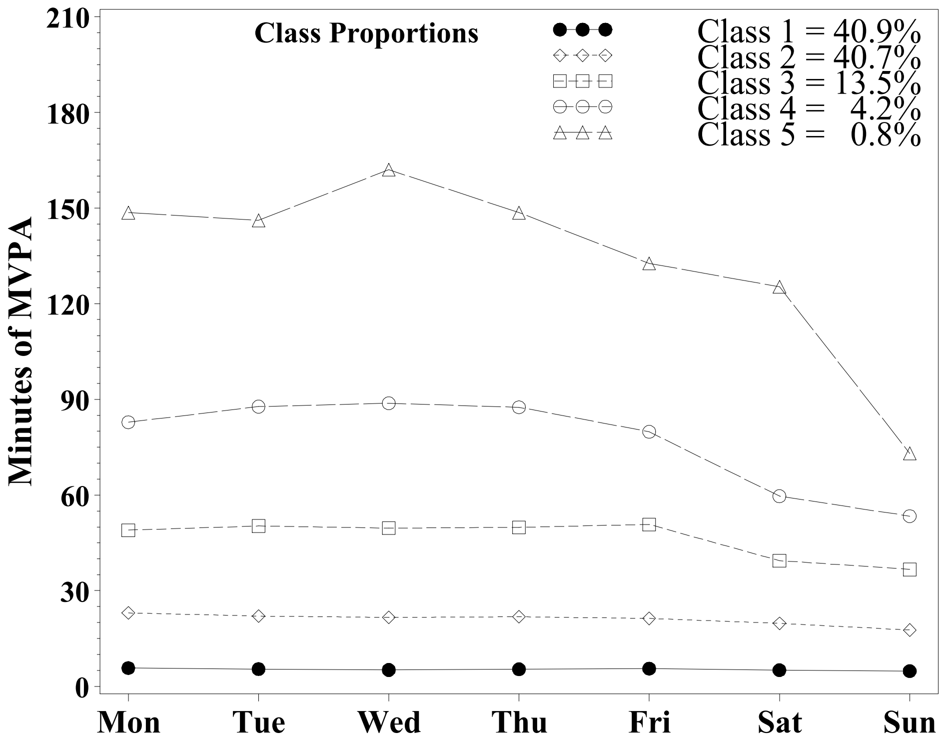
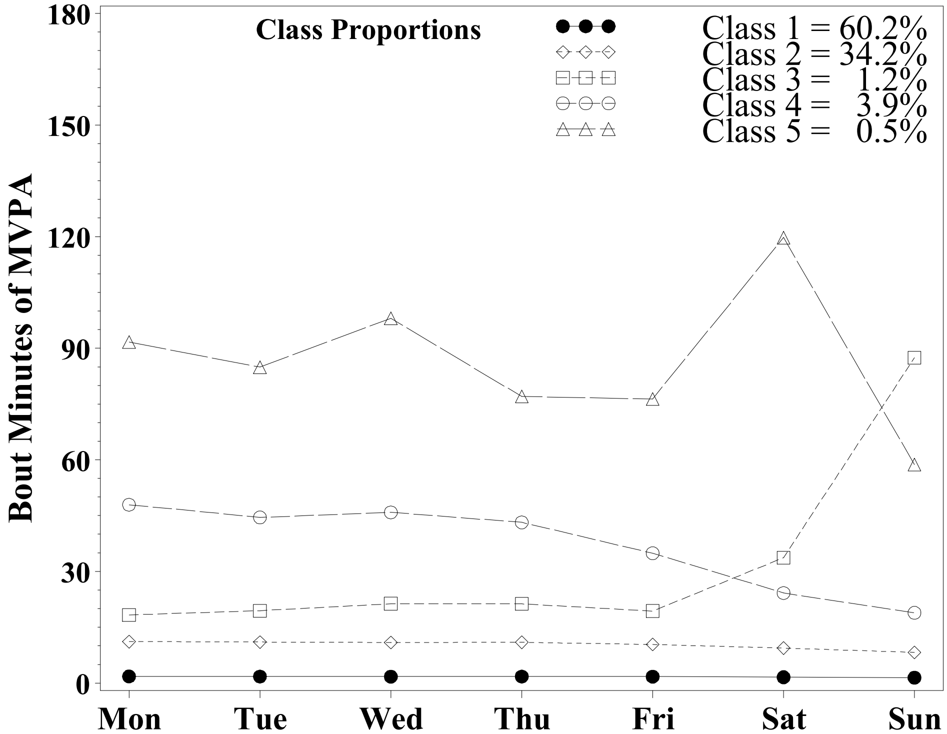


Table 4. 5. Likelihood ratio (LRT) and bootstrap LRT statistical criteria as well as entropy values for deciding on k versus k-1 number classes for bout minutes of MVPA.

Number of classes	1	2	3	4	5	6
Log Likelihood	-102,639	-72,771	-71,830	-71,524	-71,292	-71,119
Number of Parameters	9	28	45	62	79	96
Bayesian Information Criteria (BIC)	205,695	145,771	144,026	143,553	143,229	143,021
Adjusted BIC	205,533	145,682	143,883	143,356	142,978	142,716
Akaike Information Criteria (AIC)	205,381	145,599	143,750	143,172	142,743	142,431
Bootstrap LRT p-value for k-1 vs. k*	N/A	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Entropy	N/A	0.984	0.985	0.976	0.978	0.979

N/A = not applicable
* P-value is comparing whether the addition of one extra class provides statistically significant improvement in the fit of the class assignments.

Figure 4. 3. Five latent classes – bout minutes of MVPA.



Chapter Five

Associations between Adult Patterns of Objectively Measured Moderate to Vigorous Physical Activity and Sociodemographic Characteristics

Introduction

Based on information provided by the Centers for Disease Control and Prevention (CDC) using data from the Behavior Risk Factor Surveillance System (BRFSS), the prevalence of adult participation in at least the minimum recommended level of 30 minutes of at least moderate intensity activity on most, if not all, days of the week was 48.7% in 2005.[4, 7, 78] Reports of such low prevalences have led many researchers in the United States (US) to investigate what sociodemographic and psychosocial characteristics are associated with physical activity. This has become important, not just for delineating the nature and extent of the problem, but also in order to better target interventions.[68]

According to the socioecologic model, health behaviors such as physical activity are influenced through multiple levels, including intrapersonal, interpersonal, and community level (i.e., neighborhood or environmental, organizational, and policy factors).[69-71] Several review papers, covering over 300 articles, indicated numerous strong correlates of physical activity among adults reflecting these socioecologic levels.[9, 10, 70] Cognitive or emotional factors such as perceived barriers to physical activity have been shown to be correlated with leisure time physical activity.[10]

Behavior attributes such as a healthy diet were positively associated with current activity status. [10] Among social and cultural factors, women with high levels of social support were reported to be twice as likely to achieve the recommended levels of physical activity as women with low levels of social support.[83] Environmental factors such as frequency of seeing others exercising were positively associated with physical activity participation.[10]

Several demographic characteristics have also been identified as correlates. Higher age is consistently associated with lower levels of physical activity participation, as is female gender.[10] Non-white race/ethnicity has been associated with lower levels of physical activity compared to whites, although this may only reflect associations with leisure-time physical activity as research has also reported that Hispanics and blacks participate in significantly more occupational physical activity than whites.[10, 78] Socioeconomic status and education are consistent correlates of physical activity behavior, although these associations may also depend on whether occupational, leisure-time or household activity is being measured.[10, 72] For example, one study reported that males in professional occupations self-report significantly more vigorous leisure-time physical activity but significantly less vigorous occupational activity compared to skilled and less-skilled occupations.[79] When assessing whether these occupational groups met the recommendations of 20 minutes of vigorous activity at least three times per week,[73] no difference was found when all three types of activity were considered together. For females, significant differences in meeting the recommendations remained even after all occupational, leisure-time or household activity was considered, comparing those in professional and non-professional occupations.

Several questions remain about the previous physical activity research, however. First, physical activity has typically been measured by self-report, which has been shown to have a low correlation with objectively measured physical activity, with correlations ranging from 0.14-0.53.[11] In addition, reporting bias may have been an issue and this bias may vary by sociodemographic characteristics, leading to associations that are inaccurate or at least present an incomplete understanding of the true associations. Using self-report data also makes it difficult to assess the pattern in which the physical activity was accumulated over time.

In the 2003-2004 National Health and Nutrition Examination Survey (NHANES), accelerometer data was collected on a majority of the ambulatory participants 6 years old and older. This data represents the first national sample of objectively measured physical activity in the US. The accelerometer data was also collected over a seven day period, allowing for an assessment of the number of minutes of physical activity accumulated by each participant on each day of the week.

Using latent class mixture models, the purpose of our study was to determine whether patterns of moderate to vigorous physical activity (MVPA) exist among adults in this sample and whether certain sociodemographic characteristics were associated with these patterns. Specifically, the modeling is conducting using latent class analysis (LCA) for continuous variables in which unobserved (referred to as "latent") classes of activity patterns are ascertained from the observed levels of physical activity across the seven days of accelerometer data. In this type of analysis, a specified number of classes are requested a priori. Then, LCA finds the requested number of best fitting underlying normal distributions for the indicators of these classes (in this case, the daily minutes of physical activity across the seven days of a week). Once classes are established and members are assigned to these classes, the influence of the sociodemographic characteristics on class membership may be assessed. Cross-sectional associations between sociodemographic characteristics and physical activity have not been explored with objectively measured national data in the US. The analysis of the patterns of physical activity may give insight into which sociodemographic groups are insufficiently active.

Materials and Methods

Study population

We analyzed data from the 2003-2004 NHANES, an ongoing health survey with a target population of civilian, non-institutionalized citizens from throughout the entire US. The survey consists of two principle components. The first is an interview, which includes a wide array of topics ranging from tobacco use, sexual behavior, weight history, health insurance and hospital utilization. In addition, basic demographic information for our analysis, including race/ethnicity, gender, education, income and age, was drawn from the interview portion of the survey. The 2003-2004 survey over-sampled low-income persons, Mexican-Americans, African-Americans, and those age 12-19 and 60 years and older.

The second component of the survey is a physical examination, which collects a wealth of information such as anthropometric measurements, audiometry, as well as various laboratory analyses ranging from measles to sexually transmitted diseases. Most participants agreed to the physical examination, during which various health measures were assessed such as blood pressure, blood lipids, glucose and height and weight for the calculation of body mass index (BMI). In addition, the 2003-2004 NHANES collected seven consecutive days of accelerometry measurements among all ambulatory participants 6 years old and older who agreed to wear the activity monitor for a week.

Measuring Physical Activity with Accelerometry

Accelerometers are small, electronic devices that record the acceleration of change in bodily motion either in one dimension (usually the vertical plane), three dimensions, or omni-directional. They are particularly useful in measuring physical activity because they eliminate the potential for recall bias, social desirability bias, and are not dependent on literacy. NHANES 2003-2004 used the ActiGraph Model 7164 accelerometer to collect information on participant's physical activity. This lightweight uniaxial monitor is a technically reliable instrument, both within and across monitors.[54] Most participants (98.2%) wore the monitor for 7 days during normal waking hours. NHANES used one minute epochs to assign a "count' value, which is a relative measure of the changes in momentum that occurred during these periods, which may then be translated into an estimate of physical activity intensity.

Moderate physical activity cut-points based on calibration studies

The accelerometer cut-point used by this study to translate the count value into an estimate of moderate-to-vigorous physical activity (MVPA) was based on a strategy that has been adopted by NHANES researchers.[74] This strategy used a weighted average of several cut-points that have been published from previous prediction equations for adults. [65-68] Each study reported a cut-point for MVPA, which were then weighted by their sample size to arrive at an n-weighted average cut-point of 2,020 counts/min for MVPA.

Accumulating Minutes of MVPA

There are many potential strategies for assigning to an individual a level of physical activity based on their accelerometer data. The present study credited an individual for every minute that their accelerometer registered a count higher than the given 2,020 counts/min MVPA cut-point mentioned above. Then, for each of the seven days, a person is assigned a total number of minutes of MVPA.

Imputation of missing daily minutes of MVPA

The NHANES accelerometry data was very complete in terms of the total number of participant's providing all seven days of data (over 99.8%). However, within each day, there may be extended periods of zero counts, indicating either a non-wearing period or a period with no detectable movement. In order to capture true wearing periods for certain populations, such as the elderly who may remain very sedentary for extended periods of time, only periods consisting of more than one hour of consecutive zeros were treated as missing data.

Monitor malfunctions can also cause periods during which identical, consecutive non-zero values are recorded. For example, the accelerometers will sometimes malfunction and record the maximum value of 32,767 for hours or even days, indicating invalid data. For this reason, data was considered missing if more than 10 minutes of identical consecutive non-zero values were recorded.

In order to assess whether a participant contributed a sufficient amount of non-missing data, each day was divided into the following segments corresponding roughly to nighttime, daytime, early evening, and late evening: midnight to 6:00, 6:00 to 17:00, 17:00 to 21:00, and 21:00 to midnight. Then, within each time segment, a referent wearing period was determined based on how long at least 80% of participants were wearing their monitor during this period, an amount of time ranging from 0 to 100 percent of the time in that segment. If a participant provided an amount of non-missing data that was less than 70% of the length of this referent wearing period, then their data for this time segment was considered insufficient and set to missing. For periods of time in which the accelerometer recorded an insufficient amount of valid data, imputation was used to better estimate the participant's daily minutes of MVPA. This imputation strategy was similar to strategies that have been reported previously.[22] Missing data was then imputed using the Expectation Maximization (EM) algorithm, an iterative imputation technique which uses the values of an individual's other, non-missing data as predictors to estimate the expected value of the total minutes of MVPA for each missing segment of time.[22]

Self-reported measures

Age was recorded at the time of the interview and those over 85 years of age were assigned a truncated value of 85. For descriptive purposes, age was categorized into decades but was left continuous in the final LCA. Race, ethnicity and country of origin questions were recoded into the following categories: 1) Mexican-American, 2) other Hispanic, 3) Non-Hispanic (NH) Black, 4) NH-White and 5) Other Race – including Multi-Racial. Education was categorized as less than high school, high school or GED, and more than high school. The poverty income ratio (PIR) was recorded as a ratio of the self-reported family income to the poverty threshold based on family size. The smallest value of 0 indicated no family income while the highest value is truncated at 5, indicating a family income at least 5 times the poverty threshold for family size. For descriptive purposes, the poverty ratio was categorized into integer values but was left continuous in the final class analysis.

Statistical Methods

Of the 10,122 participants who completed the physical examination during 2003-2004, we excluded those under age 20 based on the fact that previous accelerometer calibration studies generally assessed adults at least 20 years old or older,[20] leaving 5,041 participants. Not all participants in the physical examination completed the accelerometer portion, leaving 4,252 participants. An additional 450 participants were excluded because they did not provide responses to their education level or household income or because they had invalid accelerometer data. Invalid accelerometer data was caused by either not wearing the accelerometer (indicated by consecutive minutes of zero counts) or because the accelerometer malfunctioned. This exclusion left a final population of 3,802 participants.

Descriptive statistics

Using SAS's survey procedures, frequency distributions, weighted distributions and sample weighted percents were computed for the sociodemographic distributions. Weighted means and medians of the average minutes of MVPA across all seven days were also computed according to levels of the sociodemographic variables.

Latent Class Analysis

Employing LCA, we used each participant's seven days of total MVPA to determine whether classes of people exist who tend to accumulate their minutes of physical activity in a similar pattern over the seven days. Classes can be thought of as groups of people who share similar means for the various indicators of class, in this case the seven days of accumulated MVPA. Covariates were added to the model, influencing both the probability density function (pdf) for y, as well as the probability of being in the specific classes. The general pdf for this type of model is defined as follows:

$$f\,[\,\mathbf{y} \mid \boldsymbol{\Sigma}(\boldsymbol{\theta}), \boldsymbol{\mu}(\boldsymbol{\theta}), \mathbf{z}_i] = \sum_{g=1}^{G} P_{g|\mathbf{z_i}} * f[\,\mathbf{y} \mid \boldsymbol{\Sigma}_g(\boldsymbol{\theta}), \boldsymbol{\mu}_g(\boldsymbol{\theta}), \mathbf{z}_i]$$

where **y** is the vector of minutes of MVPA across the seven days, conditioned on $\mu(\theta)$, the vector of mean MVPA across the seven days, and $\Sigma(\theta)$, the covariance matrix for the multivariate normal distribution of the seven days. $\mathbf{z}_i$ is the vector of sociodemographic covariates for subject i, and $Pg|z_i$ is the probability of subject i being in each class g, conditioned on $\mathbf{z_i}$. It is common to assume that the function f is a multivariate normal distribution.[60]

The probability of being a member of a particular class is assigned to an individual based on Bayesian posterior probabilities. Prior probabilities are based on the size of the individual's particular class relative to the entire population. Thus, the posterior probability of an individual being a member of class g is:

$$P_{g|\mathbf{y_i}, \mathbf{z_i}} = P_{g|\mathbf{z_i}} * f[\mathbf{y_i} \mid \boldsymbol{\Sigma}_g(\boldsymbol{\theta}), \boldsymbol{\mu}_g(\boldsymbol{\theta}), \mathbf{z}_i] \; / \; \sum_{g=1}^{G} P_{g|\mathbf{z_i}} * f[\mathbf{y_i} \mid \boldsymbol{\Sigma}_g(\boldsymbol{\theta}), \boldsymbol{\mu}_g(\boldsymbol{\theta}), \mathbf{z}_i]$$

where $Pg|z_i$ is the prior probability of being in class g, conditioned on the covariates $\mathbf{z_i}$. The numerator in this case is the prior probability that subject i belongs to class g, multiplied by the probability for the observed seven days of MVPA for $\mathbf{y_i}$, given the participants covariates and the predicted means and covariance of the seven days of MVPA in class g. The denominator is the sum of the probability densities for all possible class memberships given the individuals set of indicator values y_i, weighted by each class's specific prior probability.

After the posterior probabilities have been determined, individuals are assigned to the class with their highest posterior probability of class membership. This type of assignment is referred to as Modal Allocation. [57]

Structural Equation Modeling Perspective

Figure 1 provides a structural equation modeling representation of the LCA model. In this depiction, the latent classes are defined based on the patterns of physical activity across the seven days of the week. The sociodemographic characteristics are used to predict the derived activity classes, and, at the same time, the sociodemographic characteristics have also been allowed to have a direct influence on the indicators of class.

Given this model, the resulting parameters for the influence of the sociodemographic characteristics on class membership can be interpreted as a type of "relative risk ratio" for an individual with covariates $\mathbf{x_i}$ being in class k compared to an individual with covariates $\mathbf{x_i}$ being in the referent class, relative to someone with the referent category of the $\mathbf{x_i}$ covariates being in the two classes. See Appendix A for a derivation of this interpretation.

Selecting the Number of Classes

Many criteria were used to select the appropriate number of classes. One of the most difficult tasks of latent class analysis is determining the proper number of classes which adequately describe the population without over-specifying the number of class groupings, thereby losing the interpretative value of the classes.[57] A priori, we suspected a large group of inactive participants and a small group of highly active participants, as well as varying class variances. Given this, the bootstrap likelihood ratio test (BLRT), which compares the fit of k classes to k-1 classes, was selected over other statistical tests based on its' superior performance in accurately determining classes with varying class sizes and variance structures.[59] Entropy was also used to assess proper class membership. This measure is based on the mean of the entire study population's predicted probabilities of being in their assigned class, based on modal allocation.[60] It was also necessary to select a number of classes which would allow for the proper assessment of the effect of the sociodemographic variables on class membership, regardless of statistical significance. If too many classes are specified, the associations between class membership and the sociodemographic characteristics may become impossible to calculate due to groups with very small n. As a final criterion, substantive knowledge for establishing the appropriate number of classes is recommended.[61]

Specifying Variance Estimates

Various variance configurations were explored. Completely free estimates, zero covariance estimates with fixed variances across classes, as well as class varying variances with zero covariances were all assessed. However, due to the behavior of the various models, as well as the fact that the estimates of the mean minutes of physical activity for the lowest activity class should have a significantly lower variance than the more active classes, we ultimately settled on a model which allowed the lowest activity class to have variances that differed from all of the other activity classes. In addition, we also allowed the weekend (Saturday and Sunday) to have variances that differed from the Monday to Friday variances, while we set the Monday to Friday variances to be equal across classes. By constraining the model in this way, we tried to create a parsimonious and stable model that still captured some of the complexity of the substantive issues of the analysis. [57]

Direct effects of the sociodemographic characteristics

Lastly, the statistical significance of the direct effects on the 7 days of physical activity was tested by initially adding all of the sociodemographic variables with direct effects on the physical activity variables. The effect estimate divided by its' standard error was compared against a chi-square distribution. Backwards elimination was used until only those variables significant at the 0.10 level remained. This reduction is important due to the substantial number of parameter estimates that would be required if all of the variables' direct effects remained in the final model.

The LCA was performed using MPLUS. [75] The modeling was conducted by requesting a range from 1 to 6 classes a priori as the number of group memberships to predict. Beyond six classes, the sample size of the more active classes became very small and the activity patterns over the seven days became highly unstable. The model was then fit to these increasing numbers of groups, after which the BLRT statistics were analyzed as well as the entropy. While MPLUS allows for complex survey sampling in conjunction with LCA modeling, the software does not currently account for survey sampling when computing the BLRT statistic. As such, the initial analysis was performed without sample weights and cluster sampling. After the number of classes was determined, the analysis was re-run with the cluster and sample weights added back into the model, keeping the number of classes and variance structures constant. In this way, the variances of the effect estimates for the sociodemographic characters were properly inflated to account for the sampling procedures.

Results

The distributions of the sociodemographic characteristics from our study population are presented in Table 1, along with the weighted distributions and the weighted percents. Nearly 23% of the population was 60 years old or older. Over half of the study population had more than a high school education. Income, as measured by a ratio of the poverty index for family composition, was fairly evenly distributed from 0 to greater than 5, and nearly three-quarters of the final population was Non-Hispanic (NH) white.

Table 1 also presents the sample-weighted mean and median minutes of MVPA for each sociodemographic characteristic across all seven days of the week. Higher age was associated with a pronounced lower mean for minutes of MVPA, dropping from an average of 31.2 minutes of MVPA for those between 20 and 30 years old to only 5.2 minutes of MVPA for those 80 years old and older. Higher education was associated with a slightly higher level of physical activity. Males engaged in nearly twice as much physical activity as females. Higher levels of the poverty index were associated with increased physical activity, except for the lowest category (those below the federal poverty level) which was active at nearly the level of those between 3 and 4 times the federal poverty level. Mexicans and other Hispanics were more active on average than NH-whites, NH-blacks and other race/ethnicities. In all cases, the median minutes of MVPA was less than the mean, indicating the skewed distributions.

A five class model was ultimately selected to best represent the statistical and substantive content of this analysis. As represented in Figure 2, most of the participants fell in the two least active classes, representing over 87.5% of the population. The most active class, averaging around 130 minutes of MVPA per day, represented only 1.2% of the population (only 43 participants). Class three represented a class with a lower level of physical activity Monday through Friday but with a substantial increase in physical activity on the weekend, particularly on Sunday. This class, representing 2.1% of the population (76 participants), will be referred to as the "weekend warrior". With the exception of this class, the other four classes all demonstrated a reduction in physical activity on the weekends, particularly on Sunday.

The unweighted five-class model had a highly significant BLRT statistic of <0.0001, indicating that the addition of the fifth class explained a significant amount of the variation based on class membership as compared to a 4 class analysis. The entropy for this five class model was 0.943, indicating that the mean probability that an individual belonged in the class into which they were assigned was ~ 94%. In addition, these class assignments provided large enough groups to assess associations with the sociodemographic characteristics without generating singular covariance matrices.

Table 2 presents the relative proportion of the sociodemographic variables in each class compared to the referent population. Males were significantly ($p<0.05$) more likely to be classified into all of the more active classes compared to the least active referent class. In particular, males were substantially more likely to belong in class 3 (the weekend warrior, RR=7.3) and class 5 (the most active class, RR=8.5). For example, the predicted percentage of all males in class 1 (the referent class) was 32.4% versus 56.3% of all females. For class 3, the predicted percentage of all males is 2.5%, whereas class 3 only represents 0.59% of females.

The class by race/ethnicity analysis generated few statistically significant findings. Other Hispanics were statistically significantly more likely to be in class 5 compared to NH-whites (RR=4.8). Mexicans were 2.9 times more likely to be in class 5 compared to NH-whites, although this latter finding was possibly due to chance based on a 95% CI that included the null association.

Those with less than high school education were statistically more likely to be in class 5, compared to those with high school education. Those with more than high school education were more likely to be in classes 3 and 5, compared to those with a high school education, but these associations were also possibly due to chance based on a 95% CI that included the null association.

A 10 year increase in age was associated with a significantly lower probability that a participant was in any of the more active classes, and this relationship demonstrated a type of dose response by increasing activity level. Thus, for each 10 year increase in age, participants were half as likely, for example, to be in the highest activity class compared to referent class.

A one unit increase in the poverty index demonstrated an opposite relationship. Each one unit increase in the poverty index was associated with a 20% greater relative probability of being in the more active classes 2 and 4, and these associations were not likely due to chance based an a 95% CI that did not include the null association. A one unit increase in the poverty index was associated with a 40% greater relative probability of being in class 5, although this association was not statistically significant.

Figures 3 and 4 show the predicted probability of being in each of the five classes as age increases, stratified by gender. Similar graphs could have been produced for any combination of sociodemographic characteristics, but these two were selected for presentation because both were significantly associated with every class assignment. For females with the referent category values, Figure 4 shows that the largest proportion of the population (47%) at age 20 is in the least active class, and this proportion increases to 85% by age 80. The probability of being in the weekend warrior class is ~0.9% for 20 year old women, but this diminishes to 0.06% by age 80. For the most active class, 0.3% of 20 year old women belong to this group, while 0.01% of 80 year old women do.

For males at age 20 with the other referent category values, Figure 5 shows that the largest percentage of men are in classes 2 and 4; however, by age 30, more men are in the least active class than class 4, and by age 40, the largest single proportion of men are in the least active class. By age 80, 75% of men are in the least active class. 3.2% of 20 year old men are weekend warriors, while 1.2% of 20 year old men are in the most active class. By age 80, these proportions have dropped to 0.4% and 0.09%, respectively.

Discussion

This paper presents, for the first time, a latent class analysis of objectively measured physical activity that simultaneously describes the patterns of physical activity across the course of a week while also assessing the associations between these classes and the participants' sociodemographic characteristics. The class analysis generated a weekend warrior class as well as a highly active class, while all classes except the weekend warrior showed a reduction of activity on the weekend.

The weekend warrior reflected only 2.1% of the population, so nearly 98% of the population engaged in less physical activity during the weekend, a time when many

Americans who work Monday through Friday might actually have more time to engage in leisure time physical activity. This indicates that developing cultural norms that emphasize the importance of leisure time physical activity could lead to substantial increases in the average physical activity levels in the US.

A recent article used self-report data from NHANES and the BRFSS to describe the prevalence of the weekend warrior pattern in the US adult population based on participants accumulating ≥ 150 minutes of MVPA during 1 or 2 days in a week.[62] Because the two surveys asked a different set of questions, approximately 3% of the NHANES population demonstrated a weekend warrior pattern, while only approximately 1% of the BRFSS population fell into this pattern. Our results, while based on objectively measured accelerometer data, found that a similar proportion of the population (2.1%) could be classified as a weekend warrior based on minutes of MVPA.

An inactive class emerged which represented nearly 50% of the entire population. This class was disproportionately populated by women, older participants, and those in the lower income range. In fact, by age 60 less than 1 in 1,500 women living at the poverty level were predicted to be in the most active class and 78.2% of these women were predicted to be in this activity class. Similarly, by age 80 less than 1 in 1,000 males living at the poverty level were predicted to be in the most active class and 75% of these males were predicted to be in the least active class, averaging 12.8 minutes of MVPA per day. This reflects an amount of physical activity significantly below the recommended levels,[4, 7] which indicates that successful interventions are needed for this large inactive segment of the US population.

While the least active class only averaged 12.8 minutes of MVPA per day, the class with the next higher level of activity averaged 28.8 minutes of physical activity per day and thus represents a group of which many, if not most, would meet the physical activity recommendations. Considering classes 2 through 5 together, therefore, close to 52% of the US population met the physical activity recommendations for moderate activity.[3, 6]

Both gender (male) and age (younger populations) were found to be strongly associated with membership in the more active classes. The associations also presented a type of dose-response relationship indicated by males having higher odds of being in each of the successively more active classes. Conversely, higher age had lower odds of being in each of the successively more active classes. Higher socioeconomic status, as measured by the poverty income ratio, was associated with higher levels of MVPA, although for the classes with smaller population sizes the statistical significance was tenuous. These findings were consistent with much of the previous physical activity research.[10]

Although higher levels of educational attainment have generally been found to be associated with higher physical activity levels, this analysis showed a strong association between less than high school education and membership in the most active class. These results are consistent with a report from the National Health Interview Survey in which participants with less than a high school education were nearly 4 times as likely to report engaging in ≥ 5 hours / day of hard occupational activity compared to those with more than a high school education.[76] Although occupational information was collected during the NHANES interview, these data had not been made publicly available at the time of writing. Therefore, while the association between education and membership in the most active class could be related to occupational PA, future analysis would be needed to determine the source of this association. Similarly, those classified as non-Mexican Hispanics presented a strong association with being in the most active class, which could also be driven by occupational physical activity.[76]

The present work represents the first LCA analysis which uses objectively measured, nationally representative physical activity data sampled from across the US to assess the associations between patterns of physical activity and the sociodemographic characteristics of the study population. The results of this type of LCA analysis also provide a clear and intuitive visual representation for how certain variables, such as age and income level, affect activity class membership over the range of the respective variables. The high probability that older, lower-income women were members of the least active class was an important finding. While many of the results of this novel use of LCA correspond with previous research, a few findings need further exploration. For example, the increased probability that non-Mexican Hispanics, Mexican's and blacks belong in the most active class, while not all statistically significant, reflect an import divergence from previous results using self-reported physical activity data.[10] Determining the source of this physical activity could be an important step toward developing appropriate interventions, which in the past may not have accounted for work related activity among these sociodemographic sub-populations and could thus help address racial disparities. This analysis highlights the importance of collecting information on all modes of activity and not just leisure-time physical activity.

The primary weakness of this paper, a weakness shared with most of the other sociodemographic analyses of PA, is that the data were collected cross-sectionally and thus the results may only be viewed as correlates of physical activity. In the review by Bauman et. al.[9], they emphasize that most of the associations reported in the current literature do not necessarily reflect causal relationships. Distinguishing between determinants of physical activity and simple correlations is important both for the interpretation of results as well as for the targeting of interventions.[10] Future research is needed to separate the causal associations from mere correlates.

In addition, many of the other associations did not achieve statistical significance. This was particularly true for the "weekend warrior" class and the most active class, both of which were substantively important groups but had too few participants to adequately assess the parameter estimates, even though some of the associations were fairly large in magnitude. Future analysis of NHANES, after additional accelerometer data has been made public, may help resolve this problem since accelerometry continued to be collected in a similar manner in 2005-06.

Uniaxial accelerometers do not capture all types of physical activity, particular static activities such as raking leaves or riding a bike.[77] Therefore, while the current analyses do not rely on self-report, they may still not reflect the true activity levels of the US population. Similarly, the cut-point for what constitutes MVPA is also sensitive to the types of activities being done. Changing the cut-point would affect the amount of physical activity that participants were credited for, which in turn could have affected the outcomes of the latent class analysis.

Also, we did not explore the differences below the moderate level of physical activity and, therefore, we don't know how inactivity and light activity compare to moderate activity. We previously reported efforts to assess the patterns of vigorous physical activity in the same NHANES population, but the very low participation in this type of physical activity made the analysis of class membership impossible.

One analytical weakness is worth noting. The use of the BLRT test statistic was not available with the simultaneous use of the sample weights, which could have affected the final decision for the number of classes. However, because the BLRT only assesses the statistical benefit of adding an additional class, which in this case was highly significant, we felt that by re-running the analysis with the sample weights added back in, we were capturing a meaningfully relevant number of classes while at the same time producing effect estimates with appropriate variances and activity classes with proper patterns.

In conclusion, both gender and age emerged as significant predictors of membership in the different patterns of physical activity. A combination of certain sociodemographic characteristics such as older females with lower family income was associated with a high probability of being in the least active class, which averaged only 12 minutes of MVPA per day. The higher odds of Mexicans, other Hispanics, and NH-blacks being in the most active class, although not all statistically significant, was novel and needs future research to determine the source of the high level of activity.

Figure 5. 1. Structural Equation Model for the prediction of the latent classes based on the minutes of physical activity across the seven days of the week, with sociodemographic characteristics influencing class membership as well as direct effects on each day's minutes of physical activity.

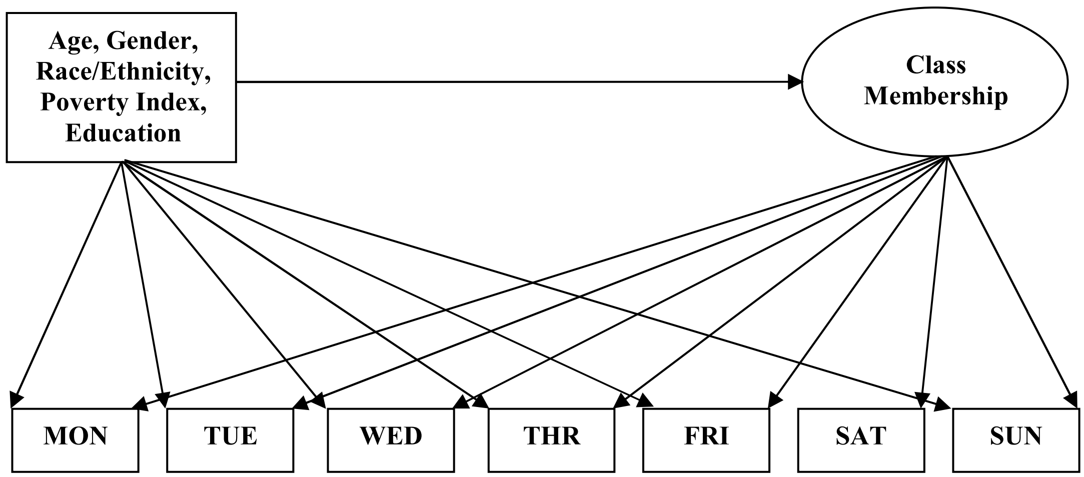


Table 5. 1. Sample weighted frequency distributions of the demographic variables for the final study population.

		N	Weighted N	Weighted %	Minutes of Daily MVPA	
					Mean	Median
Age	**20 to <30**	645	38,382,093	18.7	31.2	25.3
	30 to <40	618	41,376,198	20.2	30.3	24.4
	40 to <50	637	44,500,615	21.7	26.2	20.5
	50 to <60	487	34,470,493	16.8	21.4	16.2
	60 to <70	614	22,448,718	10.9	14.2	8.7
	70 to <80	484	16,538,140	8.1	8.5	4.2
	80+	317	7,568,412	3.7	5.2	2.8
Education	**Less than High School**	1,077	35,395,144	17.2	22.5	13.4
	High School	940	53,985,575	26.3	23.1	17.8
	More than High School	1,785	115,903,950	56.5	24.7	18.7
Gender	**Female**	1,956	106,855,170	52.1	17.7	12.8
	Male	1,846	98,429,499	47.9	30.5	24.3
Poverty Index Ratio	**0 to <1**	678	25,432,107	12.4	23.9	16.7
	1 to <2	1,032	43,570,060	21.2	22.3	14.2
	2 to <3	640	35,028,892	17.1	22.0	16.0
	3 to <4	456	30,364,379	14.8	23.5	16.9
	4 to <5	368	26,126,000	12.7	22.8	18.5
	5+	628	44,763,232	21.8	27.6	22.6
Race/Ethnicity	**Mexican**	792	15,940,237	7.8	30.8	23.4
	Other Hispanic	106	726,1321	3.5	32.6	25.7
	NH-White	2,037	148,475,909	72.3	22.8	17.1
	NH-Black	714	23,034,729	11.2	23.6	17.0
	Other	153	10,572,473	5.2	23.5	16.2

Figure 5. 2. Five latent class analysis for Moderate-to-Vigorous Physical Activity across the seven days of the week.

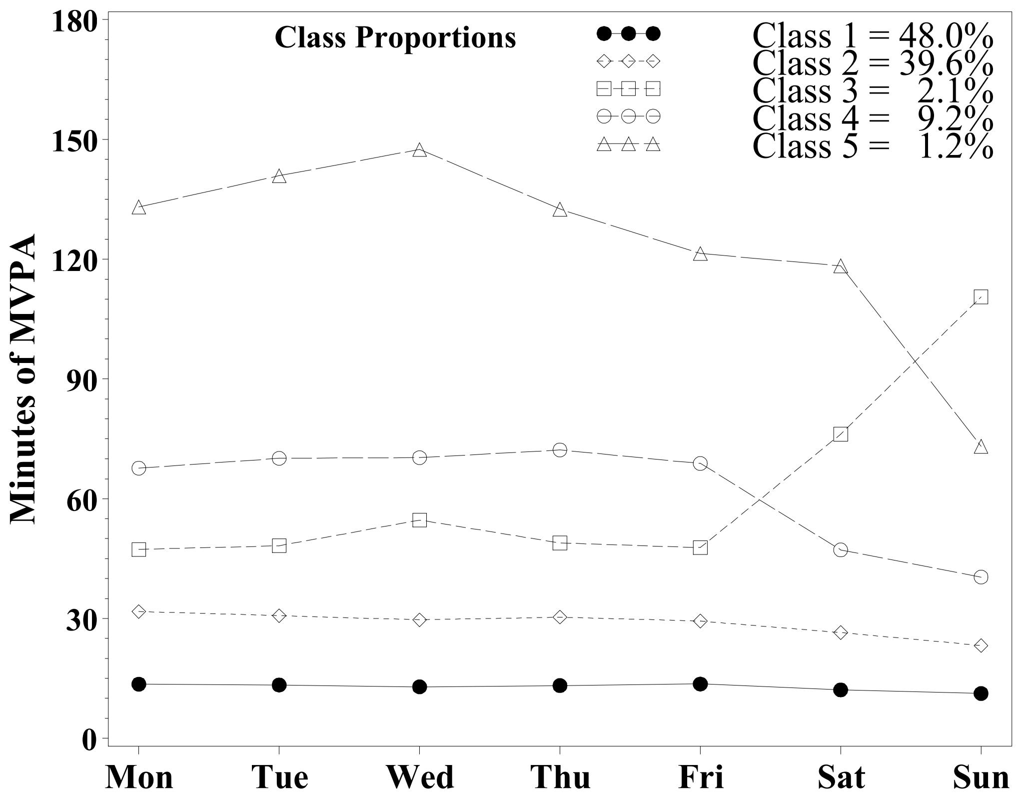


Table 5. 2. Relative proportion of the sociodemographic variables in each class compared to the referent population (white, female, high school education, aged 30 and with a poverty index ratio of 1), relative to their proportions in the least active class.*

Gender – Relative proportion (and 95% confidence internal) of males in each class compared to the least active class (Class 1)

	Males
Class 5	8.5 (3.6, 20.2)
Class 4	5.1 (3.5, 7.6)
Class 3	7.3 (1.8, 28.6)
Class 2	2.1 (1.7, 2.4)
Class 1 - Referent	1.0

Race/Ethnicity – Relative proportion (and 95% confidence internal) of each race/ethnicity category in each class compared to the least active class (Class 1)

	Blacks	Mexicans	Other Hispanic	Other Race/Ethnicity
Class 5	1.6 (0.5, 4.4)	2.9 (0.8, 10.0)	4.8 (1.7, 13.3)	0.3 (0.1, 1.8)
Class 4	0.9 (0.5, 1.7)	1.6 (0.8, 3.0)	2.3 (0.9, 6.2)	0.5 (0.1, 2.2)
Class 3	0.5 (0.2, 1.1)	1.0 (0.4, 2.2)	0.4 (0.0, 5.0)	1.9 (0.7, 5.3)
Class 2	0.8 (0.6, 1.1)	1.3 (1.0, 1.7)	1.3 (0.6, 2.8)	0.7 (0.5, 1.1)
Class 1 - Referent	1.0	1.0	1.0	1.0

Education– Relative proportion (and 95% confidence internal) of less than high school and more than high school education in each class, compared to the least active class (Class 1)

	Less than High School	More than High School
Class 5	2.8 (1.0, 7.4)	1.9 (0.6, 6.5)
Class 4	1.1 (0.7, 1.7)	0.7 (0.5, 1.1)
Class 3	1.1 (0.2, 5.1)	2.3 (0.6, 8.4)
Class 2	0.9 (0.6, 1.2)	1.1 (0.8, 1.4)
Class 1 - Referent	1.0	1.0

Age – Relative proportion (and 95% confidence internal) of a 10 year increase in age in each class, relative to the least active class (Class 1)

	10 year increase in Age
Class 5	0.5 (0.4, 0.7)
Class 4	0.6 (0.5, 0.6)
Class 3	0.6 (0.4, 0.8)
Class 2	0.7 (0.7, 0.8)
Class 1 - Referent	1.0

Poverty Index – Relative proportion (and 95% confidence internal) of a 1 unit increase in the poverty index in each class, relative to the least active class (Class 1)

	1 unit increase in Poverty Index
Class 5	1.4 (0.9, 2.0)
Class 4	1.2 (1.0, 1.4)
Class 3	1.2 (0.9, 1.7)
Class 2	1.2 (1.2, 1.3)
Class 1 - Referent	1.0

*All associations are adjusted for the other sociodemographic characteristics.

Figure 5. 3. Probability that a female with the referent category values belongs in each of the five activity classes (corresponding to those presented in figure 3), according to their age.

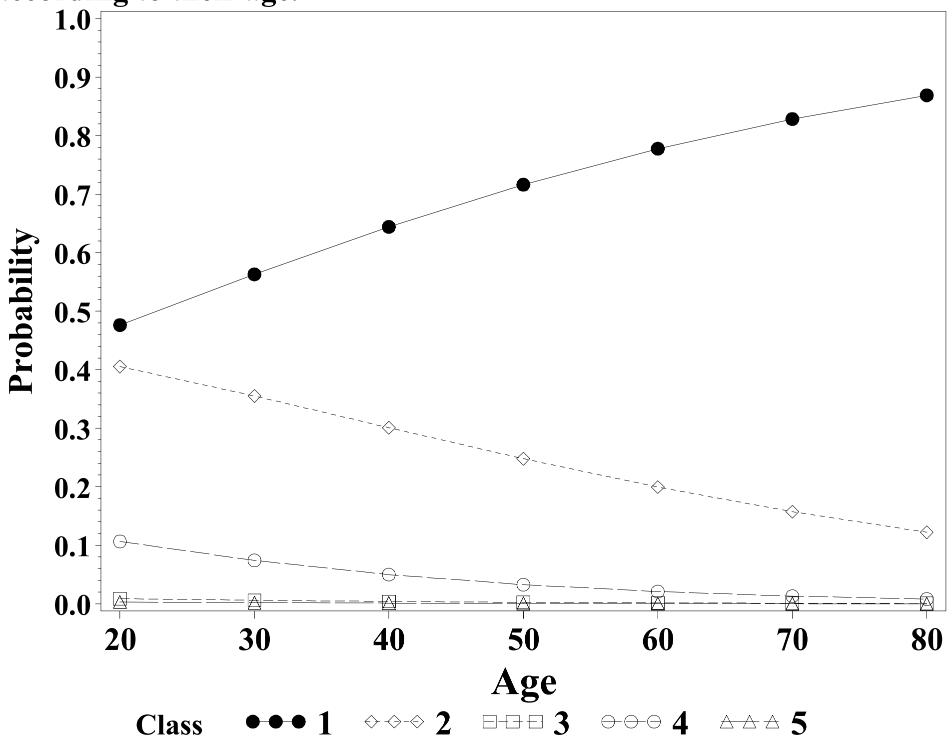


Figure 5. 4. Probability that a male with the referent category values belongs in each of the five activity classes (corresponding to those presented in figure 3), according to their age.

Chapter Six

Associations between Patterns of Objectively Measured Physical Activity and Risk Factors for the Metabolic Syndrome

Introduction

The last several decades have produced a substantial body of literature indicating the health benefits of physical activity, including reduced risk of all-cause mortality, coronary heart disease (CHD), and CHD risk factors.[31] Many recent review articles also separate the benefits of physical activity into both preventive as well as palliative effects on disease and disease progression.[32, 38] Nevertheless, the prevalence of physical activity in the US continues to be suboptimal for most as work and daily activities become more and more sedentary.[8, 9] In 2004, the National Center for Health Statistics (NCHS) reported that 32.2% of adults were obese (as defined by a body mass index (BMI) ≥ 30 kg/m^2). Extreme obesity (BMI ≥ 40 kg/m^2), which in 1990 only affected 0.5% of men and 1.2% of women, presently affects 2.8% of men and 6.9% of women.[2, 47]

According to the National Cholesterol Education Program's (NCEP) Adult Treatment Panel III report (ATP III), these two factors (overweight/obesity and physical inactivity) along with genetic factors are the primary root causes of the metabolic syndrome, described as a constellation of CHD risk factors of metabolic origin.[27] This syndrome and its' risk factors have become "a coequal partner to cigarette smoking as contributors to premature coronary heart disease".[27] As such, the ATP III report indicated that treating the metabolic syndrome is one of the most important clinical goals for reducing the risk of CHD, second in importance only to the primary goal of controlling high levels of low-density lipoproteins (LDL).[27]

From a clinical perspective, the diagnosis of the metabolic syndrome requires at least three of the following: high waist circumference, low levels of high-density lipoprotein (HDL), and elevated levels of triglycerides, blood pressure (BP) and fasting glucose.[27] Congruent with this diagnosis and the importance that physical activity is believed to play in the development of the syndrome, numerous research papers report negative associations between physical activity and hypertension, diabetes, obesity, triglycerides and low levels of HDL, the components of the clinical definition of the metabolic syndrome.[31, 32, 35, 40]

Many of these associations, however, may be somewhat transient in nature. For example, higher levels of insulin mediated glucose uptake have been demonstrated for up to 48 hours after exercise, but the levels return to normal after 5 days.[78] Similarly, during bouts of physical activity triglycerides are hydrolyzed by lipoprotein lipase (LPL) into glycerol and fatty acids which are used as energy for muscle contractions. LPL activity has been shown to increase during bouts of PA, but this increased activity only lasts up to 48 hours after acute endurance exercise.[29] Studies have also shown that immediately following bouts of exercise there is a reduction in systemic vascular resistance while cardiac output returns to lower levels, leading to periods of hypotension.[79] These periods can last for 2 hours among healthy individuals but up to 12 hours among hypertensives.[80]

Given the relatively short term effects of physical activity on some of the risk factors for the metabolic syndrome, those who demonstrate regular activity patterns across a seven days week would be associated cross-sectionally with fewer diagnoses of the metabolic syndrome compared to those with irregular activity. Therefore, using the seven days of accelerometer data from the 2003-2004 National Health and Nutrition Examination Survey (NHANES), the purpose of this analysis is to employ latent class analysis (LCA) to determine the whether certain patterns of objectively measured physical activity among adults in this sample are disproportionately associated any of the risk factors for or the diagnosis of the metabolic syndrome.

In LCA analysis, a specified number of classes are requested a priori. Then, LCA finds the requested number of best fitting underlying activity patterns using the indicators of these classes (in this case, the daily minutes of moderate-to-vigorous physical activity (MVPA) across the seven days of a week). New developments in LCA methods then allow for the simultaneous assessment of the associations between these derived patterns of physical activity and the risk factors for the metabolic syndrome.

Determining whether certain patterns of physical activity are associated with the metabolic syndrome could help target interventions for those who do not accumulate physical activity in an optimal way. For example, while the current recommendations are to be moderately active at least 30 minutes on most, and preferably all days of the week,[3, 6] a large portion of the population has employment which requires them to be sedentary for the majority of the day throughout the work week. This would potentially allow for greater time during the weekend for activity. If this pattern of physical activity is insufficient, then interventions incorporating activity during the typical work-week would be important. Conversely, it may be that a significant amount of physical activity only on the weekend (a "weekend warrior") is sufficient for desired health benefits. This analysis was thus performed to help fill in these very important gaps in our understanding of the importance of PA.

Because it was not known a priori what patterns would be found, a secondary analysis was also performed in order to directly assess the associations between regular physical activity and the clinical diagnosis of and the risk factors for the metabolic syndrome. Participants were classified into quartiles of the co-efficient of variation (CV) based on their minutes of MVPA across the seven days. A low CV would indicate that an individual accumulated their minutes of MVPA consistently over the course of the week, while a high CV would indicate days of high and days of low MVPA accumulation, similar to a weekend warrior. The quartiles of CV were then used to assess whether the variation in the accumulated MVPA was associated with the metabolic syndrome.

Materials and Methods

Study population

We analyzed data from the 2003-2004 NHANES, an ongoing health survey with a target population of civilian, non-institutionalized citizens from throughout the entire United States. The survey consists of two principle components. The first is an interview, from which the basic demographic information for our current analysis was obtained, including race, gender, education, income and age. In the 2003-2004 NHANES, low-income persons, Mexican-Americans, African-Americans, and those age 12-19 and 60 years old or older were over-sampled.

The second component of the survey is a physical examination. Most participants agreed to the physical examination, during which the various health measures for our analysis were assessed, including blood pressure, blood lipids, fasting blood glucose and height and weight for the calculation of body mass index (BMI). In addition, the 2003-2004 NHANES collected seven consecutive days of accelerometry measurements among all ambulatory participants 6 years old and older who agreed to wear the monitor for a week.

Risk Factors for the Metabolic Syndrome

For analysis purposes, all of the variables were categorized according to their relevant clinical cut-points. Hypertensive status was classified based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).[81] Thus, normotensive was based on a systolic blood pressure (SBP) of <120 mm Hg and a diastolic blood pressure (DBP) of <80 mm Hg. Pre-hypertensive was based on a SBP of 120-139 mm Hg or a DBP of 80-89 mm Hg. And Hypertensive was based on a SBP of 140+ mm Hg or a DBP of 90+ mm Hg or if the participant was taking medication for hypertension. A fasting blood glucose of 126 mg/dL or greater was considered the clinical cut-point for the diagnosis of diabetes,[82] as well as whether the participant was taking insulin or pills for high blood glucose levels. Clinical categories used to classify triglycerides and HDL were based on the NCEP cut-points.[27] Thus, normal triglycerides levels were considered <150 mg/dL, borderline-high triglycerides were considered 150 to 199 mg/dL, and high triglycerides were considered ≥ 200 mg/dL or taking medication for high cholesterol. HDL levels were categorized as low (high risk) if below 40 mg/dL or taking medication for cholesterol. BMI was based on the standard calculation of weight in kilograms divided by standing height in meters squared. According to the cut-points published by the National Heart, Blood and Lung Institute (NHLBI)[83], BMI was categorized into four categories: <18.5 kg/m^2 = Underweight, 18.5-24.9 kg/m^2 = Normal, 25-29.9 kg/m^2= Overweight, and 30+ kg/m^2 = Obese. Finally, for the purposes of this analysis, participants were classified as having the metabolic syndrome if they fell into the highest risk category of at least 3 of these risk factors.

The analysis software treats the risk factor variables as ordinal, not simply categorical, which we did not feel reflected the true relationship for the associations with the four BMI categories, specifically comparing the odds for the lowest BMI category to the next three higher BMI categories. In addition, because only 42 participants fell into the lightest BMI category, they were excluded leading to a modeling strategy that we believe was more appropriate given the model assumptions and the sample size requirements needed for the associations between the activity classes and the risk factors.

Measuring physical activity with accelerometry

Accelerometers are small, electronic devices that record the acceleration of change in bodily motion either in one dimension (usually the vertical plane), three dimensions, or omni-directional. They are particularly useful in measuring physical activity because they eliminate the potential for recall bias, social desirability bias, and are not dependent on literacy. NHANES 2003-2004 used the ActiGraph Model 7164 accelerometer to collect information on participant’s physical activity. This lightweight uniaxial monitor is a technically reliable instrument, both within and across monitors.[54] NHANES used one minute epochs to assign a “count’ value, which is a relative measure of the changes in momentum that occurred during these periods, which may then be translated into an estimate of physical activity intensity.

Moderate physical activity cut-points based on calibration studies

The accelerometer cut-point used by this study to translate the count value into an estimate of moderate-to-vigorous physical activity (MVPA) was based on a strategy that has been adopted by NHANES researchers.[74] This strategy used a weighted average of several cut-points that have been published from previous prediction equations for adults.[22-25] Each study reported a cut-point for MVPA, which were then weighted by their sample size to arrive at an n-weighted average cut-point of 2,020 counts/min for MVPA.

Accumulating minutes of MVPA

There are many potential strategies for assigning to an individual a level of physical activity based on their accelerometer data. The present study credited an individual for every minute that their accelerometer registered a count higher than the given 2,020 MVPA cut-point. Then, for each of the seven days, a person was assigned a total number of minutes of MVPA.

Imputation of missing daily minutes of MVPA

The NHANES accelerometry data was quite complete in terms of the total number of participants providing all seven days of data (over 99.8%). However, within each day there may be extended periods of zero counts, indicating either a non-wearing period or a period with no detectable movement. Periods consisting of one hour or more of consecutive zeros were treated as missing data. In addition, periods of monitor malfunctioning were also considered missing (e.g., 10 minutes of identical consecutive non-zero count values). Occasional missing accelerometry data within a participant's 7-day record was then imputed using the expectation maximization (EM) algorithm, an iterative imputation technique which uses the values of an individual's other, non-missing data as predictors to estimate the expected value of the total minutes of MVPA for each missing segment of time.[22]

Self-reported variables

Gender was recorded at the time of interview as was age, which, for those over 85 years of age, was assigned a truncated value of 85. Race, ethnicity and country of origin questions were recoded into the following categories: 1) Mexican-American, 2) other Hispanic, 3) Non-Hispanic (NH) Black, 4) NH-White and 5) Other Race – including Multi-Racial. Education was categorized as less than high school, high school or GED, and more than high school. The poverty income ratio (PIR) was recorded as a ratio of the self-reported family income to the poverty threshold based on family size. The smallest value of 0 indicated no family income while the highest value is truncated at 5, indicating a family income at least 5 times the poverty threshold for family size.

Statistical Methods

Of the 10,122 participants who completed the physical examination during 2003-2004, we excluded those under age 20 based on the previous accelerometer calibration studies for adults which generally assessed those at least 20 years old or older.[19] This left 5,041 participants. Not all participants in the physical examination agreed to complete the accelerometer portion, leaving 4,252 participants. An additional 450 participants were excluded because they did not provide responses to their education level or household income or because they had no days of valid accelerometer data with which to impute the other, missing days. A lack of valid accelerometer data was caused by either not wearing the accelerometer (indicated by consecutive zeros) or because the accelerometer malfunctioned. This left 3,802 participants. In the end, 344 were removed for missing height, weight, HDL levels or blood pressure, leaving a final population of 3,458. For the analysis of triglycerides and fasting blood glucose, which were only collected on members of the morning examination, only 1,620 were available for analysis. There were no differences in the distributions of either the sociodemographic characteristics or the relevant risk factors (BP, blood glucose, and BMI) comparing those who sat for the morning examination and those who sat for the afternoon examination (chi-square and t-test p-values > 0.15 for all comparisons).

Using SAS's survey procedures, the distribution of each of the risk factors were produced, along with their sample-weighted n, sample weighted percent and standard error.

Interested readers may refer to our earlier papers for an in depth description of the statistical foundations of the LCA modeling as well as an overall description of the LCA modeling strategy employed.[84, 85] Figure 2 provides a structural equation representation of the model. In this depiction, the latent classes are defined based on the patterns of physical activity across the seven days of the week. The socio-demographic characteristics are used to help predict membership in the derived activity classes, and, at the same time, the socio-demographic characteristics have been allowed to have a direct influence on the indicators of class as well as the six biological markers of health.

Finally, the classes derived from the levels of physical activity across the seven days are used as a categorical indicator for predicting the risk factors.

Given this strategy (classes predicting the multiple risk factors), the ordinal variables representing the risk factors are assumed to follow an ordered polytomous logistic regression.[60] Thresholds, analogous to intercept parameters, are established above which a subject is assumed to fall into the next higher category of the ordinal variable.[86] With this model structure, the exponentiated difference between the thresholds of any two classes may be interpreted as the odds ratio that a member of one class falls above the ordinal category, compared to the odds that a member of the other class falls above the ordinal category. See the appendix for a derivation of this interpretation.

The least active class was used as the referent class. Odds ratios for each of the risk factors in each class were calculated with respect to this lowest activity class. The odds ratios were based on comparing the thresholds of the highest level of each ordinal variable.

Secondary analysis

The current physical activity recommendations call for 30 minutes of physical activity on most days of the week.[3] Because for the secondary analysis we were primarily interested in whether the regularity of physical activity is associated with the metabolic syndrome, we only included those participants meeting the current physical activity recommendations in order to remove the possibility that any associations found would be driven by the underlying level of activity. By defining “most days of the week” as 5 days, then only participants who accumulated at least 150 minutes of MVPA over the seven days were selected. Critical for this analysis, however, was that we allowed these 150 minutes to be accumulated in any way, for example, two days of 75 minutes of MVPA, and not just on days of 30 minutes or more. 1,392 participants from the final study population accumulated 150 minutes of physical activity in this way, while 710 were available for analysis of the triglycerides and 692 for blood glucose due to the reduced population who participated in the morning exam. Finally, 643 were available for the analysis of the metabolic syndrome.

Among this population, participants were classified into quartiles of the co-efficient of variation (CV) based on the minutes of MVPA across the seven days. The CV quartiles were then regressed on the each of the risk factors, adjusting for the socio-demographic variables, in order to assess whether "how" the participants accumulated their MVPA was associated with the metabolic syndrome or its' risk factors.

Results

The frequency distributions of the five risk factors and the metabolic syndrome are presented in Table 1. 33.7 percent of the population was classified as having hypertension or taking medicine for hypertension. Only 6.4 percent of the population was classified as having high blood glucose or taking medication for blood glucose levels. Roughly a third of the population fell into each of the three BMI categories, while 26.9% had low HDL levels and 28.3% had high triglycerides levels. Overall, nearly 20% of the population was classified as having the metabolic syndrome.

A five class model was ultimately selected to best represent the statistical and substantive content of this analysis. Figure 2 represents the five class LCA analysis for the larger population with non-missing BMI, HDL and blood pressure. Most of the participants were classified into the two least active classes, representing 87.3% of the population. The most active class averaged 122.6 minutes of MVPA per day and represented only 1.3% of the population. Class three represents a class with a lower level of physical activity Monday through Friday but with a substantial increase in physical activity on the weekend, particularly on Sunday. This class, representing 1.9% of the population, will be referred to as the "weekend warrior". With the exception of this class, the other four classes all demonstrated a reduction in physical activity on the weekends, particularly on Sunday.

Figure 3 represents the LCA results for the subset of the population for which triglycerides and fasting blood glucose levels were recorded during the morning interview. The patterns for this reduced population were similar in appearance to those in Figure 2, with the exception of class 3, which resembles that of the "weekend warrior" but with substantially more accumulated minutes of MVPA from Monday through Thursday. For purposes of comparison, however, this class, too, will be referred to as the "weekend warrior", representing 1.1% of the population. Most of the participants were classified into the two least active classes, representing 89.1% of the population. The most active class again represented 1.3% of the population, and all but the weekend warrior demonstrated a reduction in physical activity on the weekends.

Figure 4 presents the results of the odds-ratio (OR) associations between the class assignments and the risk factors for the metabolic syndrome comparing the four more active classes with class 1, the most sedentary class. The results for the ordinal variables with more than two levels (BMI, BP, and triglycerides) reflect the comparison of the highest level of the risk factor to the lower levels.

Membership in all of the more active classes led to statistically significantly lower odds of obesity compared to the least active class, based on a 95% confidence interval (CI) that did not include the null association.

Classes 2 through 4 had significantly lower odds of high blood pressure, with the weekend warrior having nearly one-fifth of the odds compared to the least active class. While the most active class had slightly lower odds of high blood pressure than the least active class, this result was not significant.

Classes 2 and 4 had significantly lower odds of having low levels of HDL, with class 4 experiencing 26% of the odds of low HDL levels compared to the least active class. The weekend warrior and the most active class both demonstrated lower HDL levels, but neither result was significant based on CIs that included the null.

The blood glucose, triglyceride and metabolic syndrome analyses represented roughly half of the overall study population, causing less stability in the results. No participants in classes 3 and 5 experienced high blood glucose, leading to an OR of zero with no variance estimates. Class 4 experienced significantly lower odds of high glucose levels, odds that were nearly 10% of the odds of the least active class.

Both classes 2 and 4 indicated statistically significant lower odds of high triglyceride levels compared to the least active class. The associations between classes 3 and 5 and high triglyceride levels were close to the null but had CIs that were very wide, indicating unstable results or imprecise estimates.

Similarly, classes 2 and 4 indicated statistically significant reductions in the odds of being classified as having the metabolic syndrome, while class 3 presented no participants with the metabolic syndrome. The odds ratio for class 5 was very close to the null association with wide CIs.

Figure 5 presents the odds ratios and 95% CIs from the secondary analysis of the risk factors comparing the three higher quartiles of CV with the lowest quartile of CV, among those study participants who achieved at least 150 minutes of MVPA over the seven days. BMI, high BP, and low HDL all demonstrated associations that, for all three quartiles of CV, were very near the null association compared to the lowest quartile of CV. For high blood glucose, only the 3rd quartile of CV demonstrated lower odds compared to the 1st quartile, while the 2nd and 4th quartiles of CV had ORs very near the null with wide CIs, compared to the lowest quartile of CV. The ORs for high triglycerides were farther from the null, but all three quartiles included the null association compared to the lowest quartile of CV. Finally, the odds ratios for the metabolic syndrome demonstrated the 3rd quartile of CV with lower odds compared to the 1st quartile, while the 2nd and 4th quartiles had ORs somewhat above the null but with wide CIs.

Discussion

For the first time, objectively measured physical activity data sampled from throughout the US has been analyzed to determine the patterns of physical activity across a seven day week while simultaneously examining the associations between these patterns and several biological markers of health. The primary observation from the analysis of the five physical activity classes is that, in nearly all cases, the four more active classes were associated with lower odds of the five risk factors and the metabolic syndrome itself compared to the most sedentary class. The one exception was the association between class 5 and triglyceride levels, although even this result was close to the null and had a very wide CI. The consistency of these results across the various risk factors provides encouraging evidence of the potential benefits of physical activity.

Classes 2 and 4 comprised roughly 40 and 9 percent of the population, respectively, and thus produced point estimates which were much more stable than those produced for classes 3 and 5 which composed 1.9 and 1.3 percent of the larger population, respectively. Comparing, then, only these two larger classes, class 4 had notably lower odds of all of the risk factors compared to class 2, and class 2 had significantly lower odds of all of the risk factors compared to the least active class, indicating a consistent dose response relationship. This is important because class 2 represents a class of which most participants would meet the physical activity recommendations of 30 minutes of physical activity on most days of the week. Nevertheless, these results indicate that participating in physical activity at roughly twice this recommended amount may be associated with lower odds of being classified with any of the risk factors used in this study.

One recent article has attempted to assess the effect of the "weekend warrior" activity pattern on the risk of mortality.[45] In this study, the mortality outcomes of the weekend warrior, defined as those who accumulate a large quantity of physical activity (≥1000 kcal/week) over a short period of time (1-2 days/week), were compared to those who accumulate a similar amount of activity (≥1000 kcal/week) over a longer period of time (3+ days/week), along with those who are insufficiently active (500-999 kcal/week) or sedentary (<500 kcal/week). Among low risk men, weekend warriors demonstrated the lowest relative risk of mortality, while among high risk men only the regularly active showed improved mortality risks as compared to the most sedentary group.

In the current study, comparing classes 3 and 4 represents a similar assessment. Class 3, the weekend warrior, accumulated a large portion of their minutes on the weekend, while class 4 accumulated a consistently larger amount of activity Monday through Friday, with a reduction on the weekend. For obesity, low HDL, and high triglycerides, the weekend warrior had higher odds compared to class 4, while the weekend warrior had lower odds of high blood pressure, blood glucose and the metabolic syndrome. However, the small sample size for the weekend warrior makes these comparisons tenuous. Thus, it is unclear from this analysis whether an individual benefits to a greater degree from a consistently active daily lifestyle or from a highly active weekend lifestyle.

The secondary analysis resolved some of the problems related to small class sizes. In this analysis, no association was observed between the amount of variation in the accumulation of physical activity over a seven day week and the respective risk factors, with the exception of the 3rd quartile's association with significantly lower blood glucose levels and the metabolic syndrome. These results in combination with the previous results present a relatively consistent picture that meeting the recommendations for physical activity is indeed associated with lower odds of all of the biological markers related to the metabolic syndrome, i.e. BP, triglycerides, blood glucose, HDL, BMI as well as the syndrome itself. It may also be that more physical activity may be better. However, among those participants who met the minimum requirement for total physical activity in a week, acquiring that physical activity consistently over the week had associations with all of the risk factors that were similar to acquiring physical activity erratically. For example, two days in which 75 minutes of MVPA are accumulated may lead to similar benefits as 30 minutes of MVPA spread over 5 days.

The lack of association between the quartiles of CV and any of the risk factors for the metabolic syndrome was interesting given our initial hypothesis. Among those who are regularly active, the cross-sectional assessment should have had a higher probability of sampling during a post-activity period compared to those who were irregularly active. As such, the post-exercise reductions in certain measures including blood glucose, triglycerides and blood pressure might have been apparent in the odd ratio analyses, but in this case were not. One possible explanation is that, while physical activity is known to affect all of the relevant risk factors, it may not affect classification according to the clinical cut-points used in this study. Another possibility is that there was some non-random selection for when participants were assessed, i.e. those who were irregularly active chose to be assessed on the day that they also set aside for physical activity. Another possibility is that the sample size was insufficient to adequately assess associations which were only small in magnitude.

This paper has many strengths worth noting. The present work represents the first LCA analysis which uses objectively measured, nationally representative physical activity data sampled from across the United States to assess the associations between patterns of physical activity and several biological markers of health. Structuring the analysis around those factors believed to be associated with the metabolic syndrome helped present a clearer view of how physical activity may influence the risk factors for cardiovascular disease. The five classes provided a potent indicator of overall activity level by capturing many important aspects of physical activity including frequency, intensity and time at or above the moderate-to-vigorous intensity level. For analysis purposes, therefore, this data reduction very concisely captures many of the important aspects needed to adequately assess the associations between physical activity and health status. A large study population led to many statistically significant and clinically meaningful results. The secondary analysis provided an important contribution to the understanding of whether the overall health benefits received from physical activity are altered by "how" it is accumulated.

The primary weakness of this paper is that the data were collected cross-sectionally. As such, the results, while compelling, may only be viewed as associations between physical activity and the various risk factors. While effort was made to control for potential socio-demographic confounders, residual confounding may still be the source of the observed associations. Similar analysis of prospectively measured physical activity and health status may help separate the causal relationships from mere associations.

Accelerometers do not capture all types of physical activity, particular static activities such as raking leaves or riding a bike.[19] Therefore, while the current analyses do not rely on self-report, they may still not reflect a complete picture of the activity levels of the US population. Similarly, the cut-points for what constitutes MVPA are also sensitive to the types of activities being done. Changing these cut-points would affect the amount of physical activity that participants were credited for, which in turn could have affected the outcome of the latent class analysis. It also might have been informative to examine the potential effects of lighter intensity activity.

In conclusion, these results indicate that accumulating the total amount of physical activity recommended for a week is consistently associated with positive profiles of the biological risk factors related to the metabolic syndrome, and that accumulating substantially more physical activity than what the recommendations suggest may be even better. However, the manner in which you accumulate this activity, either spread over many days of the week or compressed into just a couple, may have similar associations with the risk factors for the metabolic syndrome as well as the syndrome itself.

Figure 6. 1. Structural equation model for the prediction of the latent classes of physical activity as well as the associations between the latent classes and the risk factors. Socio-demographics have direct effects on the risk factors, the seven days of MVPA and the class memberships themselves.

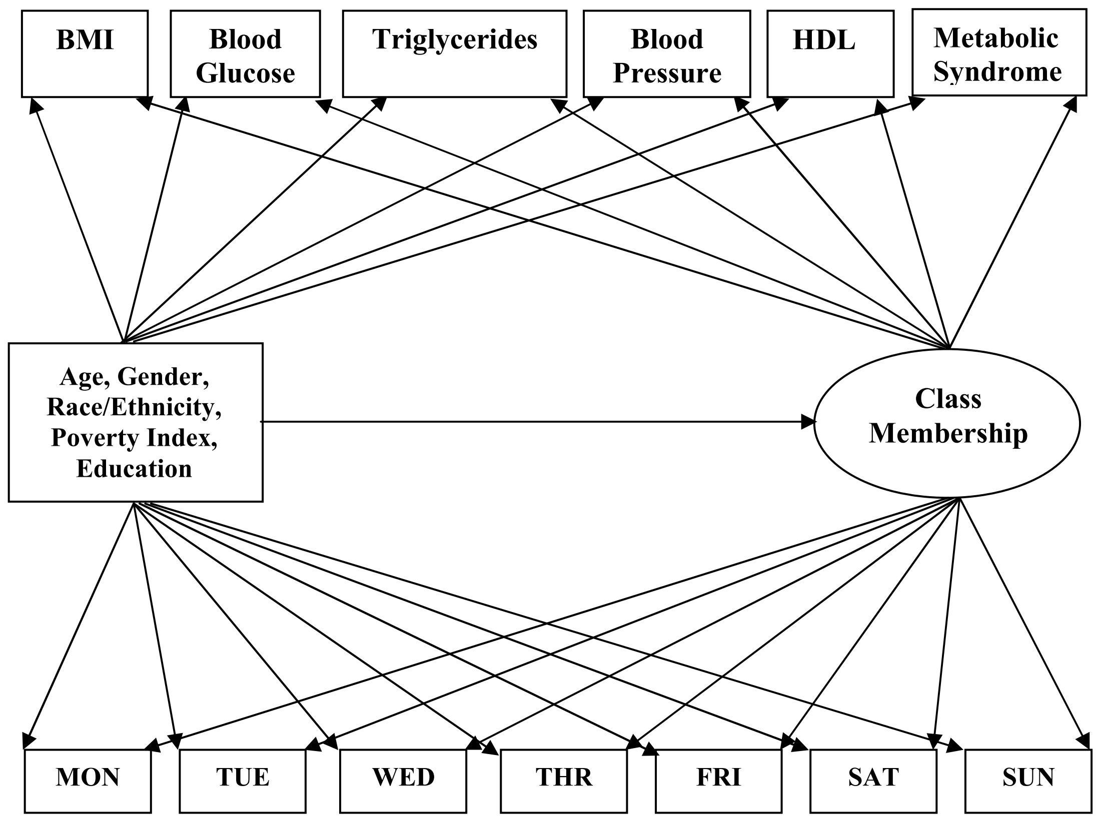


Table 6. 1. Unweighted frequency, sample weighted frequency, sample weighted percent, and standard error of percent of the categorized risk factors for the final study population.

Risk Factors / Metabolic Syndrome	N	Weighted N	Weighted %	SE of %
JNC 7 Classification of BP with Meds				
Normal	1,197	81,306,738	39.6	1.5
Pre-Hypertension	817	54,802,015	26.7	1.2
Hypertension or medication	1,444	69,175,916	33.7	1.3
Blood Glucose (mg/dL)				
< 126	1,481	192,160,947	93.6	0.8
>= 126 or insulin or pills	139	13,106,621	6.4	0.8
BMI (kg/m^2)				
18.5-24.9	1,029	65,678,847	32.0	1.3
25.0-29.9	1,264	72,172,568	35.2	1.4
30+	1,165	67,433,254	32.8	1.4
HDL (mg/dL)				
≥ 40	2,452	150,049,559	73.1	1.3
< 40 or medication	1,006	55,235,110	26.9	1.3
Triglycerides (mg/dL)				
Normal (<150)	910	124,488,133	60.6	1.8
Borderline High (150-199)	207	22,642,237	11.0	1.0
High (≥ 200 or medication)	503	58,137,198	28.3	1.2
Metabolic Syndrome				
No	1,250	164,408,975	80.1	1.5
Yes	370	40,858,592	19.9	1.5

Figure 6. 2. Five class analysis for entire study population for which BMI, HDL and blood pressure was available.

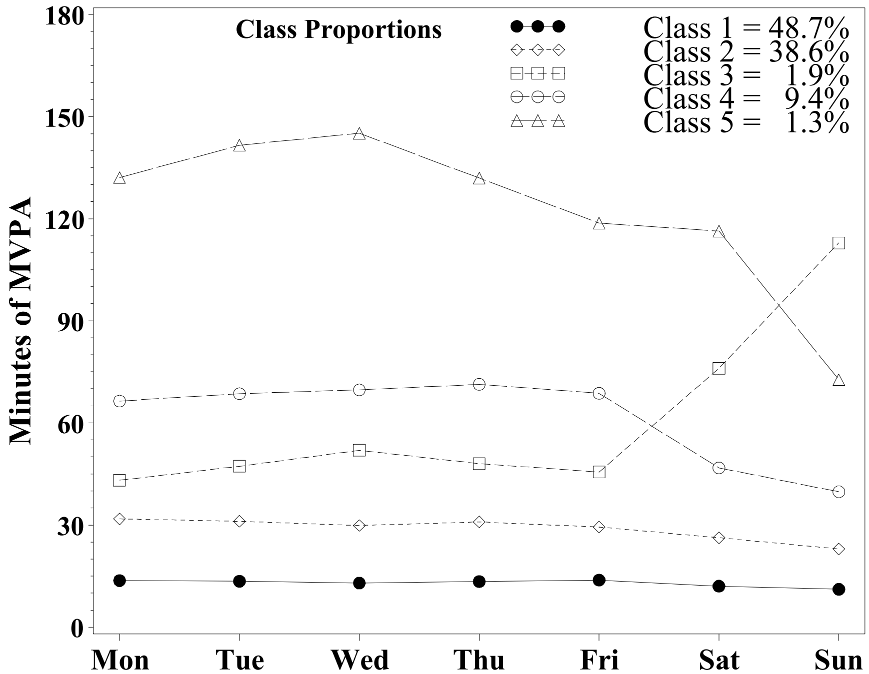


Figure 6. 3. Five class analysis for the subset of the population for which triglycerides and fasting blood glucose levels were recorded during the morning interview.

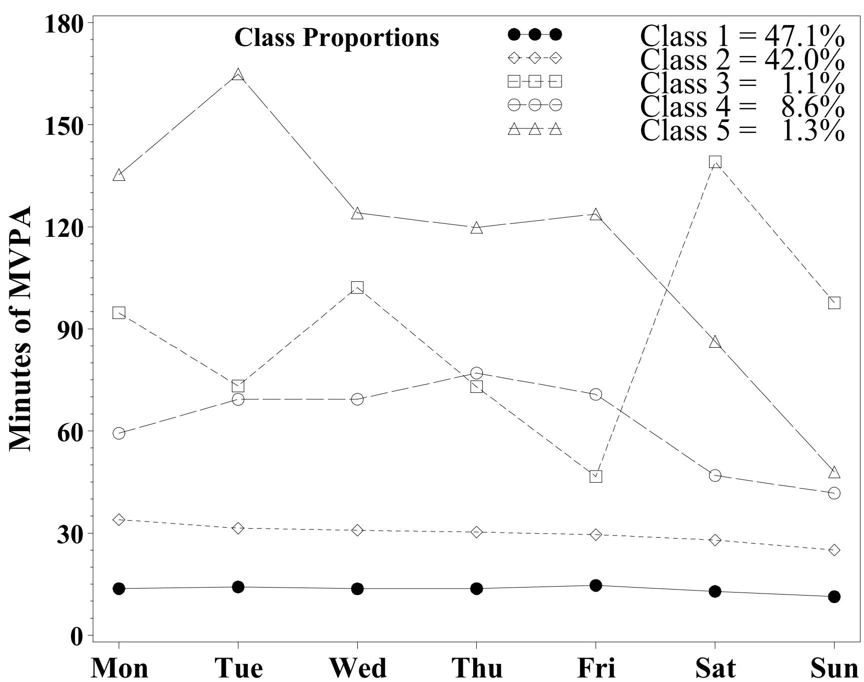
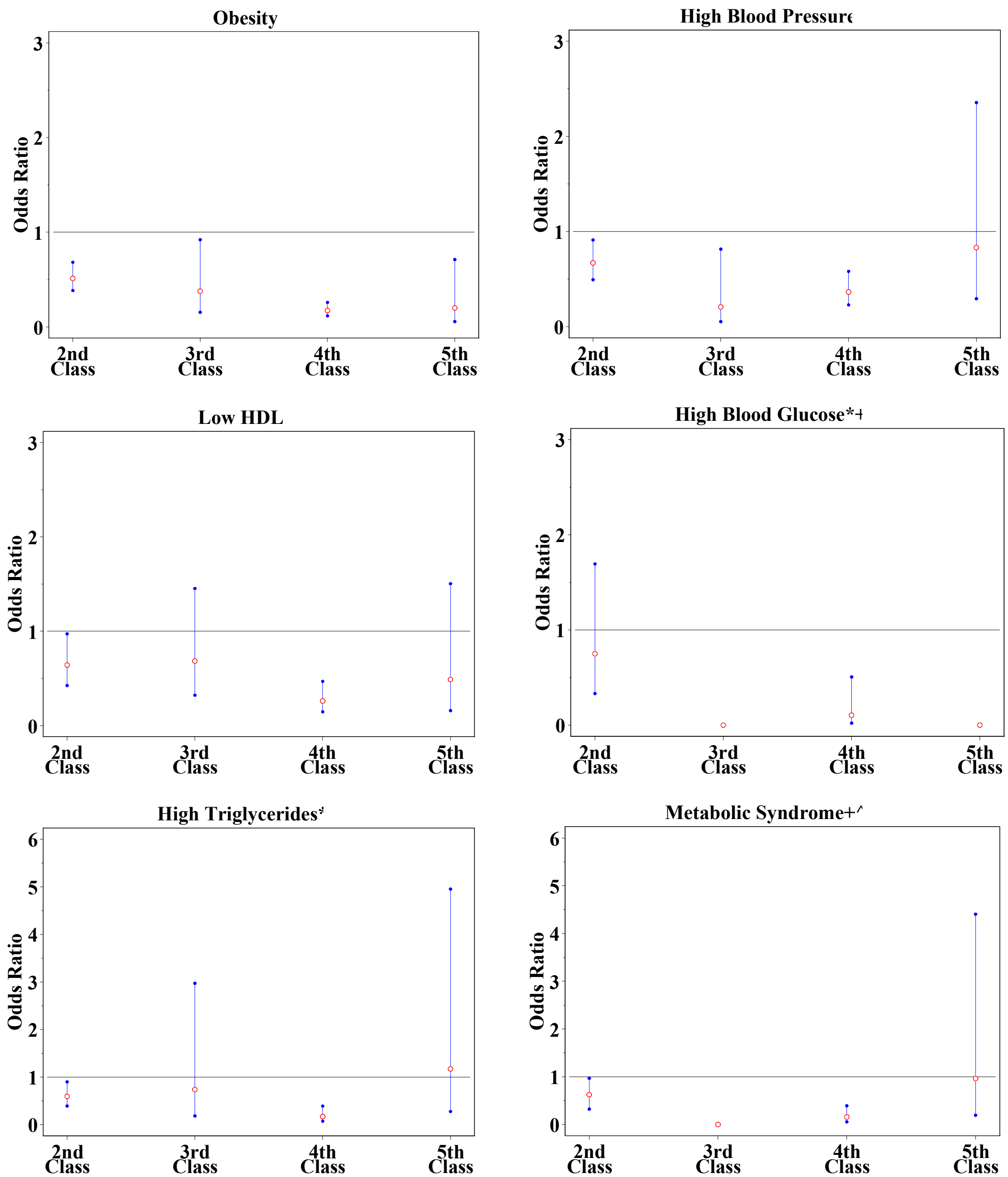


Figure 6. 4. Odds ratios and 95% confidence intervals for each of the risk factors comparing the four more active classes with the least active class (class 1).

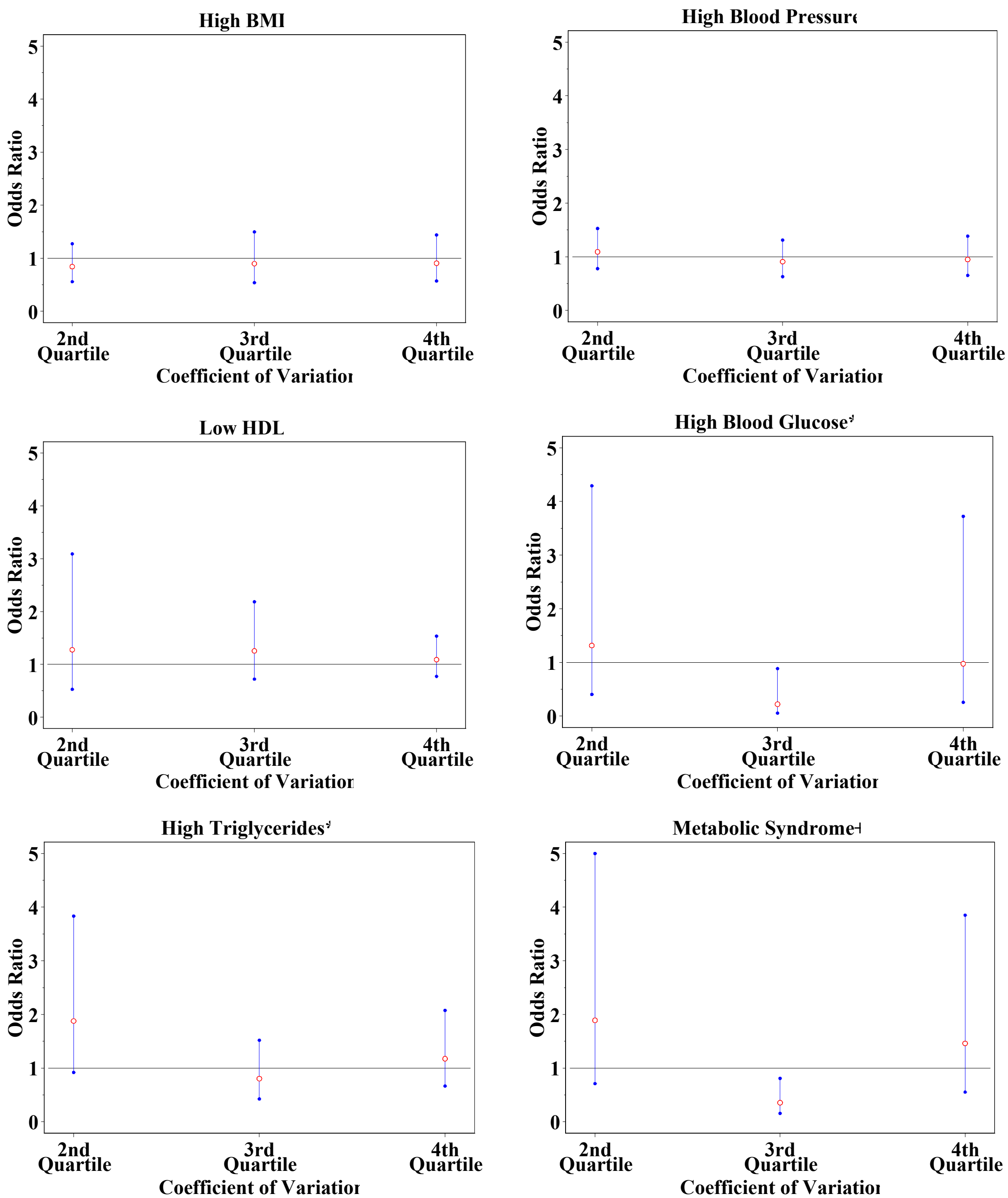


* Blood glucose and triglycerides were only collected during the morning session of the physical exam, so these analyses represent a subset of the final study population.

\+ For fasting blood glucose, no participants were classified with elevated levels in classes 3 and 5, and thus the odds ratios were zero. No participants were classified as having the metabolic syndrome in class 3.

^ Analysis represents a subset of the final study population among those with all non-missing risk factors.

Figure 6. 5. Odds ratios and 95% confidence intervals for the secondary analysis of the risk factors comparing the three higher quartiles of the co-efficient of variation with the lowest quartile of the co-efficient of variation, among those study participants who achieved at least 150 minutes of MVPA over the seven days.



* Blood Glucose and Triglycerides were only collected during the morning session of the physical exam, so these analyses represent a subset of the final study population.

\+ Analysis represents a subset of the final study population among those with all non-missing risk factors.

Chapter Seven

Conclusions

The findings from this research support many of the initial hypotheses from the specific aims. In addition, when taken as a whole, the findings could provide new avenues for behavioral interventions which have potentially realistic and achievable goals while still providing important personal and public health benefits.

Specific Aim 1

The first aim of the research was to develop a set of descriptive physical activity classes. Even though software was developed to generate LCA results, the process still requires a great deal of statistical sophistication in order to ensure that the generated results were those that were actually desired. The MPLUS software allows the researcher to select nearly all aspects of the variance/covariance structures for the latent class modeling. In addition, there are the inherent complexities of selecting the appropriate direct effects of covariates on the indicators of class and the risk factors, as well as the prediction of class membership based on covariates. Simultaneous with this is the primary task of selecting the appropriate number of classes. These analytical challenges mean that there still remains a significant amount for user input which could affect the end results. The numerous decisions made by the researcher ensure that LCA is not entirely a purely data driven statistical technique.

While the lack of one single empirical path to a final model may be concerning, much of the process toward developing the final 5 class model provided confidence in the final results. Due to the large sample size, the bootstrap statistical tests were uniformly significant and thus provided less guidance than other consideration for the final model. After all of the various arrangements were explored with regards to the variance structures and the influence of the covariates on both the risk factors and the indicators of class, the patterns presented in our final 5 class model emerged and re-emerged in nearly all model configurations (with the important exception of the final model presented in chapter 4). At the same time, the 6 class model produced a large amount of variation in the underlying patterns as different model arrangements were explored, indicating a possible over-specification of the number of classes which led to the unstable results. The 4 class model, while generally stable, failed to delineate the weekend warrior pattern nor the highly active class, thus missing important sub-populations. The stability of the 5 class model along with the regularity of the appearance of those sub-groups of public health interest led to a great deal of confidence that the 5 class model was the most appropriate.

The first hypothesis of Aim 1 was that a weekend warrior class would emerge. The five class analysis presented in chapter 4 did not include direct effects on the indicators of class. With this model structure, the presence of the weekend warrior for the overall MVPA was not indicated. This group was clearly present, however, for the bout minutes of MVPA. The analyses which followed in chapters 5 and 6 only included overall MVPA and not VPA, but added direct effects on the indicators of class. In these analyses, the weekend warrior consistently emerged. Unfortunately, the VPA analysis failed in nearly all cases due to the low number of participants accumulating any VPA.

The last three hypotheses were also supported by our results. A consistently active class, a highly active class with less activity on the weekend, and a class that was inactive on all days emerged for overall MVPA and bout minutes of MVPA.

Specific Aim 2

The second aim was to determine whether sociodemographic characteristics were associated with the established activity classes identified through Aim 1. Even though males were consistently associated with higher activity classes as hypothesized, African-Americans and those with less education were not associated with membership in the least active class as hypothesized. In fact, those with less education were significantly associated with membership in the most active class, as were African-Americans, even though this latter association was not significant. An interesting area of future research would be to determine whether the source of the high levels of activity among these important sub-populations originate from leisure-time, occupational, or some other type of activities.

Hispanics were hypothesized to be in the more active classes, which was found to be true based on these results, particularly for non-Mexican Hispanics. Acquiring additional information on occupational activities, time spent in these activities, and intensity of these activities would be an interesting area of future research. Higher age was consistently associated with membership in the less active classes, as hypothesized. Finally, higher household income was associated with all of the more active classes. An interesting area of future research would be to determine if family income simply serves as a proxy for occupational activities. Therefore, future analysis could include the association of family income among those with similar occupational activities.

Specific Aim 3

The goal of Aim 3 was to determine which, if any, of the physical activity classes were associated with the risk factors related to the metabolic syndrome. The two hypotheses were that 1) higher overall physical activity would be positively associated with the biological markers of health and that 2) certain patterns of physical activity are associated with positive profiles, regardless of overall activity. With the exception of the weekend warrior class, the final patterns reflected groups which had increasing mean levels of physical activity on all days. Thus, the risk factor analysis using these activity patterns was not able to fully assess the associations of the patterns of activity independent of overall activity level because the classes only represented increasing mean activity.

This challenge led to the secondary analysis. By using the coefficient of variation (CV) as a tool for categorizing the participants, the associations between the risk factors and the regularity of physical activity over a seven day period could be assessed. Although the CV does not provide information on the exact pattern of physical activity, the essential goal of determining whether intermittent activity leads to health benefits that are similar to regular physical activity was still possible.

The final analysis of the risk factors provided the most compelling results. In all cases, class 2, the class of which most would have met the physical activity recommendations of 30 minutes of MVPA on most days, was consistently less associated with the health risk factors compared to class 1, the least active class, as hypothesized. Most members of class 2 would have met the US physical activity recommendations, thus supporting the previous research on the beneficial effects of achieving the recommendations. In addition, class 4, the second most active class, consistently showed lower associations with all of the risk factors compared to class 2.

Assessing the risk factor associations of the weekend warrior were less informative for several reasons. While the weekend warrior had a lower odds of all of the risk factors compared to the least active class, the magnitude of the odds ratios ranged from only slightly lower (OR=0.9 for triglycerides) to much lower (OR = undefined for blood glucose). This variability in the magnitude of the associations was possibly due to the small sample size resulting in the large confidence intervals around the estimates. In addition, the weekend warrior's level of physical activity Monday through Friday far exceeded the US physical activity recommendations, even though their level of activity on the weekend was even higher. Thus, any association seen for the weekend warrior class could simply have reflected a generally high level of physical activity, and was not necessarily related to the increased level of activity on the weekend.

The secondary analysis provided a key piece of additional information which helped clarify some of the questions that remained from the class analysis. By categorizing people into quartiles of the CV, the question could then be asked whether consistent daily activity was associated with better health profiles. Even though the CV attempts to remove the effects of heteroscedasticity on the variance estimates, restricting this analysis to just those participants who achieved 150 minutes of MVPA over the seven days reduced the possibility that any associations found were only residual associations with the underlying levels of physical activity. In addition, the restriction attempted to remove the possible threshold effect among those who accumulated at least the recommended levels of physical activity.

These results also have the additional advantage of assessing the associations with physical activity only among those who are active. This reduced the possibility of confounding caused by inactive participants being inactive for reasons associated with the health risk factors. For example, those who have a high BMI and are diabetic might be less likely to be employed in occupations which require physical activity or participate in leisure-time physical activity due to the discomfort that physical activity causes them. It might not have been their physical activity levels, however, but rather their eating habits, that led to their high BMI and diabetes.

The final results from the secondary analysis indicated with a high level of consistency that, among those who achieved the recommended levels of physical activity, the regularity of how one accumulated their MVPA was not associated with the risk factors related to the metabolic syndrome.

Overall conclusions

These results indicate that a very large portion of the US population may be classified into patterns of physical activity that represent low levels of MVPA throughout the week. Fewer than 1% of the population met the VPA recommendations least 20 minutes on 3 or more days per week. In addition, a weekend warrior class emerged for approximately 1% of the population. Both gender and age emerged as significant predictors of membership in the different patterns of physical activity. The higher odds of Mexicans, other Hispanics, and NH-blacks being in the most active class was novel and needs future research to determine the source of the high level of activity.

Taken together, these results indicate that physical activity accumulated at the level of the current recommendations of 30 minutes of moderate physical activity on most days of the week is beneficial for all of the risk factors associated with the metabolic syndrome. Additional activity appears to offer additional benefits. Finally, accumulating physical activity regularly over many days or in long periods on fewer days may offer similar benefits. However, these conclusions are tempered by the fact that this is cross-sectional data.

Thus, in order to target appropriate physical activity interventions, it may be important to assess whether a strategy of regular or concentrated physical activity is most appropriate. For those groups who appear to accumulate physical activity at lower levels, such as females, older people or those with lower income, different approaches more be necessary. For example, females and those with lower levels of family income may, due to work obligations, be more capable of finding a day or two per week in which to engage in extended periods of exercise than dedicate a small part of each day toward physical activity. Conversely, older populations may need to limit the length of their periods of physical activity due to physical limitations. In addition, dedicating a small part of each day to physical activity may be more realistic for older populations, many of whom may not be working.

The primary weakness of this work, which has also been previously explored, is the cross-sectional nature of the NHANES survey. Because of this, the results have to be viewed with caution. The primary concern is that the health status of an NHANES participant may affect the participant's level of physical activity, or that some other unmeasured confounding factor is associated with both the risk factors and the participant's level of physical activity. If this were true, and it is entirely possible, then the associations found between physical activity and the biological markers of health would be spurious. In fact, quite to the opposite, they could represent the affect of poor health status. This issue can not be resolved with the current NHANES data.

Appendix A

The probability that an individual i belongs in class k is modeled based on the following equation:

$$\Pr(c_{ik} = 1 \mid \mathbf{X}_i) = \frac{e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}{\sum_{k=1}^{K} e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}$$

Where $c_{ik} = 1$ if subject i belongs to class k and 0 otherwise, a_{c_k} is the logit intercept for class k, $\boldsymbol{\gamma}'_{c_k}$ is the set of sociodemographic parameter estimates for class k, and $\mathbf{x}_i$ is the set of sociodemographic variable values for subject i. For the referent class, the co-efficients of a_{c_k} and $\boldsymbol{\gamma}'_{c_k}$ are standardized to zero for the referent class.

The standardization of the referent class beta co-efficients leads to a useful interpretation. The ratio of the probability that subject i with sociodemographic characteristics $\mathbf{x_i}$ is in class k compared to the probability that someone with the same sociodemographic characteristics $\mathbf{x_i}$ belongs to referent class is:

$$\frac{\Pr(c_{ik} = 1 \mid \mathbf{X}_i)}{\Pr(c_{ik=ref} = 1 \mid \mathbf{X}_i)} = \frac{\dfrac{e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}{\sum_{k=1}^{K} e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}}{\dfrac{e^{a_{c_k=ref} + \boldsymbol{\gamma}'_{c_{k=ref}} \mathbf{x}_i}}{\sum_{k=1}^{K} e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}} = \frac{\dfrac{e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}{\sum_{k=1}^{K} e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}}{\dfrac{e^{0}}{\sum_{k=1}^{K} e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}}} = e^{a_{c_k} + \boldsymbol{\gamma}'_{c_k} \mathbf{x}_i}$$

Similarly, the ratio of the probability that subject i with the referent sociodemographic characteristics $\mathbf{x_i}$ is in class k compared to the probability that someone with the referent sociodemographic characteristics belongs to the referent class is:

$$\frac{\Pr(c_{ik}=1\,|\,\mathbf{X}_{ref})}{\Pr(c_{ik=ref}=1\,|\,\mathbf{X}_{ref})}=\frac{\dfrac{e^{a_{c_k}+\boldsymbol{\gamma}'_{c_k}\mathbf{x}_{ref}}}{\sum_{k=1}^{K}e^{a_{c_k}+\boldsymbol{\gamma}'_{c_k}\mathbf{x}_{ref}}}}{\dfrac{e^{a_{c_{k=ref}}+\boldsymbol{\gamma}'_{c_{k=ref}}\mathbf{x}_{ref}}}{\sum_{k=1}^{K}e^{a_{c_k}+\boldsymbol{\gamma}'_{c_k}\mathbf{x}_{ref}}}}=\frac{\dfrac{e^{a_{c_k}}}{\sum_{k=1}^{K}e^{a_{c_k}}}}{\dfrac{e^{0}}{\sum_{k=1}^{K}e^{a_{c_k}}}}=e^{a_{c_k}}$$

Given this:

$$\frac{\dfrac{\Pr(c_{ik}=1\,|\,\mathbf{X}_i)}{\Pr(c_{ik}=1\,|\,\mathbf{X}_{ref})}}{\dfrac{\Pr(c_{ik=ref}=1\,|\,\mathbf{X}_i)}{\Pr(c_{ik=ref}=1\,|\,\mathbf{X}_{ref})}}=\frac{e^{a_{c_k}+\boldsymbol{\gamma}'_{c_k}\mathbf{x}_i}}{e^{a_{c_k}}}=e^{\boldsymbol{\gamma}'_{c_k}\mathbf{x}_i}$$

And thus the beta co-efficients $\boldsymbol{\gamma}'_{c_k}$ can be seen as the log transformation of a type of "relative risk ratio". For a practical interpretation, the exponentiated beta co-efficients represent the "relative risk" that a participant with covariates xi is in class k, relative to their proportion in the referent class, as compared to the ratio of a subject with the referent sociodemographics being in the same two classes.

Appendix B

The modeling of the ordinal health risk factors is conceptualized as the modeling of continuous variable representing a probability continuum. Thresholds, indicated by the symbol τ_s, are established along this continuum above which the ordinal variable is assumed to be in the next higher level of the risk factor. Thresholds can be thought of as a type of intercept parameter. As such, different thresholds are established for each activity class based on the likelihood that the individuals in that class will take on each of the ordinal values, while covariates may affect where an individual falls along this continuum.

Muthen, the author of our statistical software, has established what he refers to as a Framework B, a generalized modeling scheme in which the risk factors may be predicted by latent class levels, while latent variables, typically conceptualized as an intercept and slope parameters, may also simultaneous predict class membership as well as the risk factors. In this regression framework, an individual's value along the continuum, indicated by $\boldsymbol{\mu}_i^*$ and conditioned on class k, is defined by:

$$\boldsymbol{\mu}_i^* = \boldsymbol{\Lambda}_{\mu_k} \boldsymbol{\eta}_{\mu_i} + \mathbf{K}_{\mu_k} \mathbf{x}_i \qquad (1)$$

$$\boldsymbol{\eta}_{\mu_i} = \boldsymbol{\alpha}_{\mu_k} + \boldsymbol{\Gamma}_{\mu_k} \mathbf{x}_i \qquad (2)$$

Where $\mathbf{K}_{\mu_k}$ is the logit parameter matrix for the covariates and $\mathbf{x}_i$ is the matrix of covariates for subject i. $\boldsymbol{\Lambda}_{\mu_k}$ represents the factor loadings for each of the latent variable values and $\boldsymbol{\eta}_{\mu_i}$ represents the vector of latent variables.

This modeling can be conceptualized by referencing Figure B.1. This graph represents an risk factor variable with 3 ordinal levels. The thresholds for transitioning between these levels are indicated by τ_1 and τ_2. An individual with covariates $\mathbf{x_1}$ has a predicted $\boldsymbol{\mu}_i^*$ that makes it most likely they will have the lowest ordinal value, somewhat likely that they will have the next higher value, and unlikely that they will take on the highest level of the risk factor. Similarly, an individual with covariates $\mathbf{x_2}$ has a predicted $\boldsymbol{\mu}_i^*$ that makes it most likely they will be in the highest (3^{rd}) level of the ordinal risk factor.

In Latent Class Growth Analysis (LCGA) or Growth Mixture Modeling (GMM), in which latent growth factor variables are added to the structural equation model, $\boldsymbol{\Lambda}_{\mu_k} \boldsymbol{\eta}_{\mu_i}$ in equation 1 represents the random effects (typically the intercept and slope terms) of the latent variables on the predicted risk factor, $\boldsymbol{\mu}_i^*$, conditioned on class K. Because we did not model with growth factors, and opted instead for LCA, this part of the equation drops out. In addition, in our analysis the parameter estimates for K were not allowed to vary across classes, leaving simply:

$$\boldsymbol{\mu}_i^* = \mathbf{K}_\mu \mathbf{x}_i \qquad (3)$$

Thus, when all of the risk factor variables are modeled simultaneously (and indexed by j), then the categorical vector representing these values, $\boldsymbol{\mu}_{ij}$ (j = 1, 2,…., r), with S_j ordered categories, is assumed to follow an ordered polytomous logistic regression, where r is the total number of risk factor variables and s = 0, 1, …, S_j -1, and $\tau_{j,k,o} = -\infty, \tau_{j,k,S_j} = \infty$.

$$\mu_{ij} = s \text{ if } \tau_{j,k,s} < \mu_{ij}^* \le \tau_{j,k,s+1} \qquad (4)$$

$$P(\mu_{ij} = s \mid c_i x_i) = F_{s+1}(\mu_{ij}^*) - F_s(\mu_{ij}^*) \qquad (5)$$

$$F_s(\mu_{ij}^*) = \frac{1}{1+\exp(-(\tau_s + \mu_{ij}^*))} \qquad (6)$$

$F_s(\mu_{ij}^*)$ is thus the probability that subject i falls below the threshold τ_s of ordinal variable j. Clearly, then, the probability of being above the threshold is 1 - $F_s(\mu_{ij}^*)$. And thus the odds of being above vs. below the threshold is:

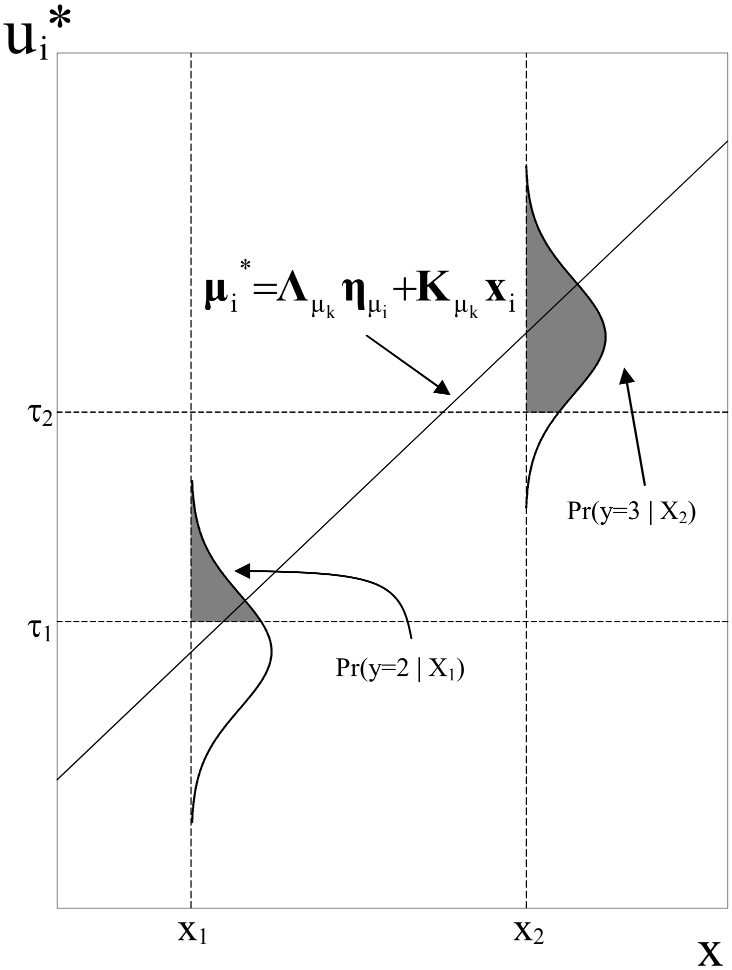
$$\frac{1-F_s(\mu_{ij}^*)}{F_s(\mu_{ij}^*)} = \frac{1-\dfrac{1}{1+\exp(-(\tau_s+\mu_{ij}^*))}}{\dfrac{1}{1+\exp(-(\tau_s+\mu_{ij}^*))}} = \frac{\dfrac{\exp(-(\tau_s+\mu_{ij}^*))}{1+\exp(-(\tau_s+\mu_{ij}^*))}}{\dfrac{1}{1+\exp(-(\tau_s+\mu_{ij}^*))}} = \exp(-(\tau_s+\mu_{ij}^*)) \qquad (7)$$

Because the predicted threshold values (analogous to intercept parameters) vary between activity classes, then the odds ratio of hypothetical class 2 being above the threshold of level s of ordinal variable j compared to class 1 is:

$$OR = \frac{\exp(-(\tau_{s-class2} + \mu_{ij}^*))}{\exp(-(\tau_{s-class1} + \mu_{ij}^*))} = \exp(-(\tau_{s-class2} - \tau_{s-class1})) \qquad (8)$$

And thus, the inverse of the exponentiated difference between the threshold levels of class two versus class one can be interpreted as the odds ratio of being in level s or higher of health variable j comparing class 2 to class 1.

Figure B. 1. Latent variable model for predicting the log-odds of experiencing one of the risk factors given an individual's covariates and latent variable.



Modified from Agresti[86] and Muthen[60]
τ 1 and τ 2 represent thresholds for a 3 level ordinal risk factor.

References

1. National Center Health Statistics (U.S.). National Health and Nutrition Examination Survey, 2005-2006 - Overview. 2006. http://www.cdc.gov/nchs/data/nhanes/OverviewBrochureEnglish_May05.pdf.

2. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006; 295: 1549-55.

3. Pate RR, Pratt M, Blair SN, 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* 1995; 273: 402-7.

4. Byrne NM, Hills AP, Hunter GR, Weinsier RL, Schutz Y. Metabolic equivalent: one size does not fit all. *J Appl Physiol* 2005; 99: 1112-9.

5. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 2000; 32: S498-504.

6. United States. Public Health Service. Office of the Surgeon General., National Center for Chronic Disease Prevention and Health Promotion (U.S.), President's Council on Physical Fitness and Sports (U.S.). *Physical activity and health : a report of the Surgeon General*. Atlanta, Ga. [Washington, D.C.] Pittsburgh, PA: U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, 1996: xvii, 278 p. p.

7. Adult participation in recommended levels of physical activity--United States, 2001 and 2003. *MMWR Morb Mortal Wkly Rep* 2005; 54: 1208-12.

8. Trends in leisure-time physical inactivity by age, sex, and race/ethnicity--United States, 1994-2004. *MMWR Morb Mortal Wkly Rep* 2005; 54: 991-4.

9. Bauman AE, Sallis JF, Dzewaltowski DA, Owen N. Toward a better understanding of the influences on physical activity: the role of determinants, correlates, causal variables, mediators, moderators, and confounders. *Am J Prev Med* 2002; 23: 5-14.

10. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W. Correlates of adults' participation in physical activity: review and update. *Med Sci Sports Exerc* 2002; 34: 1996-2001.

11. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. *Res Q Exerc Sport* 2000; 71: S1-14.

12. Montoye HJ. *Measuring physical activity and energy expenditure*. Champaign, IL: Human Kinetics, 1996: vii, 191 p. p.

13. Rzewnicki R, Vanden Auweele Y, De Bourdeaudhuij I. Addressing overreporting on the International Physical Activity Questionnaire (IPAQ) telephone survey with a population sample. *Public Health Nutr* 2003; 6: 299-305.

14. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc* 2005; 37: S531-43.

15. Leenders N, Sherman WM, Nagaraja HN. Comparisons of four methods of estimating physical activity in adult women. *Med Sci Sports Exerc* 2000; 32: 1320-6.

16. Leenders NY, Sherman WM, Nagaraja HN, Kien CL. Evaluation of methods to assess physical activity in free-living conditions. *Med Sci Sports Exerc* 2001; 33: 1233-40.

17. Hendelman D, Miller K, Baggett C, Debold E, Freedson P. Validity of accelerometry for the assessment of moderate intensity physical activity in the field. *Med Sci Sports Exerc* 2000; 32: S442-9.

18. Welk GJ, Blair SN, Wood K, Jones S, Thompson RW. A comparative evaluation of three accelerometry-based physical activity monitors. *Med Sci Sports Exerc* 2000; 32: S489-97.

19. Matthew CE. Calibration of accelerometer output for adults. *Med Sci Sports Exerc* 2005; 37: S512-22.

20. Swartz AM, Strath SJ, Bassett DR, Jr., O'Brien WL, King GA, Ainsworth BE. Estimation of energy expenditure using CSA accelerometers at hip and wrist sites. *Med Sci Sports Exerc* 2000; 32: S450-6.

21. Masse LC, Fuemmeler BF, Anderson CB, et al. Accelerometer data reduction: a comparison of four reduction algorithms on select outcome variables. *Med Sci Sports Exerc* 2005; 37: S544-54.

22. Catellier DJ, Hannan PJ, Murray DM, et al. Imputation of missing data when measuring physical activity by accelerometry. *Med Sci Sports Exerc* 2005; 37: S555-62.

23. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. *Med Sci Sports Exerc* 2005; 37: S523-30.

24. Eston RG, Rowlands AV, Ingledew DK. Validity of heart rate, pedometry, and accelerometry for predicting the energy cost of children's activities. *Journal of applied physiology (Bethesda, Md* 1998; 84: 362-71.

25. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1595-607.

26. Grundy SM, Brewer HB, Jr., Cleeman JI, Smith SC, Jr., Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation* 2004; 109: 433-8.

27. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; 106: 3143-421.

28. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *Jama* 2001; 285: 2486-97.

29. Dishman RK, Washburn RA, Heath G, Kaplan RL, Kaplan BH. *Physical activity epidemiology*. Champaign, IL: Human Kinetics, 2004: 467 p. p.

30. Cleroux J, Kouame N, Nadeau A, Coulombe D, Lacourciere Y. Aftereffects of exercise on regional and systemic hemodynamics in hypertension. *Hypertension* 1992; 19: 183-91.

31. Physical activity and cardiovascular health. *NIH Consens Statement* 1995; 13: 1-33.

32. Grundy SM, Blackburn G, Higgins M, Lauer R, Perri MG, Ryan D. Physical activity in the prevention and treatment of obesity and its comorbidities: evidence report of independent panel to assess the role of physical activity in the treatment of obesity and its comorbidities. *Med Sci Sports Exerc* 1999; 31: 1493-500.

33. Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann Intern Med* 2002; 136: 493-503.

34. Votey SR, Peters AL. Diabetes Mellitus, Type 2 - A Review. 2005. http://wwwemedicinecom/emerg/topic134htm.

35. American College of Sports Medicine and American Diabetes Association joint position statement. Diabetes mellitus and exercise. *Med Sci Sports Exerc* 1997; 29: i-vi.

36. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C, White RD. Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care* 2006; 29: 1433-8.

37. Hill JO, Melanson EL. Overview of the determinants of overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc* 1999; 31: S515-21.

38. DiPietro L. Physical activity in the prevention of obesity: current evidence and research issues. *Med Sci Sports Exerc* 1999; 31: S542-6.

39. Jebb SA, Moore MS. Contribution of a sedentary lifestyle and inactivity to the etiology of overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc* 1999; 31: S534-41.

40. Bassuk SS, Manson JE. Physical activity and the prevention of cardiovascular disease. *Curr Atheroscler Rep* 2003; 5: 299-307.

41. McLachlan GJ, Peel D. *Finite mixture models*. New York: Wiley, 2000: xxii, 419 p. p.

42. Greenbaum PE, Del Boca FK, Darkes J, Wang CP, Goldman MS. Variation in the drinking trajectories of freshmen college students. *J Consult Clin Psychol* 2005; 73: 229-38.

43. Croudace TJ, Jarvelin MR, Wadsworth ME, Jones PB. Developmental typology of trajectories to nighttime bladder control: epidemiologic application of longitudinal latent class analysis. *Am J Epidemiol* 2003; 157: 834-42.

44. National Health and Nutrition Examination Survey - Data Accomplishments. 2005. http://www.cdc.gov/nchs/about/major/nhanes/DataAccomp.htm.

45. Lee IM, Sesso HD, Oguma Y, Paffenbarger RS, Jr. The "weekend warrior" and risk of mortality. *Am J Epidemiol* 2004; 160: 636-41.

46. Ryan A, ed. *Exercise and Health: Lessons from the past*. Champaign: Human Kinetics Publishers, 1984.

47. Freedman DS, Khan LK, Serdula MK, Galuska DA, Dietz WH. Trends and correlates of class 3 obesity in the United States from 1990 through 2000. *JAMA* 2002; 288: 1758-61.

48. Coakley EH, Rimm EB, Colditz G, Kawachi I, Willett W. Predictors of weight change in men: results from the Health Professionals Follow-up Study. *Int J Obes Relat Metab Disord* 1998; 22: 89-96.

49. Lewis CE, Smith DE, Wallace DD, Williams OD, Bild DE, Jacobs DR, Jr. Seven-year trends in body weight and associations with lifestyle and behavioral characteristics in black and white young adults: the CARDIA study. *Am J Public Health* 1997; 87: 635-42.

50. LaPorte RE, Montoye HJ, Caspersen CJ. Assessment of physical activity in epidemiologic research: problems and prospects. *Public Health Rep* 1985; 100: 131-46.

51. Lohr SL. *Sampling : design and analysis*. Pacific Grove, CA: Duxbury Press, 1999: xv, 494 p. p.

52. Hughes E, McCracken M, Roberts H, et al. Surveillance for certain health behaviors among states and selected local areas--behavioral risk factor surveillance system, United States, 2004. *MMWR Surveill Summ* 2006; 55: 1-124.

53. Chowdhury PP, Balluz L, Murphy W, et al. Surveillance of certain health behaviors among states and selected local areas--United States, 2005. *MMWR Surveill Summ* 2007; 56: 1-160.

54. Metcalf BS, Curnow JS, Evans C, Voss LD, Wilkin TJ. Technical reliability of the CSA activity monitor: The EarlyBird Study. *Med Sci Sports Exerc* 2002; 34: 1533-7.

55. Conor V. Dolan, Brenda R. J. Jansen, Han L. J. van der Maas. Constrained and Unconstrained Multivariate Normal Finite Mixture Modeling of Piagetian Data. *Multivariate Behavioral Research* 2004; Vol. 39: 69-98.

56. Bollen KA, Curran PJ. *Latent curve models : a structural equation perspective*. Hoboken, N.J.: Wiley-Interscience, 2006: 188-228 p.

57. Hagenaars JA, McCutcheon AL. *Applied latent class analysis*. Cambridge ; New York: Cambridge University Press, 2002: 97 p.

58. Lo Y, Mendell NR, Rubin DB. Testing the number of components in a normal mixture. *Biometrika* 2001; 88: 767-78.

59. Nylund KL, Asparouhov T, Muthén BO. Deciding on the Number of Classes in Latent Class Analysis and Growth Mixture Modeling:A Monte Carlo Simulation Study. *Structural Equation Modeling, An Interdisciplinary Journal (in press)* 2007.

60. Muthen BO. *MPlus Technical Appendices*. Los Angeles, CA: Muthen & Muthen, 1998-2004: 34 p.

61. Muthen B. Statistical and substantive checking in growth mixture modeling: comment on Bauer and Curran (2003). *Psychol Methods* 2003; 8: 369-77; discussion 84-93.

62. Kruger J, Ham SA, Kohl HW, 3rd. Characteristics of a "weekend warrior": results from two national surveys. *Med Sci Sports Exerc* 2007; 39: 796-800.

63. U.S. Department of Health and Human Services. Healthy People 2010. Understanding and Improving Health and Objectives for Improving Health. 2 vols. Washington, DC: U.S. Government Printing Office, November 2000: p. 22-11. http://www.healthypeople.gov/document/tableofcontents.htm.

64. Centers for Disease Control and Prevention. *Behavioral Risk Factor Surveillance System Survey Data*. Atlanta, Georgia: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2005. http://apps.nccd.cdc.gov/brfss/index.asp.

65. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc* 1998; 30: 777-81.

66. Brage S, Wedderkopp N, Franks PW, Andersen LB, Froberg K. Reexamination of validity and reliability of the CSA monitor in walking and running. *Med Sci Sports Exerc* 2003; 35: 1447-54.

67. Leenders NY, Nelson TE, Sherman WM. Ability of different physical activity monitors to detect movement during treadmill walking. *Int J Sports Med* 2003; 24: 43-50.

68. Sherwood NE, Jeffery RW. The behavioral determinants of exercise: implications for physical activity interventions. *Annual review of nutrition* 2000; 20: 21-44.

69. National Cancer Institute, National Institutes of Health, US Department of Health and Human Services. Theory at a Glance: A Guide for Health Promotion Practice (Second Edition). Bethesda, MD, downloaded July 23, 2007: 52 pages. http://www.nci.nih.gov/cancer_information/cancer_literature/.

70. Sallis J, Owen N. Health Behavior and Health Education: Theory, Research, and Practice. In: Glanz K, Lewis F, Rimer B, eds. *Ecological models*. San Francisco, CA: Jossey-Bass, 1997: 403-24.

71. McLeroy KR, Bibeau D, Steckler A, Glanz K. An ecological perspective on health promotion programs. *Health Educ Q* 1988; 15: 351-77.

72. Salmon J, Owen N, Bauman A, Schmitz MK, Booth M. Leisure-time, occupational, and household physical activity among professional, skilled, and less-skilled workers and homemakers. *Prev Med* 2000; 30: 191-9.

73. Pollock ML, Gaesser GA, Butcher JD, et al. American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 1998; 30: 975-91.

74. Physical Activity Measured by Accelerometry in that National Health and Nutrition Examination Survey 2003-2004. *Active Living Research Annual Conference*, February 2007. http://www.activelivingresearch.org/alr/node/11471.

75. Mplus. Fourth Edition. Los Angeles, California, 2006.

76. Prevalence of leisure-time and occupational physical activity among employed adults--United States, 1990. *MMWR Morb Mortal Wkly Rep* 2000; 49: 420-4.

77. Metzger JS, Catellier DJ, Evenson KR, Treuth MS, Rosamond WD, Siega-Riz AM. Patterns of Objectively Measured Physical Activity in the United States. 2007.

78. Mikines KJ, Sonne B, Farrell PA, Tronier B, Galbo H. Effect of physical exercise on sensitivity and responsiveness to insulin in humans. *Am J Physiol* 1988; 254: E248-59.

79. Halliwill JR. Mechanisms and clinical implications of post-exercise hypotension in humans. *Exerc Sport Sci Rev* 2001; 29: 65-70.

80. Kenney MJ, Seals DR. Postexercise hypotension. Key features, mechanisms, and clinical significance. *Hypertension* 1993; 22: 653-64.

81. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; 289: 2560-72.

82. Redefining Diabetes Control,. *Diabetes & Cardiovascular Disease Review*, 2002: 8.

83. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: executive summary. Expert Panel on the Identification, Evaluation, and Treatment of Overweight in Adults. *The American journal of clinical nutrition* 1998; 68: 899-917.

84. Metzger JS, Catellier DJ, Evenson K, Treuth M, Rosamond W, Siega-Riz A. Patterns of Objectively Measured Physical Activity in the United States: a Latent Class Analysis of the Accelerometer Data from the 2003-2004 NHANES 2007.

85. Metzger JS, Catellier DJ, Evenson K, Treuth M, Rosamond W, Siega-Riz A. Associations between Patterns of Objectively Measured Physical Activity and Sociodemographic Characteristics 2007.

86. Agresti A. *Categorical data analysis*. New York: Wiley, 1990: xv, 558 p. p.