FAMILIAL AGGREGATION OF PHYSICAL ACTIVITY LEVELS IN THE STRONG HEART FAMILY STUDY

by

Kristi Leigh Storti

B.S., Exercise Science, Slippery Rock University, 1994

M.S, Exercise Physiology, University of Pittsburgh, 1997

M.P.H., Epidemiology, University of Pittsburgh, 2003

Submitted to the Graduate Faculty of

Graduate School of Public Health in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

University of Pittsburgh

2007

UNIVERSITY OF PITTSBURGH

GRADUATE SCHOOL OF PUBLIC HEALTH

This dissertation was presented

by

Kristi Leigh Storti

It was defended on

April 10, 2007

and approved by

Dissertation Advisor:
Andrea M. Kriska, PhD, Associate Professor, Department of Epidemiology
University of Pittsburgh, Graduate School of Public Health

Vincent C. Arena, PhD, Associate Professor, Department of Biostatistics
University of Pittsburgh, Graduate School of Public Health

M. Michael Barmada, PhD, Associate Professor, Department of Human Genetics
University of Pittsburgh, Graduate School of Public Health

Clareann H. Bunker, PhD, MPH, Associate Professor, Department of Epidemiology
University of Pittsburgh, Graduate School of Public Health

Joseph M. Zmuda, PhD, MPH, Assistant Professor, Department of Epidemiology
University of Pittsburgh, Graduate School of Public Health

Robert L. Hanson, MD, MPH, Staff Scientist, DECRS/National Institutes of Diabetes & Digestive & Kidney Diseases/National Institutes of Health; Phoenix, AZ

Sandra L. Laston, PhD, RN, Staff Scientist, Department of Genetics, Southwest Foundation for Biomedical Research; San Antonio, TX

Jeun-Liang Yeh, PhD, MPH, Associate Professor, Center for American Indian Health Research, University of Oklahoma Health Sciences Center, Oklahoma City, OK

FAMILIAL AGGREGATION OF PHYSICAL ACTIVITY LEVELS IN THE STRONG HEART FAMILY STUDY

Kristi Leigh Storti, PhD

University of Pittsburgh, 2007

Physical inactivity is a major risk factor for complex metabolic diseases such as obesity, diabetes, and hypertension. Traditionally, these diseases and conditions have been the specific burden of adulthood, but they are now being diagnosed more frequently in younger populations. There has been some suggestion that, as is true in adults, children are becoming less physically active and that this decline in physical activity may help to explain the sudden increase in the incidence of metabolic diseases among children. Understanding the factors that are impacting on decreased physical activity levels in children will provide clues on how to approach this problem.

Similar to findings in obesity, where obese parents tend to have overweight and obese children, physical activity appears to be related between parent and offspring. Although the literature regarding familial aggregation of physical activity levels is limited, it does allude to an association of physical activity levels among parents and children to varying degrees. Using several different approaches, we examined the familial resemblance of physical activity levels, determined by pedometry, in 96 extended Native American families from three geographic locations (Arizona, North/South Dakota, Oklahoma) in the Strong Heart Family Study.

Based upon correlational analyses, physical activity levels were significantly and positively related among parent-offspring pairs. More specifically, correlations between father-daughter pairs (< 18 years of age) and father-son pairs (>18-30 years of age) were rho = 0.30 and

0.26, respectively ($p = 0.01$). No significant associations were noted between physical activity levels of mother-offspring pairs. For our main investigation, we examined the familial effects, of physical activity using variance components analyses. Despite the fact that this study was conducted in three separate geographic locations, had limited household data, was not designed specifically to examine aggregation of physical activity levels, and was not limited to 2-parent families, when modeled as a heritable effect, physical activity achieved statistical significance ($p = 0.007$) explaining approximately 9% of the trait variance.

Since physical activity can provide health benefits in youth, and since many young people are not meeting established guidelines, improving physical activity levels of youth is a key public health challenge. However, in order to develop effective physical activity interventions for youth, factors that impact on a child's physical activity levels need to be better understood. The findings of the current study indicate a significant, albeit weak, degree of aggregation of physical activity levels among parent-offspring pairs and among families. This supports the need to establish family based lifestyle interventions studies where both parent and child may benefit.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PREFACE

I would like to thank first and foremost my advisor, Dr. Andrea Kriska, for the opportunity to work on such an exciting project and for pushing me to my limits in order to realize my true potential. I am forever grateful to you! To my committee members, Drs. Vincent Arena, Clareann Bunker, Joe Zmuda, Robert Hanson, Sandy Laston, and Jeun-Liang Yeh, you have my sincere appreciation for the time, input, and dedication that you provided to me on this project. To Dr. Michael Barmada, there are not enough words to say thank you for the help and guidance that you provided to me and for the crash course in genetic epidemiology.

To my friends and colleagues, Drs. Jennifer Brach and Kelley Pettee, your friendship is invaluable and I thank you for all of the times that you provided me with an open ear to listen. To Marquis Hawkins, Darcy Underwood, and Vanisha Brown for allowing me to bounce ideas off of you and for helping me out when the times got tough. Your friendship and input are priceless.

Finally, I would like to acknowledge those closest to me and those who have weathered every storm. My husband, Anthony, for your love, support, and encouragement. Without you, I don't know if this seemingly endless journey would have come to an end. To my parents, especially my father, who always told me that the best things in life take a lot of hard work and an inordinate amount of time to accomplish; I guess the Shevchik stubbornness finally paid off. To my brother, Michael and sister-in-law, Kiersten (Anastasia too!), thank you for believing in me when I couldn't believe in myself. To Shannon, thank you for the encouragement and for always being there no matter what the circumstances were, you are a blessing and a true best friend. And to my dear children, Maggie and Philip, who deserve the most thanks for the many days and nights that they spent alone with their father or in the care of others, so that I could finish this project. You are the reason why I get up each day and why I would never quit, even when the times got tough. I love you both!!!

1.0 INTRODUCTION

1.1 THE PREVALENCE OF INACTIVITY

It has been suggested that physical activity provides numerous health benefits including the prevention of many chronic diseases[1-3]. Research has demonstrated that habitual physical activity is associated with reduced morbidity and mortality from various chronic diseases and conditions such as cardiovascular disease[4-6], diabetes[7-9], hypertension [10-12], obesity[13], and cancer[14, 15]. Despite this well documented evidence, many individuals continue to lead relatively sedentary lifestyles [16].

According to a 2004 Vital and Health Statistics Report, at least 4 in 10 United States (U.S.) adults were physically inactive defined as engaging in no leisure-time physical activity (LTPA) within a two-week period[17]. Additionally, only 31.3% of adults engaged in activity that would meet current minimum recommendations established by the U.S. Surgeon General, defined as engaging in 30 minutes of moderate intensity activity, (such as that of a brisk walk), on most, if not all, days of the week[18, 19]. Of minority and ethnic groups assessed in the 2004 report, 26.4% of Native Americans, 24% of non-Hispanic Blacks, and 22.4% of Hispanics were least likely and 33.9% of non-Hispanic Whites were most likely to meet the Surgeon General's activity recommendations.

Unfortunately, the problem of inactivity in U.S. youth is beginning to mirror that of U.S. adults. Data from multiple national surveys indicate that approximately 14% of youth and adolescents do not participate in any activity,[18] and that at least 50% of those 12 to 21 years do not participate in levels of physical activity that would meet minimum recommendations (defined as engaging in 60 minutes of moderate to vigorous intensity activity most days per week, preferably daily) established by the U.S. Surgeon General[20]. Furthermore, an age-related decline in physical activity from adolescence to young adulthood has been documented in several longitudinal studies [21-25] with an additional decrease throughout young adulthood[23, 24, 26, 27]. This decline may be largely due to increasingly common sedentary ways of life. For example, fewer children walk or cycle to school, and excessive time is devoted to watching television, playing computer games, and using computers. Very often theses activities are done at the expense of time and opportunities for physical activity and sports.

Since physical activity can provide health benefits in youth and many young people are not meeting established guidelines, improving physical activity levels of youth is a key public health challenge. However, in order to develop effective physical activity interventions for youth, factors that impact on a child's physical activity levels need to be well understood.

1.2 THE PREVALENCE OF PHYSICAL ACTIVITY IN NATIVE AMERICANS

As previously indicated, physical inactivity is a problem in all facets of the U.S. population, especially among minority populations. Although, there is a limited body of evidence available regarding physical activity levels in Native American populations, the sparse data that is available indicates that many Native Americans are inactive [17, 28-32]. In Native American youth, data is even more limited but does imply that Native American children spend significantly less time engaged in sport and leisure activities than in other subgroups of the U.S. population[33].

In addition to decreased physical activity levels, Native Americans of all ages and both sexes tend to have a higher prevalence of obesity than the general U.S. population[34]. Reports from the Strong Heart Study, a longitudinal study of cardiovascular disease and its risk factors in American Indians, indicate that the prevalence rates of overweight (defined as a body mass index (BMI) of 25 to 29.9 kg/m^2) in Arizona, Oklahoma, and the Dakotas for the years 1989-1992 were 67%, 65%, and 54% respectively, for adult men and were considerably higher for adult women at 80%, 71%, and 66% respectively[28, 35]. These rates are noticeably higher than the Third National Health and Nutrition Examination Survey (NHANES III; 1988-1991) all-races rate of 27% and 28% overweight for same-age men and women, respectively[36]. Additionally, according to the NHANES II reference data, the prevalence of overweight and obesity among Native Americans children is higher than those in all races combined in the United States. These data suggest that approximately 16 % of all U.S. children and adolescents are overweight[37, 38]. The prevalence of overweight among Native American youth is at least 38%[39]. Furthermore, it has been suggested that the prevalence of obesity among all U.S. children and adolescents is approximately 17%[37, 38], whereas the prevalence of obesity among Native American preschoolers and adolescents may be much higher ranging anywhere from 20 to 50% [39-41].

1.3 THE FAMILY APPROACH TO INCREASING PHYSICAL ACTIVITY LEVELS

Factors that increase physical activity during childhood are currently being investigated. It has been suggested that parents play a pivotal role in childhood activity. It is believed that parents who encourage, facilitate, and role model physical activity, and who participate in activity with their children will possibly impact on their child's activity behavior as they approach adolescence[42, 43]. Therefore, parents can clearly have a major impact on the development of active lifestyles in their children. More work is needed to characterize and document the nature and extent of parental influence on physical activity behavior in children [44].

From a theoretical point of view, participation in sport and physical activity may be considered a modeling process for which family members, especially parents, are powerful role models[25, 45]. Longitudinal studies indicate that certain social, cultural, genetic, and environmental factors may predict consistent physical activity participation [21, 22, 24]. Studies suggest that both a parents' exercise pattern and their encouragement have an effect on their children's physical activity behavior, and that physically active parents tend to have physically active children [43, 46-59]. This concept is often referred to as familial aggregation, which can be defined as the combination of genetic and environmental influences within a family.

The literature regarding familial aggregation of physical activity is somewhat limited, but it does allude to an association of physical activity levels among parents and children to varying degrees [43, 48, 50-53, 55, 56, 58]. Most of these studies relied on subjective assessment methods such as self-report questionnaires[44, 48-50, 53, 55, 56, 58-62], diaries[57], or one or two questions to assess physical activity levels[59, 61, 63, 64], but very few provided information regarding the validity and reliability of such instruments. It is well known that subjective measures are often the most practical tool to assess physical activity, but they are not without limitations. Two key limitations are recall bias and an inability to accurately capture most lower-intensity physical activities. These and other subsequent limitations of subjective assessment methods will be discussed in more detail in the review of literature provided in Chapter 2.

Alternatively, a few familial aggregation studies utilized objective physical activity monitors to assess physical activity levels among parents and children[43, 51, 52]. Using objective assessment methods, three studies out of the twenty familial aggregation studies found moderate to strong associations of physical activity levels among family members. Despite the positive findings, it must be noted that the sample sizes included in these studies were fairly small ranging from only 30 – 100 participant pairs. In addition, these studies were conducted in predominantly Caucasian samples therefore limiting their generalizability to other populations.

1.4 THE STRONG HEART FAMILY STUDY

The Strong Heart Study (SHS) is a multi-site clinical trial of cardiovascular disease (CVD) and its risk factors in American Indian men and women from 13 communities in three geographical areas of the U.S.: Arizona (AZ), Oklahoma (OK), and North/South Dakota (DA). In its earlier stages, the SHS included three main components. The first was a survey to determine cardiovascular disease mortality rates from 1984 to 1994 among tribal members aged 35-74 years of age residing in the 3 geographic study areas (the community mortality study). The second component was the initial clinical examination and morbidity and mortality surveillance of the 4,500 resident tribal members (the cohort). The third component was the continued morbidity and mortality (M&M) surveillance of these 4,500 participants. To date, the SHS has completed three clinical examinations of the original Cohort (Phase I: 1989-1991; Phase II: 1993-1995; Phase III: 1998-1999, respectively).

Preliminary findings from the SHS noted that CVD mortality rates among American-Indians were higher than corresponding state rates [65]. These findings prompted further research examining the importance of genetics in the occurrence of CVD, since many CVD risk factor phenotypes are significantly heritable[66]. Thus, the SHS expanded into the genetic epidemiology area to examine and localize genes influencing CVD risk factors within family cohorts during Phase III.

In Phase III, in addition to the Cohort examination, the study conducted a pilot family study. Each field center recruited about 10 large extended families. The family pilot study recruited approximately 30 families, which consisted of more than 900 family members. Due to the success of the pilot study, Phase IV was funded to conduct a full-blown family study to investigate the heritability of CVD and its risk factors.

In 1999, the Strong Heart Family Study (SHFS) or Phase IV was initiated to investigate genetic effects on cardiovascular risk factors among family members. The overall goal of this research was to further establish links with family members relating to development of CVD and other morbidities and mortalities. To date, the SHFS has recruited a total of 96 extended families (33 – AZ, 36 – OK, and 27 – DA) totaling approximately 3,800 genetically linked participants from all three centers who range in age from 14-93 years. Information regarding biological relationships and physical activity (assessed by activity monitors, more specifically pedometers) has been collected. In addition, information regarding household structure, which identifies which family members live in the same household, has been collected since these family members may share certain environmental risk factors.

1.5 STUDY GOAL

The Association of Physical Activity Levels between Genetically Linked Family Members of the Strong Heart Family Study (SHFS).

The aim of the current investigation is to examine the association of objectively measured physical activity levels (i.e., pedometer) between genetically linked family members from 96 extended families in the SHFS. In particular, this effort will examine the relationship of physical activity levels between parent and offspring. To accomplish this goal, we will utilize the SHFS cohort that contains roughly 3,800 genetically linked participants, of which approximately 3,300 have complete physical activity data.

Utilizing this unique data, the proposed investigation will examine the association of physical activity levels between biologically related family members. We will examine both the heritability of physical activity levels between genetically linked pairs as well as the effect of household environment. Specifically, the study objective is as follows:

Objective:

To examine the association of physical activity levels between biologically related family members, more specifically parent and offspring.

Hypotheses:

1a: It is hypothesized that physical activity levels assessed by objective activity monitor (i.e., pedometer) will be significantly and positively associated between parent and offspring pairs in the Strong Heart Family Study.

1b: It is hypothesized that physical activity is a heritable trait among family members in the Strong Heart Family Study.

Public Health Significance

The potential benefits of regular physical activity are extensive. Unfortunately, there is a growing body of evidence that physical activity among children and adolescents in the U.S. is declining. Preventing the decline of physical activity participation in children has the potential to decrease the burden of chronic disease in the U.S. population, indirectly through decreasing obesity, and directly by beneficially impacting on risk factors for both cardiovascular disease and diabetes. Determining if physical activity levels are heritable among family members could provide future insight as to where and how to focus lifestyle intervention efforts.

2.0 REVIEW OF LITERATURE

Previous investigations regarding the familial aggregation of physical activity levels have not been conducted in minority populations utilizing an objective measure of physical activity. The purpose of the proposed study is to examine whether familial aggregation of physical activity levels is present within the Strong Heart Family Study. The population of interest for this study is Native Americans, a minority subgroup at high risk for cardiovascular disease and diabetes. To date, limited information is available regarding physical activity levels of Native Americans and most of the information that has been collected has been through the use of subjective questionnaires.

The following chapter will provide a brief review of physical activity levels among Native Americans in order to better understand the prevalence of inactivity within this population. Later, a review of both subjective and objective physical activity assessment methods used in epidemiological studies will be provided. This section will discuss the strengths and weaknesses of these techniques and their appropriateness for use in the proposed study. In addition, this information will be provided to better understand the assessment techniques used to assess physical activity within the familial aggregation literature. Lastly, an extensive review of the literature concerning familial aggregation of physical activity levels will be provided.

2.1 PHYSICAL ACTIVITY LEVELS OF NATIVE AMERICANS

A limited body of evidence is available regarding physical activity levels among Native Americans. The available data does, however, suggest that Native Americans participate in relatively low levels of physical activity [17, 28-32, 67], in many instances, lower than their minority counterparts[31]. According to Schoenborn et al, (2004)[17] at least 5 in 10 Native Americans adults are physically inactive, with women more likely to be inactive than men (55.5% vs.42.5%). This same report suggests that roughly 26.4% of this population does not meet the Surgeon General's recommendations for physical activity participation. Both the Strong Heart Study and the Inter-Tribal Heart Project have reported estimates of inactivity among their respective tribal groups. In the Strong Heart Study, estimates of no LTPA ranged from 32.3% to 53.1% during the past week and from 10.4% to 25.2% during the past year in men. In women, estimates of no LTPA for the past week ranged were slightly higher ranging from 39.5% to 59.7% and from 14.5% to 28.2% for the past year [28]. The Inter-Tribal Heart Project provided estimates of inactivity over the past month ranging from 15% to 28% for women and from 10% to 25% for men [28, 29].

In regard to Native American children, there are few quantitative data on the activity levels. Fontvieille et al.[33] is one of the few to report that Pima Indian boys and girls spend significantly less time engaged in sport leisure activities than their Caucasian counterparts. Although not statistically significant, Pima Indian boys were found to participate in fewer hours per week of physical activity when compared with Caucasians boys (8.8 vs. 9.7 hrs/week, respectively). Likewise, Pima Indian girls were found to participate in significantly fewer hours of physical activity compared with their Caucasian female counterparts (1.0 vs. 5.6 hrs/week, respectively; $p < 0.01$). Furthermore, both Pima Indian boys and girls reported participation in significantly fewer physical activities (4 vs. 7, boys; 2 vs. 6, girls) than their Caucasian counterparts. In regard to sedentary behavior, no differences were noted in regard to television/video viewing among Pima Indian and Caucasian boys. However, Pima Indian girls were found to watch significantly ($p < 0.001$) more TV than their Caucasian counterpoints.

2.2 PHYSICAL ACTIVITY ASSESSMENT IN EPIDEMIOLOGICAL STUDIES

Physical activity is a complex behavior and selecting the proper assessment tool(s) is challenging, particularly among free-living populations. The lack of a simple gold standard measure and inconsistent use of physical activity terminology has contributed to confusion in this field. Measurement is further complicated by the fact that there are several health-related dimensions of physical activity, which may require the use of different assessment tools[68]. When examining the relationship between physical activity and a disease or condition, it is important to focus on the dimension(s) of physical activity that is most likely to be associated with the specific outcome of interest.

Energy expenditure is defined as the exchange of energy required to perform biological work. There are three components that make up total energy expenditure; they include basal metabolic rate, which typically encompasses 50-70% of total energy and the thermic effect of food, which accounts for another 7-10%. The remaining component is energy expended through various types of physical activities[69]. Physical activity is defined as any bodily movement produced by skeletal muscles that result in increased energy expenditure[70]. Therefore, housework, transportation, occupational, and leisure activity may all be considered types of physical activity. It is this specific component of energy expenditure that we attempt to measure in most population studies.

All physical activity falls across a range of intensity levels, as presented in Figure 2.1[71]. At the lower end of the physical activity intensity spectrum are general activities of daily living such as bathing, feeding, and grooming. The remainder of the intensity spectrum is comprised of various sports and leisure, household activities, care taking, transportation, and occupation activities that range in intensity from low to moderate and high levels. The relative contribution of each of these various types of activities to total energy expenditure in a specific population will vary depending on the population in question.

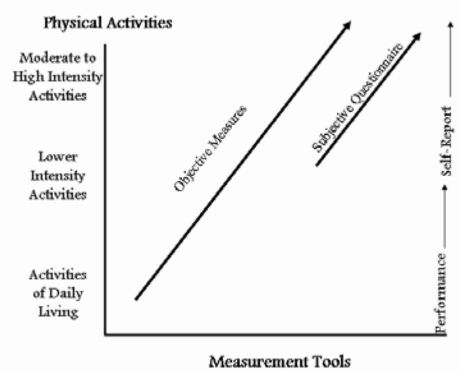

Figure 2.1 The Physical Activity Spectrum

Precise estimates of energy expenditure cannot feasibly be obtained from subjective measures such as questionnaires. In order to do so, objective measures such as a respiratory chamber, doubly labeled water, or activity monitors would be needed[69]. However, estimates obtained by activity questionnaire are valuable in relative terms, and can be used to rank individuals or groups of subjects within a population from least to most active. The end result is a relative distribution of individuals based upon their reported levels of physical activity[72].

In order for an accurate assessment of activity to be achieved, the assessment tool used must elicit information on the types of physical activities that encompass the greatest proportion of energy expenditure in the study population. Therefore in investigations where it can be assumed that low intensity activities are generally consistent across the population, such as healthy adults, a physical activity questionnaire may be appropriate for the assessment of sports and leisure physical activities. However, in certain subgroups, such as the elderly, injured/impaired, or other populations where lower intensity activities may comprise the bulk of their physical activity levels, the use of a subjective measure to assess physical activity may likely miss a significant portion of activities that comprise their total energy expenditure. In this case, an objective measure of physical activity should be considered to account for low intensity activities[72].

Subjective measures of physical activity, such as a questionnaire, alone may not be the best way to quantify these lower intensity, spontaneous, lifestyle activities. Additional measures may be needed to supplement the information collected by the questionnaire. Measurement of lower intensity activities may require the use of objective measures such as an activity monitor or a pedometer.

2.2.1 Subjective Measures – Physical Activity Questionnaires

Subjective assessment measures are the most frequently used method of assessing physical activity in free-living individuals. These measures vary in their complexity, from self-administered single-item questions to comprehensive interviewer-administered surveys of lifetime physical activity. Single-item questionnaires have been used which ask an individual whether or not they are more active than others their age and sex. These simple single item questions have often been used to adjust for the confounding influence of physical activity when exploring associations of more primary interest [68]. More complex questionnaires attempt to survey a wide range of popular activities over a selected time frame.

Questionnaires also vary according to time frame. They may inquire about usual activity or ask about activity within past day, week, month, year or even over a lifetime. Questionnaires that focus on a longer-time frame, such as 1-year, may be more likely to represent usual activity patterns and have been used extensively in epidemiologic studies. Questionnaires with a short time frame have two advantages over those with longer time frames: the estimates are less vulnerable to recall bias and they are more practical to validate with objective measures. However, assessment over a short time period is less likely to reflect "usual" behavior, as activity levels may vary with seasons, as a result of an acute illness, or time commitment[72]. In order to obtain the best estimate of physical activity levels, some questionnaires may include assessment over both a short and a long term period.

Problems and Limitations with Subjective Measures

Large epidemiologic studies often use questionnaires to assess physical activity due to cost and ease of administration[72]. However, the use of a questionnaire in the SHFS may be problematic since activity must be assessed across a wide range of ages (14-93 years). There has been some suggestion that very young children often have difficulties with self-report questionnaires because of the sporadic nature of their activity participation which makes these activities difficult to recall, quantify, and categorize[73]. In elderly adults, the use of subjective measures may also pose a problem due to issues with memory and recall. In addition, questionnaires may not adequately assess lower intensity physical activities such as unstructured physical activities like walking and housework. These activities tend to be difficult to recall and have been shown to be less reproducible when assessed by questionnaire than higher intensity activities such as many of the organized sports [74].

Several reports have indicated that the most frequent types of activities reported in minority populations include household and care-giving activities, walking for exercise, and lawn and garden activities [30-32, 75]. Data from the Third National Health and Nutrition Examination Survey (NHANES III) showed that walking was the most frequently reported activity among minority populations[76]. Therefore the use of objective physical activity measures may be warranted in order to assess physical activity across the entire spectrum of physical activity.

In the SHFS, as a large proportion of the study population, more specifically older adults, may engage in lower intensity physical activity, which is difficult to recall and quantify. It is possible that a subjective measure like a questionnaire may miss a large proportion of physical activity performed by these individuals. Therefore, the use of an objective measure of physical activity may be more appropriate to account for these lower intensity activities.

2.2.2 Objective Measures

Objective measures of physical activity include measures of total energy expenditure such as the doubly-labeled water technique and measures that estimate physical fitness such as heart rate monitoring and graded exercise testing[72]. Currently step counters/pedometers and movement counters/accelerometers have become the objective measure of choice in the assessment of physical activity and will be the focus of this review.

2.2.2.1 Accelerometers

Accelerometers are small, non-invasive, battery operated devices worn on the waist, arm, or ankle that measure the rate and magnitude of truncal or body limb movement through the use of electrical charges obtained from the distortion of piezoelectric ceramics contained within the monitor [77]. Several types of accelerometers are commercially available and measure both the quantity and intensity of movement in one or more directions, up and down, side to side, and/or forward and backward. The information collected by these accelerometers is expressed in activity counts, which incorporates the quantity and intensity of activity. In addition, some accelerometers are considered to be dual-mode, which allows them to also function like a pedometer and capture steps performed by the wearer.

Accelerometers have been validated in a variety of laboratory and field settings and have been shown to be valid and reliable in children [78-80], adults [81-83], and older adults [84, 85]. Accelerometers have been found to successfully detect bouts of moderate-intensity physical activity such as brisk walking[86] and have been used to validate physical activity questionnaires [87-89], and quantify associations between physical activity behaviors and health outcomes[90]. The accelerometer is considered to be one of the current "gold standards" in assessing physical activity levels and has often been used to validate the pedometer [91].

2.2.2.2 Pedometers

In comparison to accelerometers, pedometers are much less expensive in terms of both unit cost and data management. Pedometers are small simple digital devices usually no larger than a matchbook. They are worn on the hip on a belt or waistband along the midline of the thigh and count the number of steps taken or the distance walked by the individual. Over the past decade, they have gained much attention because of their ability to provide accurate, objective, measures of walking behaviors. Unlike a subjective questionnaire, the pedometer does not rely directly on participant recall therefore reducing the possibility of bias; however participants are still required to record their step counts manually in a diary or log. Conversely, pedometers do not afford the luxury of providing information regarding pattern of activity like subjective questionnaires. Like accelerometers, pedometers measure steps that can reflect ambulatory movement and are sensitive enough to capture the variable and subtle individual differences in patterns of sporadic or inconsistent physical activity behaviors. But, unlike an accelerometer, the pedometer is not capable of determining the intensity of activity performed.

Most pedometers are battery-operated and contain a horizontal spring-suspended lever arm that moves up and down in response to vertical accelerations of the hip. This motion opens and closes an electrical circuit, which accumulates steps and provides a digital display during activities such as walking and running.

2.2.3 Measurement Properties – Convergent Validity

The validity of an assessment instrument is commonly considered one of its most important attributes. Convergent validity is the extent to which an instrument's output is associated with that of other instruments intended to measure the same exposure of interest. The proceeding paragraphs will provide detailed information regarding the convergent validity of the pedometer more specifically the DigiWalker/Accusplit pedometer used in the Strong Heart Family Study, in a variety of laboratory and field settings.

2.2.3.1 Pedometers vs. Self-Report and Observed Distance Walking

The relationship between pedometer and self-report measures varies depending on the self-report instrument used. Self-reported and observed distance walked consistently correlates with pedometer-estimated distance walked and step counts (Tables 2.1 and 2.2)[81, 82, 91-95] . Bassett et al. (1996)[91] assessed the accuracy of five electronic pedometers for measuring steps taken and distance walked. The results of this study indicated that at walking speeds of 80-107 $m \cdot min^{-1}$, the pedometer recorded steps and distance within 1% of actual. In another study by Bassett et al. (2000)[96], correlations comparing the relationship of daily walking with distance measured by the College Alumnus Questionnaire indicated a modest association between the two assessment instruments (r = 0.35 to 0.48). When pedometer steps for distance walked were compared with instruments that determine distance, such as a calibrated measuring wheel, the correlations between two measures was 0.98. The pedometer has also been shown to be accurate in counting steps over a 400-m level walk (± 3% of actual steps taken)[93]. A more recent study by Crouter et al. (2003)[92] re-examined the validity of ten electronic pedometers for measuring steps, distance, and energy cost. As with the previous studies, the pedometer underestimated steps at speeds below 54 $m \cdot min^{-1}$, but improved with an increase in speed. At speeds greater than 80 $m \cdot min^{-1}$, the pedometer estimated steps within ±1% of actual steps. In regard to distance traveled, the pedometer estimated mean distance to within ±10% at 80 $m \cdot min^{-1}$, but overestimated distance at slower speeds.

Table 2.1 Relationship between pedometer output and self-report activity

Study	Methods	Sample	Pedometer	Monitoring frame and output	Summary Results
Leenders et al.[81]	Relationship with EE from 7-day PAR (Pearson correlations)	12 females Aged 26 ± 6 years	Yamax Digiwalker 500	7 days; steps/day	R = 0.94, p , 0.001
Bassett et al.[96]	Relationship with daily walking distance from the College Alumnus Questionnaire (linear regression)	48 males, 48 females Aged 25-70 years	Yamax Digiwalker 500	7 days	Males: r = 0.35, P = 0.02 Females: r = 0.48, p = 0.001
Welk et al.[94]	Relationship between pedometer and EE and total time in activity from 7-day PAR (correlations)	17 males, 14 females Aged 29 ± 8 years	Yamax Digiwalker	14 days; steps/day; steps/PAR category	EE: r = 0.34 Total time in activity: r = 0.39 EE in light and moderate intensity activities: r = 0.49 Time spent sitting: r = -0.38
Singh et al.[95]	Relationship with select questionnaire variables (Spearman correlations)	66 females, 38 males Aged 25 years and older	Yamax Digiwalker SW-200	10 days, 7 days analyzed; steps/day	Women: Total: r = 0.24, p < 0.05 Run-walk- jog: r = 0.26, p < 0.05 Sports/Rec. r = 0.32, p < 0.01 Vigorous; r = 0.35, p < 0.0 Men: Total: r = 0.14, NS Run-walk- jog: r = 0.17, NS Sports/Rec.: r = 0.28, p < 0.05 Vigorous; r = 0.30, p < 0.05

EE = Energy Expenditure; PAEE = Physical Activity-Related Energy Expenditure; Accelerometers: Actigraph/CSA = Computer Science Applications

Table 2.2 Relationship between pedometer output and observed time physical activity

Study	Methods	Sample	Pedometer	Monitoring frame and output	Summary Results
Crouter et al.[92]	Relationship with investigator determined steps by a hand counter (Two-way ANOVA)	5 males, 5 females Aged 33 ± 12 years	Yamax Digiwalker SW-701	Five 5 minute bouts at different walking speeds; steps	No significant difference between hand tallied steps and steps on the pedometer ($p > 0.05$)
Schneider et al.[93]	Relationship with investigator determined steps over a 400 m walk (paired t-tests; Bland-Altman scores)	10 males, 10 females Aged 34.7 ± 12.6 and 43.1 ± 19.9 years, respectively	Yamax Digiwalker SW-701	400 meter walk; steps	Mean error scores≈ -0.1, Not significantly different from O. 400 m walk: differed from actual steps by < 17 steps ($p< 0.05$)
Le Masurier et al.[82]	Relationship with observed steps on treadmill	13 males, 7 females Aged 20-55 years	Yamax Digiwalker SW-200	Five 5 minute bouts at different walking speeds; steps	No significant difference noted between actual steps taken and number of steps recorded by pedometer. Significantly underestimated steps at speeds of 54 m/min.
Motl et al.[97]	Relationship with observed steps on treadmill in MS patients (Two-way ANOVA)	1 male, 22 females Aged 40.3 ± 8.6 years	Yamax Digiwalker SW-200 & SW-401	Five 5 minute bouts at different walking speeds; steps	No significant difference noted between actual steps taken and number of steps recorded by either pedometer. Both pedometers significantly underestimated steps at speeds of 41 & 54 m/min.

EE = Energy Expenditure; PAEE = Physical Activity-Related Energy Expenditure; MS = Multiple Sclerosis Accelerometers: Actigraph/CSA = Computer Science Applications

2.2.3.2 Pedometers vs. Accelerometers

Step-counts from the pedometer have been found to correlate well with different accelerometer outputs (Table 2.3). As discussed earlier in this chapter, depending on the instrument used, accelerometer data can be expressed as either activity counts, which incorporates the quantity and intensity of activity, or simply as steps.

Several studies conducted in both children [98] and adults [81, 99-101] indicate that the output of pedometers is quite similar to that produced by accelerometers in free-living conditions. Leenders et al. (2000)[81] provides information between the steps/day from the pedometer and the activity counts from the Tritrac and CSA accelerometers, $r = 0.84$ to $r = 0.93$ under free-living conditions. These findings indicate that the number of steps recorded by the pedometer is comparable of physical activity performed during the day as estimated by counts on accelerometers. Tudor-Locke et al.[101] compared the steps/day output of the CSA accelerometer and Yamax pedometer under free-living conditions. The Pearson correlation between the two instruments steps/day was $r = 0.86$, $p < 0.001$, indicating a strong linear relationship between the two instruments. In regard to mean steps/day, participants averaged 11,483 ± 3,856 (CSA) and 9,638 ± 4,030 (pedometer) steps/day. The mean difference in steps detected between the instruments was 1,845 ± 2116 steps/day. The authors concluded that the high correlation between the two instruments does support the interchangeability of the two instruments with regard to steps taken and that differences in mean steps per day detected may be due to differences in instrument sensitivity thresholds and/or attachment.

Table 2.3 Relationship between pedometer and accelerometer output

Study	Methods	Sample	Pedometer	Monitoring frame and output	Summary Results
Kilanowski et al.[98]	Relationship with Tritrac magnitude/min. under different activity conditions (correlations)	7 males, 3 females Aged 7-12 years	Yamax Digiwalker SW-200	Classroom period: 57.0 ± 10.4 min Recreation period: 48.6 ± 7.9 min Step counts/min	Recreation: r = 0.98, p < 0.001 Classroom: r = 0.50, p < 0.41 Combined: r = 0.99, p < 0.001
Leenders et al.[81]	Relationship with Tritrac vector magnitude and CSA activity counts (Pearson correlations)	12 females Aged 26 ± 6 years	Yamax Digiwalker 500	7 days; steps/day	Tritrac-V mag: r = 0.93 Tritrac-Z: r = 0.88 CSA counts/day: r = 0.84 All significant at p < 0.0001
Bassett et al.[99]	Relationship with Caltrac kcals, CSA counts/min, Kenz kcals (Pearson correlations)	38 males, 43 females Aged 19-74 years	Yamax SW – 701	15 minutes in six different activities	Caltrac: r = 0.86 CSA: r = 0.80 Kenz: r = 0.93 All significant at p < 0.01
Leenders et al[100]	Relationship with Tritrac PAEE and CSA PAEE	13 females Aged 21-37 years	Yamax Digiwalker 500	7 days; PAEE in kcals	Specific r-values not reported; relationships between instruments were not significant
Tudor-Locke et al.[101]	Relationship with CSA counts/min ; steps/day (Pearson correlations)	27 males, 25 females Aged 38.0 ± 12.0 years	Yamax Digiwalker SW-200	7 days; steps/day	CSA counts/min: r = 0.74, p < 0.0001 CSA steps/day: r = 0.86, p , 0.0001

PAEE – Physical Activity-Related Energy Expenditure; Accelerometers: Actigraph/CSA = Computer Science Applications, Tritrac, Caltrac

2.2.3.3 Pedometers vs. Measures of Fitness and Energy Expenditure

Pedometer determined physical activity tends to correlate fairly well with different measures of energy expenditure (Table 2.4). This relationship between pedometer outputs and energy expenditure is complicated by the use of many different direct and indirect measures of energy expenditure and populations samples. Pedometers generally correlate with heart-rate estimated energy expenditure r = 0.46 to 0.88 [79, 102], and with indirect calorimetry from r = 0.49 to 0.81 [81, 92, 99, 103]depending on the monitor of use and expression of output. However, one study compared physical activity related energy expenditure (PAEE) from the number of pedometer steps taken per day with energy expenditure derived from doubly labeled water (DLW) in 13 females 21-37 years. Comparisons between these two techniques were conducted by Pearson product-moment correlations and by t-test incorporating Bonferroni adjustments. Results of the correlational analyses between PAEE from DLW and the pedometer were not presented. The results of the paired t-test analyses indicted that PAEE from the pedometer underestimated energy expenditure from doubly labeled water by as much as 59% (798 ± 83 kcals/day DLW vs. 301 ± 36 kcals/day pedometer, $p<0.05$). The authors concluded that the pedometer is a useful tool to rank individuals in regard to physical activity levels, but not to determine physical activity related energy expenditure.

Table 2.4 Relationship between pedometer output and other measures of fitness and energy expenditure

Study	Methods	Sample	Pedometer	Monitoring frame and output	Summary Results
Kahiwazaki et al.[102]	Relationship with heart rate EE (correlations after square root transformation)	10 male clerical workers an 13 male assembly workers Aged 36.3 ± 8.4 years	Yamax DX-1	24 hours; pedometer step counts	All participants: r = 0.64 Clerical workers: r = 0.72 Assembly workers: r = 0.57 All significant at $p < 0.001$
Eston et al.[79]	Relationship with VO_2 and heart rate during unregulated play and treadmill activity (Pearson product moment correlations)	15 males and 15 females Aged 8.2-10.8 years	Yamax Digiwalker DW-200	Duration of specific activity: counts/min	All activities: $p <0.001$ VO_2: r = 0.81 Heart rate: r = 0.62 Unregulated play: VO_2: r = 0.92 Heart rate: r = 0.88 Treadmill activity: VO_2: r = 0.78 Heart rate: r = 0.82
Hendelman et al.[103]	Relationship with VO_2 during self-paced walking (Pearson product moment correlation)	10 males, 15 females Aged 30-50 years	Yamax Digiwalker SW-701	Four 5 minute walks; leisure, comfortable, moderate, & brisk; steps/min	All bouts combined: VO_2: r = 0.75
Bassett et al.[99]	Relationship with indirect calorimetry EE (t-tests, Pearson correlations)	38 males, 43 females Aged 19-74 years	Yamax DW-500	15 minutes in six different activities	Mean error score ≈1.2, significantly different from 0, $p < 0.001$ Pearson correlation: r = 0.49, P , 0.01
Crouter et al.[92]	Relationship with indirect calorimetry EE (Two-way ANOVA)	5 males, 5 females Aged 33 ± 12 years	Yamax Digiwalker SW-701	Five 5 minute walks on the treadmill at different speeds; kcals	Significantly overestimated EE at all speeds ($p < 0.05$)
Leenders et al.[100]	Relationship with doubly labeled water PAEE (Pearson product moment correlation)	13 females Aged 21-37 years	Yamax Digiwalker 500	7 days; PAEE in kcals	Specific r-values not reported; relationship not significant Pedometer was found to underestimate PAEE derived from doubly labeled water by 59%

EE = Energy Expenditure; PAEE = Physical Activity-Related Energy Expenditure; CSA – Computer Science Applications

2.2.4 Measurement Properties: Construct Validity

According to the fourth edition of *A Dictionary of Epidemiology* [104], construct validity is defined as: the extent to which a measurement corresponds to theoretical concepts (constructs) concerning the phenomenon under study. For example, if on theoretical grounds, the phenomenon should change with age, a measurement with construct validity would reflect such a change. Construct validity is typically evaluated by correlational analyses, that is, the magnitude of concordance between two measures (e.g. physical activity levels and a theoretically-related parameter such as age, gender, and anthropometric measures). In examining physical activity prevalence in population based studies, there appears to be a relatively consistent decline in physical activity with age, gender, and BMI[105]. Therefore, the potential confounding effects of age, gender, and BMI should be controlled for either by study design or by analysis.

Results of the Third National Health and Nutrition Examination Survey (NHANES III; 1988-1991) demonstrated that the age-adjusted prevalence of reporting no leisure physical activity over the past month in individuals 20 years or older consistently and significantly increased with age. Fewer that 15 % of the males and 20% of the females aged 18-29 years engaged in no physical activity compared to 35% of the males and 54% of the females aged 75 years or older. Similar trends were noted in two other national physical activity surveys of adults, the National Health Interview Survey (HIS; 1985, 1990, 1991) and the Behavioral Risk Factor Surveillance System (BRFSS; 1986-1991, 1992, 1994). Most recently, results of the 2000 National Health Interview Survey conducted by the National Center for Health Statistics found that adults in 65 years and older were about five times more likely as adults in the 18-24 years age group to never be physically active[106].

In addition, several studies have documented a decline in physical activity levels with increasing BMI. On such study by Kimm et al.[107] showed a significant relation between physical activity and changes in BMI and sum of skinfold thickness in a large cohort of black and white girls during the important transition from childhood to adulthood. This cohort had a pronounced decline in physical activity while their rate of overweight and obesity doubled.

Previous studies have shown that physical activity levels appear to decline with increasing age and BMI. Furthermore, males tend to be more active than females. We would expect to see these same associations and trends in the Strong Heart Family Study. Therefore, we will examine the relationship between physical activity levels and age, gender, and BMI in the SHFS. Furthermore, we will also determine if these factors pose potentially confounding effects on physical activity levels within the SHFS and whether there is a need to control for these effects in our analyses.

Problems and Limitations with the Pedometer

There are several limitations that must be considered when using the pedometer as a physical activity assessment tool. Pedometers cannot determine intensity of physical activity. When assessing physical activity levels, pedometers cannot discriminate between steps accumulated in walking, running, or stair climbing. Hence, their ability to predict energy expenditure is limited. Pedometers assume that a person expends a constant amount of energy per step. In addition, many pedometers, such as the Accusplit pedometer used in the current study, lack internal clocks and data storage ability. Thus, the pedometer is unable to provide information on the pattern of activity leaving researchers to rely on participants to accurately record their step counts from the pedometer in a diary. This process may increase the possibility for reporting errors. In addition, the pedometer is intended to be worn specifically on the hip and is designed to capture ambulatory movement, (i.e. walking and running behaviors). Therefore, it is not capable of detecting movement and external work done in pushing, lifting, or carrying objects or in activities that do not detect the up-and-down motion of the hip such as bicycling. Furthermore, since the pedometer is not waterproof, it is not capable of capturing water activities such as swimming. Finally, participant clothing may play a role in pedometer accuracy. In order for a pedometer to accurately assess physical activity, it must be worn snug to the body and kept upright in a vertical plane, perpendicular to the ground. If the pedometer is not worn in this manner, the pedometer will not work properly and may underestimate activity levels.

It has been suggested that pedometer accuracy is compromised in obese individuals, primarily because the pedometer is worn on the waist and needs to remain upright in a vertical plane, perpendicular to the ground in order to accurately count steps[108]. Since obese individuals often have very large waists, the pedometer may tilt into a horizontal plan and may, in turn, result in an underestimation of step counts or no step counts at all. The literature in this area is limited with only a few studies available. One such study by Swartz et al. (2003)[109] examined the accuracy of the pedometer for assessing steps taken while walking in groups of adults with varying body mass index. For this study, participants were categorized according to one of three BMI categories identified by the World Health Organization: normal (N=25; < 25 kg/m^2), overweight (N=24, 25-29 kg/m^2), and or obese (N= 17; ≥ 30 kb/m^2). It was noted that category of BMI did not significantly affect pedometer accuracy. Another study by Elsenbaumer and Tudor-Locke[110] also found that BMI category was relatively unimportant and had little effect on the percent error of pedometers at self-selected normal walking speeds. In contrast, Crouter et al.[111] noted that the pedometer became less accurate in persons with increasing BMI and increasing waist circumference. However, the authors concluded that pedometer tilt angle was more important in pedometer accuracy than actual waist circumference and BMI measures and that correct placement of the pedometer is necessary for accurate measures when utilizing the pedometer.

In addition, it has been suggested that pedometer validity may be compromised in individuals, who walk at slow speeds[112]. In older adults, gait impairments were found to compromise pedometer accuracy in community dwelling stroke patients[113]. A recent study by Cyarto et al. (2004)[114] examined the accuracy of pedometers in nursing home residents and community dwelling older adults. Using self-selected speed each participant was asked to walk 100 steps while a researcher manually counted the steps. Pedometers were found to significantly underestimate observed steps taken by 74% (slow), 55% (normal) and 46% (fast) paces ($p<0.0001$) in nursing home residents. In community dwelling participants, the pedometer failed to detect 25% (slow), 13% (normal) and 7% (fast) of actual steps taken ($p<0.0001$). Our own ongoing research at the University of Pittsburgh has noted similar findings to those of Tudor-Locke in community dwelling older adults from suburban Pittsburgh [115]. In brief, our results indicate the pedometer underestimated 16% of observed steps during a 100 step test in 34 community-dwelling older adults with most of the underestimation occurring in those with slow gait speeds. When examined by gait speed, the pedometer underestimated observed steps taken by 31.2% (very slow), 12.7% (slow) and 11.1% (normal). These results indicate that slow walking speed and gait disorders may indeed hamper the utility of pedometers in the assessment of physical activity.

In conclusion, the pedometer is a useful tool for the assessment of physical activity levels but is not without limitations. How we plan to handled these limitations within the proposed study will be discussed in the next section.

2.3 PHYSICAL ACTIVITY MEASURES SELECTED FOR THE CURRENT STUDY

Most studies conducted in Native Americans, including early phases of the Strong Heart Study (SHS), assessed physical activity using subjective methods. In comparison to early phases of the SHS, the age range of the SHFS cohort is much wider and encompasses ages ranging from 14-93 years. This wide age range and the fact that many of the older/elderly participants may not participate in many moderate to high intensity activities, make the use of a questionnaire in this population difficult. It is possible that the questionnaire may miss a large proportion of physical activity performed by older and elderly participants. The use of an objective measure of physical activity in this population may help to eliminate many of the problems posed by the use of subjective measures. Although, it has its own limitation, the pedometer has been selected for use in the SHFS because it has the capability to capture physical activity across a wide range of ages.

As was discussed previously, pedometer accuracy may be affected in persons with large BMIs where the pedometer may not remain in the vertical plane or perpendicular to the ground due to excess abdominal body weight. Since the SHFS cohort has many participants classified as obese (BMI>30 kg/m^2) or extremely obese (BMI>40 kg/m^2) according to NHLBI classification of overweight and obese by BMI, the SHFS field staff was trained to instruct participants, especially obese participants where the pedometer may not be maintained in a vertical plane, to move the pedometer to the small of the back. This position has been shown to help improve the tilt of the pedometer thus improving the pedometer's ability to accurately assess physical activity and as Crouter et al.[92] suggested, the tilt of the pedometer was more important to achieving accurate step counts than actual waist circumference. However, as it is still possible that participants within the extreme BMI categories may have lower counts on their pedometer due to the pedometer's inability to correctly assess physical activity; we will examine the pedometer data in regard to extreme levels of BMI.

A majority of studies have indicated an inverse relationship between physical activity levels as determined by the pedometer and age. In elderly individuals, it is possible that the decline in physical activity levels may be due, in part, to slow gait speed and gait abnormalities, which tend to cause an under estimation of steps taken. Since the SHFS did not assess gait speed, we are not able to consider the affect of gait speed on pedometer accuracy in the older age groups during our analyses. However, we will stratify the cohort by age and examine whether removing the extreme elderly subgroup from our analyses alters our results.

In addition, functional limitation or injury may cause decreased physical activity levels. Information regarding health status and functional limitations has been collected for the entire cohort. This information will be taken into account when analyzing the pedometer data. We will plan to examine the cohort to adjust and possibly remove those who reported any major illnesses and/or injuries that may limit their physical activity levels.

2.4 FAMILIAL AGGREGATION OF PHYSICAL ACTIVITY

According to the American Heritage® Stedman's Medical Dictionary[116], familial aggregation is the occurrence of a trait in more members of a family than can be readily accounted for by chance. In other words, familial aggregation can be defined as the combination of genetic and environmental influences within a family. The concept of familial aggregation has been applied to many factors associated with health such as blood pressure[117, 118], blood lipids[119-121], cardiovascular disease[121-123], and body composition[124, 125]. Only recently has it been applied to physical activity research. Evidence of familial aggregation of physical activity levels is presented in Table 2.5. The studies included in Table 2.5 reveal that while there is evidence of familial aggregation of physical activity, the issue is still not resolved due to limitations in the existing studies to date. These limitations include: inconsistencies among physical activity assessment methods, sample size, and sample characteristics.

Table 2.5 Evidence for Familial Aggregation of Physical Activity Levels

Author & Year	Study Design	N	Methods	Results	Parental Influence
Aarnio et al., 1997[63]	Cross-sectional	3524 twin pairs and their parents and grandparents	*Children*: two questions *Parents*: two questionnaires *Grandparents*: questions answered by the parents (their children)	Correlations among twin sibships ranged from r=0.22-0.72. No relationship noted between parents and offspring or between grandparent and offspring.	-
Anderssen & Wold, 1992 [44]	Cross-sectional	904 students in Western Norway (mean age 13.3 years)	Questionnaire regarding perceived influences of parent and peers	Parental and peer physical activity level seem to influence reported activity levels of the student.	+
Bogaert et al., 2003[48]	Cross-sectional	43 children aged 6-9 and at least one biological parent	Bouchard Questionnaire (3-Day PAR)	Significant positive relationships between mothers and daughters for time spent in low or sedentary activity (r=0.44, p=0.03) and between fathers and children for percent time in low activity (r=0.43, p=0.005).	+
Duncan et al., 2002[49]	Cross-sectional	134 children (mean age 12.8 years) – parent pairs	*Children*: Four by One-Day PAR Parents: Godin Leisure Time Exercise Questionnaire (7 days)	Correlations ranged from r=0.37-0.43 for fathers PA and offspring. PA No relationship noted for mothers and offspring.	+ father - mother
Fogelholm et al., 1999 [50]	Cross-sectional	129 obese children & parents 142 normal weight children & parents	*Children*: 3DPAR & Netherlands Health Education Project Questionnaire *Parents*: 3DPAR & one question regarding habitual PA	Parent inactivity was a strong and positive predictor of child inactivity. Correlations for inactivity were stronger (r=0.29 – 0.47) than those for PA level (r=0.28-0.33).	+ - father

(+ positive association, +/- weak association, - no association) Abbreviations: PA – Physical Activity, PAR – Physical Activity Recall

Table 2.5 Evidence for Familial Aggregation of Physical Activity Levels continued

Freedson & Evenson, 1991[51]	Cross-sectional	30 children aged 5-9 and their biological parents	Caltrac accelerometer and Caltrac activity record	Using Chi-Square analyses, familial aggregation of PA occurred in 67% of the sample (fathers - offspring) and 73% of the sample (mother-offspring) using the Caltrac counts. Using the activity record, familial aggregation occurred in 70% of father-offspring pairs and 66% of mother-offspring pairs.	+
Godin et al, 1986[60]	Cross-sectional	198 12-14 year old children and their parents	Godin Leisure Time Exercise Questionnaire (7-days)	No relationship noted between parent's self-reported level of PA and offspring's self-reported level of PA	–
Kalkanis et al., 2001 [52]	Cross-sectional	51 families – one parent and one child (8-12 years)	Tritrac accelerometer	Using regression models, parent's vector magnitude explained ~19.7% of the model variance predicting child's vector magnitude. Parent's average # of bouts explained 17.3% of the model variance predicting Child's average # of bouts.	+
Kimiecik & Horn, 1998[64]	Cross-sectional	81 children (11-15 years) and their parents (79 mothers and 63 fathers)	Children: 2 day recall Parents: two questions	No relationship noted between parent's own self-reported level of PA and their child's self-reported MVPA	-
McGuire et al., 2002 [61]	Cross-sectional	Project EAT (Eating Among Teens) 900 adolescents and one parent	Adolescents: Godin Leisure Time Exercise Questionnaire (7 day) Parents: questions regarding work, sport, sweating/breathing heavy	No association noted between parental PA and offspring PA.	-

(+ positive association, +/- weak association, - no association) Abbreviations: PA – Physical Activity, PAR – Physical Activity Recall

Table 2.5 Evidence for Familial Aggregation of Physical Activity Levels continued

Mitchell et al., 2003 [27]	Cross-sectional	San Antonio Family Heart Study 1,421 participants from 42 large Mexican-American Families	Stanford 7-day physical activity recall questionnaire	No relationship noted between parent PA and offspring PA (r = -0.02, ns for parent and offspring).	-
Moore et al., 1991[43]	Cross-sectional	Framingham Children's Study 100 4 -7 year old children 99 mothers/92 fathers	Caltrac accelerometer	Child of an active mother is 2.0, of active father 3.8, and of active both parents 5.8 times more likely to be active than inactive child	+
Perusse et al., 1989 [54]	Cross-sectional	Quebec Family Study 1610 subjects 375 extended families which included 717 parents and 893 biological/adopted children (mean age 14.6 ± 3.3 years)	3-Day Activity Record	Correlations ranged from r=0.16-0.72 for Habitual Physical Activity Level (HPAL) and r=0.09-0.76 for Exercise Participation (EP). Correlations between parent and child were very low (0.16), however correlations between full siblings/twins were very strong (0.42-0.72)	+/-
Perusse et al., 1988 [53]	Cross-sectional	Canada Fitness Survey 16,477 participants aged 10 years and older from across Canada	11-page questionnaire regarding physical activity and lifestyle	Interclass correlations ranged from r = 0.09-0.21 for Energy Expenditure (EE) and from r = 0.13-0.23 for Time on Activity (TA).	+/-
Raudsepp & Viira, 2000 [55]	Cross-sectional	375 13-14 year old adolescents and their biological parents and siblings	7-Day Physical Activity Recall	Males PA was significantly related to fathers' and brothers' PA (r=0.15-0.37). Females PA was associated both with parental and siblings' moderate intensity PA as well as fathers' total weekly PA (r=0.17-0.33).	+

(+ positive association, +/- weak association, - no association) Abbreviations: PA – Physical Activity, PAR – Physical Activity Recall

Table 2.5 Evidence for Familial Aggregation of Physical Activity Levels continued

Sallis et al., 1988 [56]	Cross-sectional	95 Anglo-American + 111 Mexican-American families Children's' mean age 13 years	7-Day Physical Activity Recall	Moderate degree of familial aggregation of PA in both samples. Correlations tended to be higher in Mexican-Americans. Mother-child correlations were usually higher than father-child.	
Simonen et al., 2002 [57]	Cross-sectional	Québec Family Study 200 French-Canadian families Offspring mean age 27 years	3-Day Activity Diary	Familial aggregation of PA phenotypes adjusted for age and sex resulted in F=1.40-1.52 times more variation in PA levels between families than within families. Modeling for Maximal Heritability ranged from 10%-32%.	+
Trost et al, 2003 [62]	Cross-sectional	380 students in grades 7-12 (mean age 14.0 ± 1.6 years) and their parents	Children: 7-Day Physical Activity Recall Parents: Parents completed a questionnaire where they reported the number of days in the past week they participated in specific activities.	Parental physical activity did not directly influence child physical activity.	-
Wagner et al., 2004 [44]	Cross-sectional	3437 French children (mean age 12.1 ± 0.6 years) and their parents	Children: Modifiable Activity Questionnaire for Adolescents Parents: self-administered physical activity questionnaire	Son of both active parents is 1.97, of active mother is 1.48, and of active father is 1.36 times more likely to participate in structured physical activity. Daughter of both active parents is 1.56, of active mother is 1.80, and of active father is 1.41 times more likely to participate in structured physical activity.	+
Welk et al., 2003 [59]	Cross-sectional	994 elementary school students and parents	Children: Physical Activity Questionnaire of Children (PAQ-C) Parents: Two questions	Correlations between parent's PA and offspring activity ranged from r =0.13-0.16.	+/-

(+ positive association, +/- weak association, - no association) Abbreviations: PA – Physical Activity, PAR – Physical Activity Recall

Participation in physical activity is a behavioral trait, which is mainly determined by environmental factors such as household structure but which also shows a modest heritability level [126]. Although data on the molecular genetics of physical activity levels is scarce, previous studies indicate that certain social, cultural, genetic, and environmental factors may predict consistent physical activity participation [21, 22, 24]. Most studies reveal that parental exercise pattern and encouragement have an effect on their children's physical activity behavior, and that physically active parents tend to have physically active children [43, 46-59]. From a theoretical point of view, participation in sport and physical activity may be considered a modeling process for which family members are powerful role models [25, 45].

Parents play an influential role in their children's physical activity behavior[42, 127, 128]. Socialization within the family[42, 128], parental modeling[42, 44], and parental exercise patterns and encouragement[48-52] are believed to comprise a primary influence on children and adolescents' health related behaviors. Furthermore, it is believed that parents who are physically active are more likely to have physically active children[44, 47, 51, 55, 56, 63, 128]. Evidence of the association of physical activity levels between parents and their offspring can be noted in the genetic or familial aggregation literature in which the sample populations consist of twins (monozygotic and dizygotic) or families (parent-child, siblings), or a combination of the two. These associations will be discussed in more detail in the following paragraphs.

2.4.1 Parent and Child/Offspring Pairs

Several cross-sectional studies have utilized subjective and objective assessment techniques to demonstrate an apparent association of physical activity levels among family members to varying degrees. Despite differences in family types, physical activity assessment tools, and age of the offspring, 14 out of the 20 (~70%) studies provide evidence for the presence of familial aggregation of physical activity levels. Whereas, six studies [60-64, 129] did not. Within all of these studies, a subjective measure was utilized for the assessment of physical activity for the population of interest. Unfortunately, information regarding the validity and reliability of these subjective measures and who completed the questionnaires or interviews was often missing. Lastly, information regarding household structure/environment was often not provided, so the effect of environment may not have been considered.

As previously mentioned, 14 studies available in the literature noted the presence of familial aggregation of physical activity levels to varying degrees. These studies and their findings are as follows:

Three studies noted weak associations between parents and their offspring with correlations ranging from $r = 0.09 - 0.23$ [52-54, 59]. Two studies indicated a relationship between physical activity levels of only one parent and their offspring [49, 50]. More specifically, Duncan et al.[49] using a subjective method (questionnaire) of physical activity noted a modest relationship between activity levels of fathers and their offspring ($r = 0.37 - 0.43$), but no relationship was noted for mothers and offspring. In contrast, results from a study conducted by Fogelholm et al.[50] showed that mothers who were considered physically inactive according to a physical activity diary had children who were physically inactive, but no association was noted between fathers' physical inactivity and their offspring.

Eight studies provided fairly modest to strong familial associations of physical activity between parents and their offspring[43, 44, 48, 51, 55-58]. Five of these eight studies utilized subjective methods to assess physical activity levels within their population of interest. Wagner et al.[58] examined familial associations of physical activity among 3,437 French children and their biological parents. Physical activity was assessed in children using a standardized questionnaire, the Modifiable Activity Questionnaire for Adolescents. This questionnaire has been validated for use in adolescents and inquires about participation in leisure time physical activity during the past year[130]. For each child, the number of months, weekly frequency, and usual duration of each session of activity was recorded. This information was then used to calculate the average weekly time devoted to leisure time physical activity. Parents' physical activity was assessed using a self-administered questionnaire that inquired about regular structured sports activity participation and hours per day spent watching television. In addition, the number of biological parents living in the household was considered as the indicator of family social structure. Logistic regression models were used to examine familial associations of sports related leisure time physical activity. These results found that a son of a father who is involved in sports activity is 1.36 times and of a mother is 1.48 times more likely to participate in structured physical activity. When both parents were involved in sports activity a son is 1.97 times more likely to participate in structured activity. The same trend was noted in daughters. A daughter of a father who is involved in sports activities is 1.41 times and of a mother is 1.80 times more likely to participate in structured physical activity. When both parents participate in sports activities, a daughter is 1.56 times more likely to participate in structured activity. We plan to examine this association within the SHFS, in families for which data is available on both parents.

Additionally, three of the eight studies utilized objective physical activity monitors to assess physical activity. Interestingly, all three of these studies noted fairly strong familial aggregation. The findings of these studies will be highlighted in the following three paragraphs.

Freedson & Evenson[51] examined familial aggregation among 30 Caucasian, 5-9 year olds and their biological parents. In order to be eligible for the study, both parents must have raised the child together from the child's birth and must have currently been living at the same residence as the child. Only one child was used from each family. Physical activity was assessed using an objective activity monitor known as the Caltrac accelerometer and subjectively using an activity record. Each family member wore the Caltrac on their non-dominant hip for three consecutive 12-hour days (two weekdays and one weekend day). The Caltrac is designed to estimate energy expenditure in kilocalories, however for this study it was used solely as a physical activity counter. In order to do so, the Caltrac was programmed so that only movement was registered. The Caltrac activity scores (counts/day) for parents and children were recorded at the end of each 12 hour day by the parent. In addition, parents completed a Caltrac Activity Record for themselves and their child. This record was used to provide information regarding the frequency, intensity, duration, and types of activities in which the family participated each day. Activities reported in the diary were categorized according to intensity. Using the information obtained from both the Caltrac and the activity record, children and their parents were categorized as high active and low active according to the 50th percentile of Caltrac counts and Caltrac record activity time. Chi-square analyses were utilized, and familial aggregation in physical activity occurred in 67% of father-offspring pairs and 73% of mother-offspring pairs when using the actual counts of the Caltrac. When using the activity record, familial aggregation in physical activity occurred in 70% of father-offspring pairs and 66% of mother-offspring pairs. These results support the presence of familial aggregation of physical activity. Furthermore, since this study required that all family members reside in the same household, the investigators were able to ensure that all participants shared the same environment.

Another study conducted by Moore et al.[43] examined familial resemblance of physical activity in 100 4-7 year old children and their biological parent (99 mothers/92 fathers) from the

Framingham Children's Study. The participants included in this study are two-parent families with a biologic child 4- 7 years of age and are considered to be typical middle-class American families. Like the Freedson study[51], the Caltrac accelerometer was used to assess physical activity levels in the parent-child pairs. Each subject wore the Caltrac on the waist for two periods of 5 consecutive days, approximately 6 months apart. Subjects were asked to wear the device from the time of arising in the morning to bedtime. Parents recorded the time the monitor was attached and removed in a daily log. At the end of each day, activity counts were read from the monitor and recorded by the parents in the activity log. Average Caltrac counts per hour were calculated for each participant, and participants were categorized as active or inactive on the basis of whether their counts/hour, were above or below the median for their generation and sex-specific distribution. Contingency tables were used to examine familial resemblances of physical activity. Results of the study indicated that children of active mothers were 2.0 times more likely to be active as compared to children of inactive mothers (95% confidence interval = 0.9, 4.5). The relative odds ratio of being active for children of active fathers was 3.5 (95% confidence interval = 1.5, 8.3). When both parents were active, the children were 5.8 times as likely to be active (95% confidence interval = 1.9, 17.4) as compared to children of two inactive parents. These results support the notion that parents who are more physically active are more likely to have children who are physically active.

Lastly, Kalkanis et al.[52] examined the level and pattern of moderate-to-vigorous physical activity (MVPA) in 51 8-12 year old children and one parent using an objective Tritrac accelerometer. Children wore the Tritrac during nonschool hours and parents wore the Tritrac before and after work. Parents and children were instructed to wear the monitor on the same days and data was collected on 2 weekdays and 1 or 2 weekend days. Count data from the Tritrac accelerometer was used to determine three outcome variables: vector magnitude score (which is the culminations of the three orthogonal axes which represent vertical, anteroposterior, and mediolateral movement), the number of MVPA bouts for each subject, and duration of physical activity bouts. A bout of MVPA was defined as 1 or more minutes of activity at 4.5 or more METs. Correlational analyses and hierarchal linear regression were used to determine the association of parental physical activity and children's physical activity. Correlations between children's and parents' vector magnitude and the number of bouts of MVPA were significant (0.38, $p < 0.01$ and 0.30, $p < 0.05$, respectively). Results from the regression analyses, revealed that parent's vector magnitude explained ~19.7% of the model variance predicting child's vector magnitude from the Tritrac. Parent's average number of bouts of activity explained 17.3% of the model variance predicting child's average number of bouts of activity. Findings of this study indicated that parents' activity levels significantly and independently predicted as well as improved the prediction of physical activity level and number of MVPA bouts beyond other determinants of children's activity levels.

2.4.2 Twin and Sibling Pairs

Twin research designs and methods are valuable tools for examining genetic and environmental influences on behavioral and medical characteristics. Because Monozygotic (Mz) twins are genetically identical whereas Dizygotic (Dz) twins have only the same genetic relationship as siblings, a difference between Mz and Dz pairs with respect to some measurement of interest is customarily attributed to heredity[131]. An additional factor that must be assumed within twin studies is that Mz and Dz twins share environmental factors equally; therefore, it is easier to determine the degree of relatedness and observed similarities.

A few studies within this review utilized twin methodology and physical activity phenotypes assessed by questionnaire to determine the genetic effect of physical activity. These studies[54, 63] noted that physical activity levels between Mz twins and Dz twins were highly correlated, $r = 0.64\text{-}0.74$, $p < 0.001$ and $r = 0.41\text{-}0.76$, $p < 0.001$, respectively. In comparing Mz and Dz twins stratified by gender, both Mz twin boys and girls had stronger associations when compared to Dz twin boys and girls (Boys: 0.72 Mz vs. 0.45 Dz, Girls: 0.64 Mz vs. 0.41 Dz). Among non-twin sibships, associations of physical activity levels ranged from $r = 0.21 – 0.42$, $p < 0.001$. Findings observed in sibships of biologically related persons (siblings, dizygotic twins, and monozygotic twins) indicate a significant familial resemblance of physical activity. The findings of these studies showed that physical activity among siblings is genetically influenced, with heritability coefficients between 0.21 and 0.76, which still leaves a considerable influence of shared environmental factors. For this reason, we will begin to look at household environment and whether it influences the degree of familial aggregation of physical activity levels.

2.4.3 Extended Family Member Pairs

Lastly, a few studies[54, 63] have examined the association of physical activity among other extended family members. More specifically, the association of physical activity levels was examined among grandparent-grandchild pairs, uncle (aunt)-nephew (niece) pairs. Among extended family members, Perusse et al[54] did not find that uncles or aunts physical activity levels were associated with that of their niece or nephew. Additionally, Aarnio et al[63] did not find that physical activity patterns were associated between grandparent-grandchildren pairs. It is possible that this lack of an association between extended family members, aunt/uncle-niece/nephew or grandparent-grandchild, may be a result of an unshared household environment since physical activity may be a learned or modeled behavior.

2.4.4 Conclusions

The literature regarding familial aggregation of physical activity is sparse; yet it appears to indicate that a familial association of physical activity is present to varying degrees. Within these studies are several limitations such as inconsistencies among physical activity assessment methods, sample size, and sample characteristics.

Inconsistency among Physical Activity Assessment Methods

Many studies included in this review relied on self-report techniques for the assessment of physical activity within their population of interest. This is true for all but three studies included in this review. As previously mentioned subjective physical activity measures are decent, but may be subject to recall bias and cannot provide an accurate representation for all physical activities, particularly low intensity activities. In addition, the assessment of different components of physical activity across studies makes the comparison between studies very difficult. Some studies used total physical activity energy expenditure [49, 53, 54] calculated from several domains. Others studies assessed only occupational physical activity levels [63], leisure physical activity levels [48, 50, 54-58] and in some cases inactivity [50, 57].

In contrast, three studies utilized objective physical activity monitors to assess physical activity among family members[43, 51, 52]. The results of these studies noted fairly strong familial aggregation. There are several possible explanations for these strong findings. First, unlike subjective measures of physical activity, activity monitors do not rely on participant recall therefore they are more consistent in their assessment and reduce the possibility of bias.

Secondly, activity monitors have the ability to capture intermittent or continuous activity as well as low intensity activity, which is often missed when assessed by questionnaire. Subjective measures normally have participants quantify their activity into time periods such as hours or minutes throughout the day. In addition, all three studies utilized a valid and reliable objective assessment tool within their entire population of interest therefore reducing the possibility for inaccurate results. Lastly and most importantly, all three studies had very strict inclusion criteria requiring the parent and child of interest to reside in the same household environment and were likely to be of upper socioeconomic status.

The proposed study utilizes an objective measure, the pedometer, to assess physical activity levels. The pedometer has been selected for use in the SHFS because it is a reasonably valid and reliable assessment technique with the capability to capture physical activity across a wide range of activity intensities and ages. The use of the pedometer should help to eliminate many of the problems posed by the use of subjective measures in previous studies. Furthermore, the pedometer will allow for uniform assessment of activity levels within the entire cohort of the Strong Heart Family Study across all age ranges. Therefore, we will be able to classify participants according to activity level and make direct comparisons between related family pairs.

Sample Size and Sample Characteristics

Very few studies within this review were conducted in large cohorts. Among the 20 studies included in this review, almost half were conducted in small populations of related-pairs[43, 48-52, 56, 57, 60, 64]. Furthermore, many studies did not provide any information regarding sample characteristics such as race/ethnicity, socioeconomic status, and environmental characteristics, all factors that may impact physical activity levels. Only three studies specifically included information regarding the inclusion of minority participants[56, 61, 129]. Of these studies, one study's[129] population was entirely made up of minority individuals. A second study included 46% Mexican-Americans within their cohort[56]. While a third study's [61] population included only 22% black, 18% Asian, and 10% Hispanic participants. In addition, some studies did not provide information relating to household structure or shared environment, so the effect of environment may not have been factored into the familial aggregation analyses. However, it could be assumed that in a majority of the studies where the cohort included a child or children under the age of 18 that the child resided in the same household as their parent.

The proposed study cohort includes approximately 3,259 parent-offspring pairs (2207 mother-offspring and 1052 father-offspring pairs) with physical activity information. Among these parent-offspring pairs, 375 parent-offspring pairs with a child ≤18 years of age are available for examination of familial aggregation of physical activity levels. Moreover, the proposed study cohort consists entirely of Native Americans, an understudied minority subgroup in regard to physical activity, and is the first study to examine familial aggregation of physical activity in this population. Furthermore, information regarding household structure/environment which identifies which family members live in the same household has been collected. This information will enable us to examine what role household structure plays, beyond that of heritability, on physical activity levels.

3.0 SPECIFIC AIMS

Objectives of the Project

The primary aim of the current study is to examine cross-sectionally the association between objectively measured physical activity levels among biologically related family members, more specifically parent and offspring. We will utilize the Strong Heart Family Study (SHFS) cohort to examine familial patterns of physical activity. Within the SHFS the eligibility included a "core sibship" of at least five full siblings, of whom a minimum of three siblings were participants in the original SHS cohort. The SHS participants in the core sibship were to have a total of at least 12 offspring who are at least 15 years of age. Based upon these eligibility and recruitment requirements a total of 96 families were enrolled in the study, resulting in roughly 3,800 family participants. From these 96 extended families, 3,259 parent-offspring pairs (2207 mother-offspring and 1052 father-offspring pairs) have been identified. Of these 3,259 pairs, 375 parent-offspring pairs (247 mother-offspring and 128 father-offspring pairs) include a child ≤ 18 years of age. Information regarding household structure and environment was collected and pedometers were utilized to assess physical activity levels.

Utilizing this unique data, we intend to examine familial aggregation of physical activity between biologically related family members, parent and offspring. This will be accomplished through the use of correlation and 2 x 2 contingency table analyses. Furthermore, we plan to determine if physical activity is a heritable trait among biologically related family members and whether a shared household effect is present. This will be accomplished by using variance components modeling, which utilizes a pedigree-based maximum likelihood procedure.

3.1 STUDY HYPOTHESES

1a: Physical activity levels assessed by objective activity monitor (i.e., pedometer) will be significantly and positively associated among biologically related family members, more specifically parent and offspring pairs in the Strong Heart Family Study.

1b: Physical activity is a heritable trait among biologically related family members in the Strong Heart Family Study.

4.0 METHODS

4.1 OVERVIEW OF THE STRONG HEART STUDY PHASES I-III

The Strong Heart Study (SHS) is the largest study of cardiovascular disease (CVD) among American Indian men and women. The SHS is designed to estimate CVD mortality and morbidity and the prevalence of known and suspected CVD risk factors in American Indians. It includes cohort and family/genetic studies and was initialized in October of 1988 after community mortality data from 1984-1988 indicated differences between geographical centers in types of CVD and other causes of death compared to non-Indians[28]. The study population consists of 13 American Indian tribes in three geographical areas in the United States: Arizona, Oklahoma, and North and South Dakota (Figure 4.1). A summary of Phases I-IV can be found in Tables 4.1 and 4.2. To date, the study has completed phases I-III and is presently in the process of completing Phase IV of the Strong Heart Family Study.

Figure 4.1 Locations of Strong Heart Study communities

Phase I-III

During 1988 and 1991, 4549 tribal members ages 45-74 years (62% of the total population ages 45-74 years) from 13 American Indian Tribes (Gila River and Salt River Pima/Maricopa and the Ak Chin Pima/Papago in Arizona; the Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, and Wichita in Southwestern Oklahoma; and the Oglala Sioux, Cheyenne Rive Sioux, and Spirit Lake Communities in South/North Dakota), participated in a baseline examination (Phase I). A second examination (Phase II) was conducted between the years of 1991 and 1996 on 89% of all surviving members of the original cohort. During this phase, surveillance of the cohort for fatal and nonfatal events was instituted. A third and final examination (Phase III) was conducted between 1996 and 2000 in which 88% (3,197 participants) of all surviving participants were re-examined. Additionally, a pilot family study was begun in which 950 individuals from 32 families were examined. Of these, 198 were members of the cohort. Family size ranged from 11-56 individuals. Continuous surveillance of the cohort has been in effect since the completion of the first examination. Information on each member has been obtained yearly, and all deaths and all nonfatal CVD events are recorded and classified according to standardized criteria.

Table 4.1 Summary of Phases I Through IV of the SHS – Cohort Exams

	Community Mortality	Cohort Exams			
		N	Questionnaires	Physical Exam	Blood
I **1988-91**	35-74 yrs. 1984-88	N=4549 45-74 yrs.	Demog Med Hx Meds ROH Smoke PA Family Hx	Ht, Wt W, Hip BP Body Fat ABI Edema ECG	Lipoproteins Apo A1 & B LDL size GTT, HBA1c
II **1991-96**	35-74 yrs. 1988-1994	N=3638 All P-I Alive	All P-I +QOL+diet -Family Hx	All P-I +ECHO +gallbl +PFT +TB	All P-I +CRP +PAI-1 -apos -LP(a) -apoE pheno
III **1996-00**	Not Applicable	N=3197 All P-I Alive	All P-I +QOL +diet -Family Hx +gambling	All P-I +cartotid +tonometry +asthma	All P-I +PAI-1 -apos -LP(a) -apoE pheno
IV **2000-05**	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Case-Control (stored spec) Homocystine Adiponectin Haptoglobin Allotype MBL geno

Abbreviations: Demog = Demographic data; Med Hx = Medical History; Meds = Current Medications; ROH = Rose Questionnaire; Smoke = History of Smoking; PA = Physical Activity; Family Hx = Family History of Related Illnesses; Ht,Wt = Height & Weight; W,Hip = Waist & Hip Measurements; BP = Blood Pressure; Body fat = Impedance Measure of Body Fat; ABI = Ankle/Brachial Index; Edema = Ankle Edema; ECG = 12-lead Electrocardiogram; Apos = Apolipoproteins B and AI; GTT = Oral Glucose Tolerance Test; ApoE pheno = ApoE Phenotypes; Lp(a) = Lipoprotein (a); DNA = DNA from Lymphocytes; Ur Alb/Cr = Urinary Albumin/Creatinine Ratio; P-I = Phase I; QOL = Quality of Life Questionnaire; diet = 24-hr Recall; ECHO = Echocardiogram; gallbl = Gallbladder Sonogram; PFT = Pulmonary Function Test; TB = Tuberculin Test; CRP = C-Reactive Protein; PAI-1 = plasminogen activator inhibitor type 1; gambling = Gambling Questionnaire; carotid = carotid artery sonogram; tonometry = applanation tonometric measure of arterial stiffness; asthma = asthma substudy; MBL = Mannose Binding Lectin; FFQ = Block Food Frequency Questionnaire; pedometer = 7-day Pedometer Measure.

Table 4.2 Summary of Phases I Through IV of the SHS – Family Exams

	Family Exams				Surveillance
	N	Questionnaires	Physical Exam	Blood	
I 1988-91	Not Applicable	Not Applicable	Not Applicable	Not Applicable	All Cohort Mortality All cause CVD Morbidity-CVD
II 1991-96	Not Applicable	Not Applicable	Not Applicable	Not Applicable	All Cohort Mortality All cause CVD Morbidity-CVD
III 1996-00	N=980 ~10 families per center	All P-I +QOL	All P-I +carotid +tonometry	All P-I +PAI-1	All Cohort Mortality All cause CVD Morbidity-CVD
IV 2000-05	N=3659 ~ 30 new families per center plus re-exam of pilot	All P-I +FFQ +pedometer	All P-I +ECHO + carotid +tonometry	All P-I +PAI-1	All Cohort Same as PI-III Family Mortality All cause CVD

Abbreviations: Demog = Demographic data; Med Hx = Medical History; Meds = Current Medications; ROH = Rose Questionnaire; Smoke = History of Smoking; PA = Physical Activity; Family Hx = Family History of Related Illnesses; Ht,Wt = Height & Weight; W,Hip = Waist & Hip Measurements; BP = Blood Pressure; Body fat = Impedance Measure of Body Fat; ABI = Ankle/Brachial Index; Edema = Ankle Edema; ECG = 12-lead Electrocardiogram; Apos = Apolipoproteins B and AI; GTT = Oral Glucose Tolerance Test; ApoE pheno = ApoE Phenotypes; Lp(a) = Lipoprotein (a); DNA = DNA from Lymphocytes; Ur Alb/Cr = Urinary Albumin/Creatinine Ratio; P-I = Phase I; QOL = Quality of Life Questionnaire; diet = 24-hr Recall; ECHO = Echocardiogram; gallbl = Gallbladder Sonogram; PFT = Pulmonary Function Test; TB = Tuberculin Test; CRP = C-Reactive Protein; PAI-1 = plasminogen activator inhibitor type 1; gambling = Gambling Questionnaire; carotid = carotid artery sonogram; tonometry = applanation tonometric measure of arterial stiffness; asthma = asthma substudy; MBL = Mannose Binding Lectin; FFQ = Block Food Frequency Questionnaire; pedometer = 7-day Pedometer Measure.

4.2 CURRENT STUDY – THE STRONG HEART FAMILY STUDY(PHASE IV)

The family study was initiated in June of 2000 as a pilot study to examine the heritability of CVD and risk factors in families that included three or more siblings from the original cohort. In June of 2001, additional pedigrees were identified and recruitment of families was completed. Each center was to recruit at least 900 new family members.

In August of 2003, the Phase IV recruitment and examination of 900 additional family members was successfully met. From the family history forms completed by each participant during Phase I, families were identified for which: 1) there was a "core sibship" of at least five full siblings, of whom at least three were SHS participants and 2) the SHS participants in the core sibship had a total of at least 12 offspring who were at least 15 years of age or older. The goals of the Phase IV study are to continue mortality and morbidity surveillance of the original cohort, to continue to study the inheritance of risk factors in families, and to re-examine the members of the original families initiated in Phase III.

4.2.1 Clinical Examination

All clinical examinations were conducted at a local Indian Health Services hospital, clinic and/or tribal community facility and consisted of two parts: a personal interview and a physical examination. Each exam lasted approximately three hours. Participants were asked to arrive at the clinic fasting in the morning. After registration and before any procedure was performed, a study staff member explained the study and procedures to the participant, answered questions, if any, and obtained informed consent. A parental consent form was obtained in cases of participants under 18 years of age. All examinations were performed by trained personnel, which included nurse practitioners, registered nurses, medical assistants, health profession students, physician assistants, and/or physicians.

Components of the Clinical Examination

1) Personal Interview

During the personal interview, the following information was obtained and questionnaires were administered: 1) demographic information which included information regarding tribal enrollment, Indian heritage, income, education, residence, marital status, number of household members and employment; 2) health habits which included information regarding smoking and alcohol intake; 3) medical history; 4) a dietary survey; and 5) psychosocial information.

2) Physical Examination

The physical examination included the following procedures: 1) anthropometric measurements, 2) blood pressure measurements, 3) twelve lead electrocardiogram, 4) fasting blood samples, 5) urine collection, 6) ultrasound examination of the carotid artery, echocardiography, 7) tonometry of the radial artery, and 8) physical activity assessed by pedometry. For the purposes of this proposal we will focus on the anthropometric measurements (please see section 4.2.2) and physical activity measures (please see section 4.2.3).

4.2.2 Body Composition

Body composition was determined using anthropometry. Measurements were taken over a scrub suit or light clothing with the participant's bladder empty. Participants were to have empty pockets and any belts removed. Height and weight measurements were conducted without shoes.

a) Standing Body Height

Participants were asked to stand erect on the floor or the horizontal platform with his/her back against a vertical mounted ruler, heels together and against the vertical ruler, looking straight ahead with his/her head in the Frankfort horizontal plan. Once in this position, a right angle was brought down snugly but not tightly on the top of the head. The participant's height was recorded to the nearest centimeter.

b) Body Weight

Body weight was measured using a Tanita BWB-800 5 Adult Digital Scale (Tanita Corp. of America, Arlington Heights, IL). Once the scale was zeroed, participants were instructed to stand in the middle of the platform of the balance scale with their head erect and eyes looking straight ahead. Measures were recorded to the nearest kilogram. To maintain accuracy, the scale was zeroed daily and calibrated with a known weight (50-lb) every month or anytime the scale was moved.

c) Supine Waist (Abdominal) Girth

Abdominal girth was obtained using an anthropometric tape applied at the level of the umbilicus with the patient supine and breathing quietly. The measurement was recorded to the nearest centimeter.

d) Erect Hip Girth

Erect hip girth was measured using anthropometric tape. Participants were instructed to stand erect yet relaxed with weight distributed evenly over both feet. Hip girth was measured at the level of the maximal protrusion of the gluteal muscles (hips). The tape was kept horizontal at this level and measurements were recorded to the nearest centimeter.

e) Percent Body Fat

The measurement of body fat was assessed using the Quantum II Impedance Meter (RJL Equipment Company, Clinton Twp., MI). This procedure involves the use of a small low frequency current that travels across the body through extracellular fluids. Bioelectrical impedance measures are related to the volume of conductor material and when expressed as impedance or conductance, are proportional to fat free mass. Percent body fat will be estimated by the RJL formula based on total body water.

Quality Control for Anthropometric Measures

In order to ensure quality control in the SHFS; duplicate measures of anthropometry (height, weight, and waist, and bioelectrical impedance measurements) were performed by a second observer on a 5% random sample of participants. This data was sent to the Coordinating Center on a monthly basis for analysis. Results of these analyses were distributed to the field centers and the Steering Committee on a quarterly basis. Differences between duplicate measures exceeding the following values were considered unacceptable.

4.2.3 Physical Activity Measures

Physical activity was assessed using an Accusplit AE120 pedometer (Accusplit Inc, San Jose, CA). Participants received a pedometer, instructions for wearing the pedometer, and an activity diary at their clinical examination (please see Appendix A for a copy of the pedometer instructions and diary). Participants were asked to wear the pedometer for seven consecutive days (5 week days and 2 weekend days) and to record the number of steps taken daily in the activity diary. Participants were also asked to record the time the monitor was put-on and removed each day. At the end of the seven-day period, participants were asked to return their pedometer diary to the clinic in a postage paid envelope. The mean number of steps the participant takes per day was calculated by averaging the number of steps recorded each day during the seven-day period. Furthermore, previous research has suggested that 3 days of activity can provide a sufficient estimate of weekly physical activity[132]; therefore, only participants with 3 or more days of data will be used in the analyses. Participants were able to keep the pedometer as a token of appreciation from the SHFS.

<u>Pedometer Data Clean-Up and Considerations for Data Analysis</u>

Once the data collection was complete, the following four procedures were conducted to ensure that that the pedometer data was clean and ready for data analysis:

1. All data points < 100 steps have been coded as missing.
2. All zeros have been coded as missing.
3. All data points of 888 from the Arizona site have been coded as missing.
4. All data points greater than 99,999 steps have been eliminated. It is impossible to have a number greater than 99,999.

Considerations for data analysis:

1. All data points >35,000 steps/day should be considered extreme and examined for accuracy.
2. The minimum number of days used to represent a week is 3.
3. Look at the data stratified by age, gender, body mass index or some body composition variable and by site.

For all analyses, the variable of interest was steps per day averaged over the week. This variable was calculated for any person who had data for 3 or more days, taking the sum of steps per day divided by the number of available days. Alternatively, we will consider steps per day averaged over the week eliminating the highest and lowest data point. This variable is derived by first eliminating the highest steps per day and the lowest steps per day then taking the average of the remaining days.

4.2.4 Family Data

The goal of the SHFS is to study the family patterns of heart disease and diabetes in American Indians. The intent of the SHFS was to recruit a few large families in the community, including parents, children, and grandchildren. For each participating family, a family tree was constructed. Each family member underwent a physical examination and completed questionnaires that inquire about diet and other lifestyle factors.

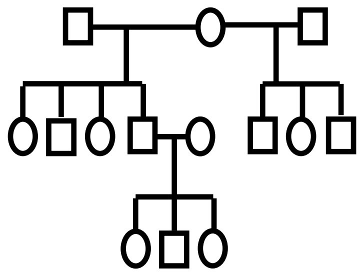

Figure 4.2 Example of Family Tree used in the Strong Heart Family Study

For each enrolled family member, the SHS Family Information Form was administered. The SHS Family Information Form requests information about the participant and his/her family. Information was first recorded about the core participant, his/her mother and father, all four grandparents, any sons and daughters, and the other parent of each son or daughter (which may include previous spouses of core sibship members). Additionally, information is recorded about the participant's siblings (half and full). In the instance of a half sibling, information regarding the other (unshared) parent of the half sibling was collected.

Household Information

For each participant, household information was collected because family members may share certain environmental risk factors. For each member of the family, a number was assigned on the family tree indicating whether or not the participant resides in the household. For example, when the first member of a family was interviewed they were assigned a (1); each additional family member that resides in same household was also assigned a (1). A family member that does not reside in the household was assigned a (2) and each member of that household was assigned (2). For each additional household, family members residing in the same household were assigned (3), (4), etc as necessary.

It must be noted that, a priori, there were concerns raised about the accuracy of the household information, more specifically the reproducibility of the information. These concerns centered around the fact that many SHFS participants often moved around from home to home, making it difficult to assign a single residence to any one individual.

Information on Relatives and Defining Relationships

For a family study, it is important to distinguish between full and half siblings, and between biological and adoptive relationships. Therefore, each participant was queried on siblings and whether they share the same mother and same father with each sibling. In the case that one parent is different; information on this parent was recorded. For information regarding a participant's children, information regarding each offspring was obtained.

Current Tallies of Parent-Offspring Pairs for the 3 Centers

For the current study, parents and offspring have been linked by pairs (i.e. offspring & mother, offspring & father) and only those participants with physical activity and body mass index information are included in this cohort. The table below provides a breakdown of these links by study center.

Table 4.3 Tallies of Parent and Offspring Pairs with both physical activity and body mass index (BMI) data for the entire SHFS cohort regardless of age of the offspring

Study Location	Offspring & Mother	Offspring & Father
Arizona	589 pairs	243 pairs
Dakotas	626 pairs	258 pairs
Oklahoma	432 pairs	205 pairs
Totals	1647 pairs	706 pairs

Table 4.4 Tallies of Parent & Offspring Pairs with both physical activity and body mass index (BMI) data that include an offspring ≤18 yrs of age

	Offspring & Mother	Offspring & Father
SHS Participants ≤18 yrs linked with a parent	247 pairs	128 pairs

4.3 STATISTICAL ANALYSES

4.3.1 Hypotheses

Hypothesis 1a: *Physical activity levels assessed by objective activity monitor (i.e., pedometer) are positively associated among parent-offspring pairs in the Strong Heart Family Study.*

In order to address this hypothesis we will use identified biologically related pairs (parent-offspring) enrolled in the Strong Heart Study. All relevant information from each individual has been linked together for each pair. In order to determine the relationship of physical activity levels between parent and offspring, we have established physical activity phenotypes based on pedometer step counts (i.e., high active/low active) specific for each age group. We will examine the role of heritability by examining the association of each biological parent's (mother/father) physical activity level with that of their biological offspring.

4.3.1.1 Descriptives

Descriptive statistics were used to describe demographic factors, such as BMI, physical activity, and chronic condition prevalence for each member of the SHFS pair. For all analyses, significance was set at an alpha level of $p<0.05$. All continuous data was assessed for normality. Normally distributed data is reported as mean (SD), non normal variables as median (25^{th}, 75^{th} percentile). Depending on the characteristics of the variable and hypothesis to be tested; analysis of variance (ANOVA), Kruskal-Wallis, or χ^2 tests of proportions were used to describe and compare differences between pairs or offspring, stratified by gender or location. If cells in the contingency table contained less than 5 individuals, Fisher's Exact Methods were used instead of the χ^2 test to compare between physical activity groups.

4.3.1.2 Correlation Analyses

Spearman Rank Order Correlation coefficients were used to examine the association of physical activity levels between offspring and their parents. We first compared the combined sample of offspring regardless of sex with their fathers and their mothers. Next we stratified the offspring cohort by sex and reran the analyses. Lastly, we limited the analyses to only those offspring who had both parents enrolled in the study to determine the association of physical activity levels when the offspring was exposed to both parents. These analyses were only performed in the ≤ 18 year old offspring cohort.

4.3.1.3 2 x 2 Contingency Tables

Two by two contingency tables were utilized to test for proportions and to compare parent-offspring pairings with respect to physical activity level. Each member of the parent-offspring pair was coded as high active or low active based upon the median (50^{th} percentile) pedometer steps relevant to each member of the pair. Concordance rates were then calculated for members in the parent-offspring pair using the physical activity grouping variables. Concordant pairs, where each member of the pair was considered either low active or high active, were used to determine familial aggregation of physical activity levels between parent and offspring. Odds ratios were then calculated using (cell c/ cell b) to predict the odds of a low active parent having a high active offspring. McNemar's statistic was used to assess statistical significance. For each age group, we examined offspring stratified by sex by each parent (mother vs. father) to determine which parent's physical activity level influence their offspring.

4.3.2 Hypothesis 1b

Hypothesis 1b: *Physical activity is a heritable trait among biologically related family members in the Strong Heart Family Study.*

Heritability is defined as a ratio of variances, specifically, the ratio of the genetic variance (i.e., that attributable to genotypic or allelic differences among individuals) to the total phenotypic variance in the population[133]. In order to determine whether physical activity is a heritable trait in the Strong Heart Family study, we will utilize variance components analysis. This approach assumes an underlying linear model where the observed phenotype, Y, is a linear function of genetic, environmental, and/or household factors, that is

$$Y_{kl} = \mu + g_k + c_l + e_{kl}$$

and where neither the effects of different genotypes (g_k, where k = 1….., K) nor the various environmental factors (c_l, where l = 1,….L) are directly observable. If genotypes and environments are independent, the total variance of the trait, Y, can be written as

$$\text{Var}(y) = \sigma^2 = \sigma^2_g + \sigma^2_c + \sigma^2_e$$

and is merely a sum of these separate components of variance. From this breakdown, the heritability of a trait in a broad sense $h^2_B = \sigma^2_g/\sigma^2$ can be obtained.[133]

4.3.2.1 Variance Components Analyses

Genetic variance components analysis, including linkage analysis, quantitative genetic analysis, and covariate screening allows for calculation of marker-specific or multipoint identity-by-descent (IBD) matrices in pedigrees of arbitrary size and complexity, and for linkage analysis of quantitative traits (or a single discrete trait) which may involve multiple loci (*oligogenic* analysis), dominance effects, household effects, and interactions.

Data obtained on 3665 family members with 19 covariates were analyzed using the Sequential Oligogenic Linkage Analysis Routines (SOLAR) software package (Southwest Foundation for Biomedical Research).[134] SOLAR performs a variance components analysis of family data that decomposes the total variance of the phenotype (physical activity levels) into components that are due to genetic (polygenic) effects, measured covariates, household effects, and random environmental effects. The relative contribution of genetic factors to physical activity level variation is then estimated by the heritability (h^2), defined by the ratio of the genetic variance component to the residual (after removal of covariates) phenotypic variance. A series of five models were developed that incorporated a large number of covariates related to physical activity levels to determine the extent of genetic factors contributing to the variation in physical activity levels independent of the covariates. For all models, in order to normalize the trait of interest, physical activity, we transformed the variable using the square root. Model 1 was conducted using the entire SHFS cohort, followed by three separate models (Models 2 - 4), which were performed using pedigrees from each study location (Arizona, Dakotas, Oklahoma). Additionally, since the assessment of physical activity levels may be compromised in persons with high BMI (> 40 kg/m^2), the very old (> 70 years of age) due to possible gait speed issues, and the disabled, we created a fifth model (Model 5) in which data was eliminated on these individuals. All models included the following covariates: age, sex, age*sex, age^2, age^2*sex, smoking (current vs. never/ever), alcohol consumption (current vs. never/ever), waist-to-hip ratio, BMI, BMI*sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), SBP*DBP, % body fat, hypertension status (yes/no), diabetes status (yes/no), years of education, study location (Arizona, Dakotas, Oklahoma), and disabled (yes/no). A person was considered disabled if they reported having any of the following conditions that may limit their physical activity:

rheumatic heart disease, renal dialysis, kidney failure, cirrhosis of the liver, emphysema, above or below knee amputation, unable to walk, or indicated that their moderate activity was limited a lot by their health. Covariate selection is done using a backwards-stepwise method, and is done in conjunction with the estimation of genetic and household effects. Model likelihoods are calculated in a sequential fashion beginning with the simplest model, where all effects are due to random environmental fluctuations (the sporadic model), and then including individual effects (genetic, household) one at a time, and in all possible combinations, and culminating with the most general model (including all effects). Model comparisons are via simple likelihood ratio tests (for nested models), and comparison of parsimony criteria (Aikike's Information Criteria or AICs) for non-nested models. Significance of the estimated heritabilities was determined by likelihood ratio tests, in which the likelihood of the models with the additive genetic and household variance component and covariates was compared with the model likelihood in which the additive genetic and household variance component was constrained to be 0.

4.4 POWER CALCULATIONS

It is our intention to complete several types of analyses regarding the association of physical activity levels between biologically related pairs, more specifically parent-offspring pairs, in the Strong Heart Family Study. As mentioned previously, there are approximately 2,353 parent-offspring pairs with complete physical activity and BMI data available. Out of these pairs, there are 375 parent-offspring pairs that include an offspring < 18 years of age. Our power calculations are based upon this subgroup of 375 pairs, since this is likely to be our smallest subgroup.

PairwiseAssociations using Correlation Analyses

H_1 = Physical activity levels between parent and offspring will be positively associated

H_0 = There is no association of physical activity levels between parent and offspring

Numeric Results when Ha: R0<>R1

Power	**N**	**Alpha**	**R1**
0.05000	375	0.05000	0.00000
0.97469			0.20000
1.00000			0.40000
1.00000			0.60000
1.00000			0.80000

Summary Statements

For example, a sample size of 375 achieves 97% power to detect a correlation of 0.20000 assuming a two-sided test conducted at an α level of 0.05.

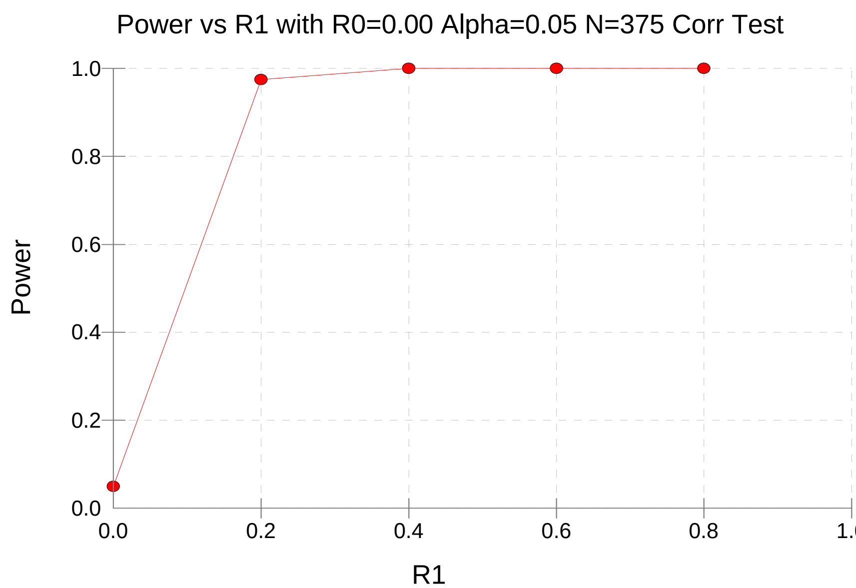

Figure 4.3 Power calculation grid for pairwise comparisons using correlation analysis for an N= 375.

5.0 RESULTS

The following chapter will provide results of statistical analyses performed on data from the Strong Heart Family Study. The physical activity literature suggests that a relatively consistent decline in physical activity levels occurs with increasing age and BMI, as well as gender with females being less active than males. This was examined in the SHFS dataset and section 5.1 presents the results of the construct validity of physical activity levels in the Strong Heart Family Study with regard to age, gender, and BMI.

Sections 5.2-5.4 present results of univariate analyses examining the association of physical activity levels specifically between parent-offspring pairs. Since it can be assumed that age of the offspring may affect the association of physical activity levels between parent and offspring, we will present our results broken down into four age groups of offspring: ≤18, >18-30, >30-50, and >50 years of age. Lastly, section 5.5 will present the variance components analyses results, which will examine the heritability of physical activity levels in the entire SHFS cohort.

5.1 PHYSICAL ACTIVITY LEVELS OF THE SHFS COHORT

As discussed in section 2.2.4, in the literature, there appears to a relatively consistent decline in physical activity levels with increasing age, gender (males having higher levels of physical activity compared to females), and increasing BMI. Therefore, to determine if these same trends are found within the SHFS, the relationship of physical activity levels in regard to age, sex, and body mass index (BMI) was examined.

Spearman Rank-Order Correlation Coefficients were used to first evaluate the association of physical activity determined by pedometer steps with age and BMI for the entire cohort and stratified by sex. The results of these analyses are presented in Table 5.1 and indicate a significant negative association between pedometer steps and age, and BMI.

Table 5.1 Spearman Rank-Order Coefficients between Age and BMI and Pedometer Steps for the total Cohort and by Gender

	Entire Cohort	Males	Females
Age and Pedometer Steps	-0.25	-0.23	-0.26
BMI and Pedometer Steps	-0.30	-0.25	-0.33

* All correlations significant at $p<0.0001$

Figure 5.1 shows a statistically significant decline in physical activity levels ($p<0.0001$) based on median pedometer step counts with increasing age within the entire cohort (n = 3254). There was a 4,127.8 step count difference between the 14-20 year old age group and the 70+ year old age group (6381.9 and 2254.1, respectively).

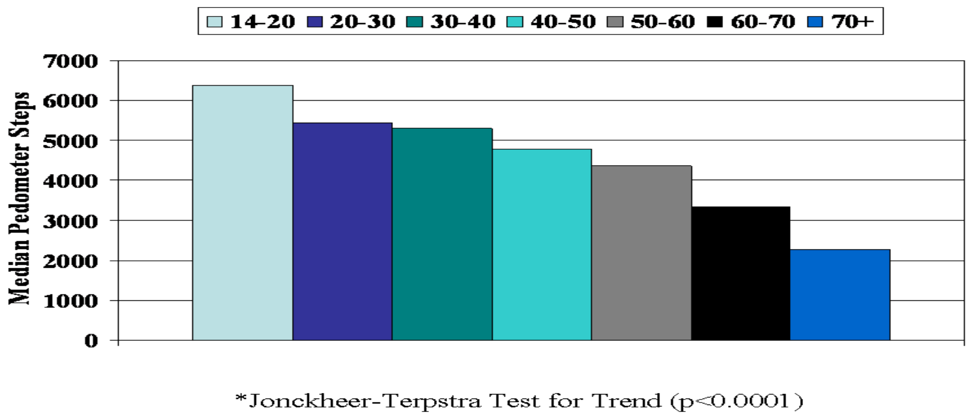

Figure 5.1Median pedometer steps by age category in the Strong Heart Family Study Cohort (n = 3254*)

When stratified by sex, the same significant trend of decline in physical activity levels remained regardless of gender (p<0.0001) (Figure 5.2). For each age group, males appeared to have higher levels of pedometer step counts compared to females.

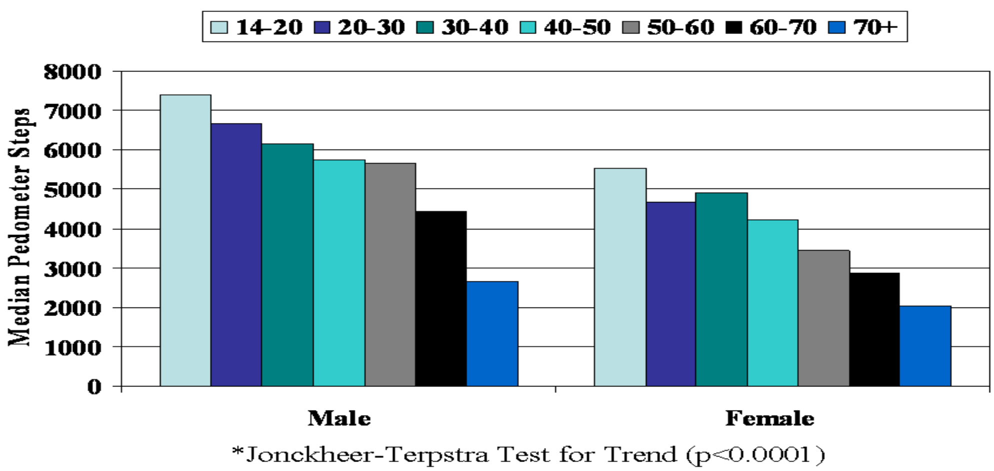

Figure 5.2 Median pedometer steps by age category stratified by sex in the Strong Heart Family Study Cohort (n = 3254)*

Figure 5.3 shows a considerable decline in physical activity levels with increasing body mass index (BMI) within the entire cohort of the SHFS (p<0.0001). Much like the findings between median pedometer step counts and age, a statistically significant decline of median pedometer steps (p<0.0001) with increasing BMI was consistent across both genders (Figure 5.4). As with age, women appeared to have lower median pedometer step counts than men in all BMI categories.

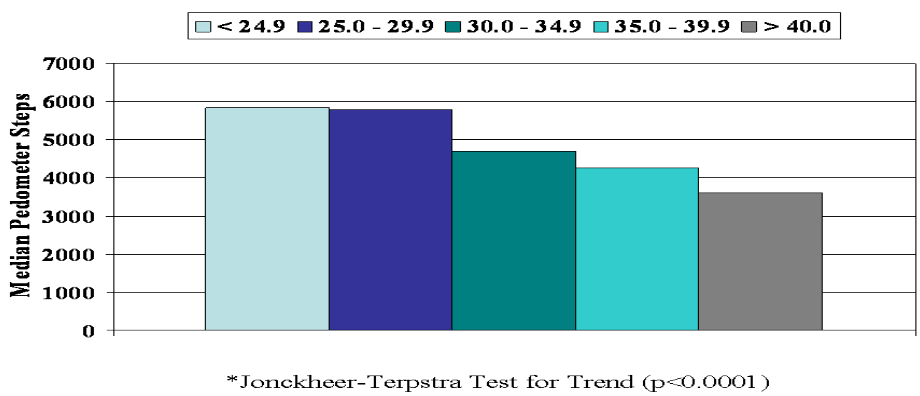

Figure 5.3 Median Pedometer Steps by NHLBI BMI Cutpoints of Overweight and Obesity in the Strong Heart Family Study Cohort (n = 3254)*

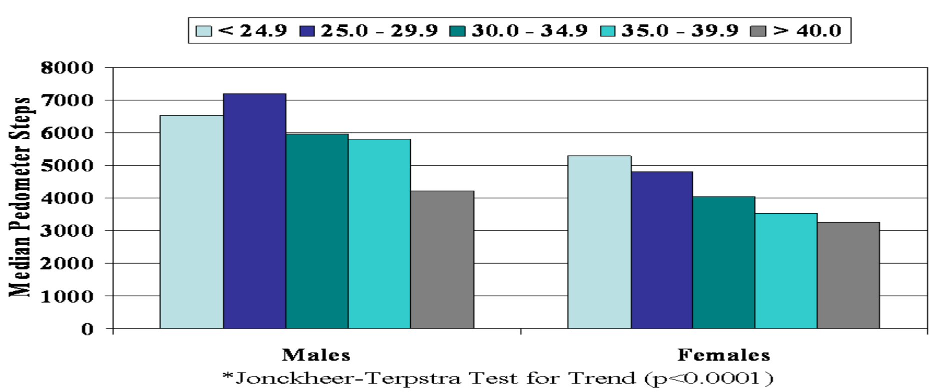

Figure 5.4 Median Pedometer Steps by NHLBI BMI Cutpoints of Overweight and Obesity stratified by sex in the Strong Heart Family Study Cohort (n = 3254)*

Lastly, Figure 5.5 presents physical activity levels by NHLBI BMI cutpoints stratified by sex and by study location. From the figure, it appears that regardless of gender and study site, physical activity significantly declines with increasing BMI.

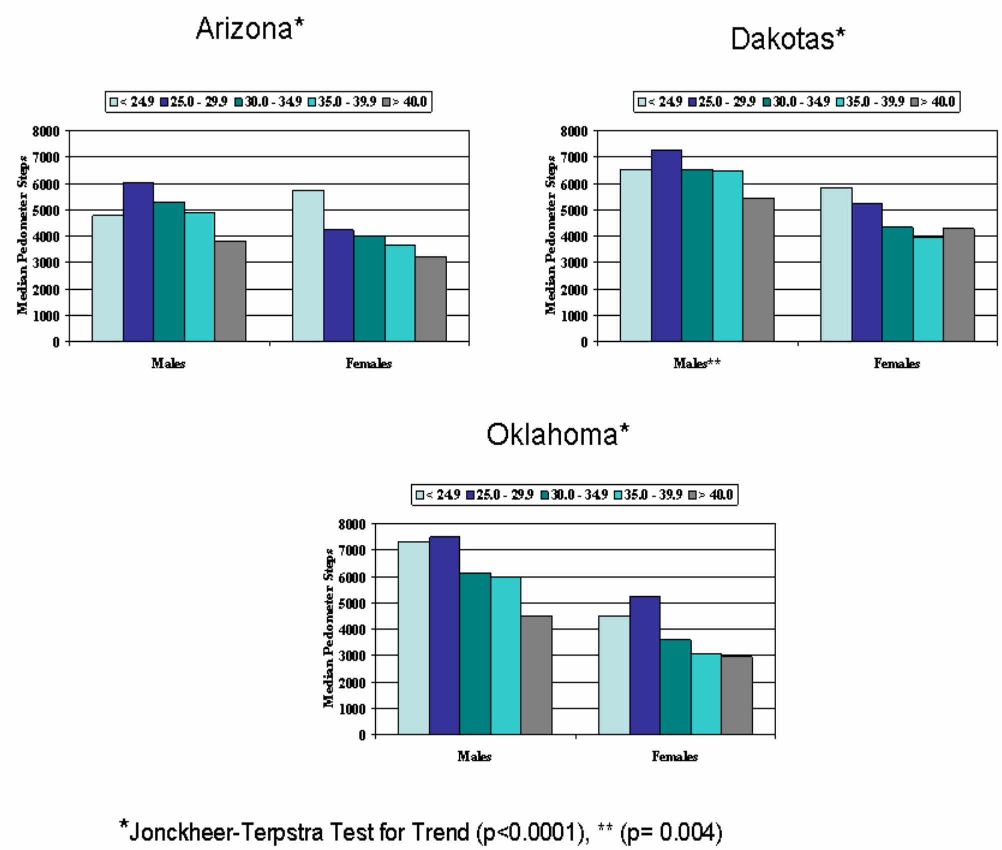

Figure 5.5 Median Pedometer Steps by NHLBI BMI Cutpoints of Overweight and Obesity stratified by sex and by study location in the Strong Heart Family Study Cohort (n = 3254)*

Similar to what is noted in the literature in other populations; data presented from the SHFS suggest that age, gender, and BMI are significantly related to physical activity levels within the SHFS. These relationships will be important to remember when considering the association of physical activity levels between parent and offspring.

5.2 DESCRIPTIVES

5.2.1 Offspring < 18 Years of Age

Of the 2062 offspring in the total SHFS cohort, 280 offspring were between the ages of 14 and 18 years of age. Table 5.2 presents descriptive characteristics of these 280 offspring along with their parents stratified by gender. The mean age of offspring among this sample was 16.4 years. In regard to parents, pairwise comparisons indicated that fathers were significantly older than mothers (44.3 vs. 41.4 years, p<0.0001) and had significantly higher WHR (0.96 vs. 0.89 cm, p< 0.0001). Fathers also had significantly higher diastolic (84.6 vs. 77.0 mmHg, p<0.0001) and systolic blood pressures (126.7 vs. 118.0 mmHg, p<0.0001), LDL cholesterol levels (109.1 vs. 100.9 mg/dl, p = 0.01) and percentage of current drinkers (70.9% vs. 54.3%, p = 0.05) compared to mothers. Conversely, mothers had significantly higher HDL cholesterol levels (53.0 vs. 49.1 mg/dl, p = 0.02) and had significantly higher percentage of current smokers (44.9% vs. 34.4%, p = 0.002) compared to fathers. There were no statistically significant differences noted for BMI, total cholesterol, triglycerides, prevalence of hypertension, or median pedometer steps.

Table 5.2 Descriptive Characteristics for Offspring≤ 18 years of age and Parents

	Offspring n = 280	Fathers n = 128	Mothers n = 247	p*
Age (years)	16.4 ± 0.90	44.3 ± 6.8	41.4 ± 5.3	<0.0001
BMI (kg/m^2)	28.5 ± 8.0	33.2 ± 7.6	33.2 ± 7.8	0.99
WHR (cm)	0.86 ± 0.11	0.96 ± 0.07	0.89 ± 0.06	<0.0001
Diastolic BP (mmHg)	68.6 ± 9.0	84.6 ± 9.7	77.0 ± 9.7	<0.0001
Systolic BP (mmHg)	112.6 ± 11.4	126.7 ± 13.8	118.0 ± 13.9	<0.0001
Total Cholesterol (mg/dl)	153.2 ± 28.5	193.4 ± 42.3	185.4 ± 33.8	0.07
LDL (mg/dl)	82.6 ± 24.0	109.1 ± 32.1	100.9 ± 27.1	0.01
HDL (mg/dl)	47.6 ± 12.3	49.1 ± 14.9	53.0 ± 15.5	0.02
Triglycerides (mg/dl)	124.3 ± 133.0	183.0 ± 109.2	162.5 ± 98.3	0.08
Smoking Status (Current)	9 (3.2 %)	44 (34.4%)	111 (44.9%)	0.002
Alcohol Status (Current)	123 (43.9 %)	90 (70.9%)	134 (54.3%)	0.05
Diabetes Status (ADA Definition)	9 (3.2%) DM 7 (2.5%) IFG	33 (25.8%) DM 17 (13.3) IFG	60 (24.3%) DM 19 (7.7%) IFG	0.31
Hypertension Status (Yes)	9 (3.2%)	61 (47.7%)	55 (22.3%)	0.08
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	5456.6 (3582.3, 7743.9)	5233.3 (3186.3, 8073.7)	4970.9 (3034.4, 7277.7)	0.48

*p for comparison between mothers and fathers; All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for offspring in the ≤18 cohort by gender are presented in Table 5.3. Females were found to have significantly higher BMI (29.8 vs. 26.9 kg/m^2, p = 0.0004) when compared to males; whereas males were found to have a significantly higher systolic blood pressure (11.6 vs. 110 mmHg, p < 0.0001) compared to females. No other statistically significant differences were noted in this cohort.

Table 5.3 Descriptive Characteristics of Offspring ≤ 18 for the total cohort and stratified by sex

	Offspring n = 280	Males n = 131	Females n = 149	p*
Age (years)	16.4 ± 0.90	16.5 ± 0.90	16.4 ± 0.9	0.26
BMI (kg/m^2)	28.5 ± 8.0	26.9 ± 8.2	29.8 ± 7.7	0.0004
WHR (cm)	0.86 ± 0.11	0.87 ± 0.2	0.85 ± 0.1	0.59
Diastolic BP (mmHg)	68.6 ± 9.0	68.2 ± 9.3	69.0 ± 9.5	0.41
Systolic BP (mmHg)	112.6 ± 11.4	116.0 ± 12.2	110.0 ± 9.7	< 0.0001
Total Cholesterol (mg/dl)	153.2 ± 28.5	154.0 ± 31.5	153.0 ± 25.7	0.59
LDL (mg/dl)	82.6 ± 24.0	82.8 ± 26.1	82.4 ± 22.1	0.76
HDL (mg/dl)	47.6 ± 12.3	46.7 ± 10.7	48.3 ± 13.5	0.59
Triglycerides (mg/dl)	124.3 ± 133.0	136.0 ± 181.0	114.0 ± 65.3	0.82
Smoking Status (Current)	9 (3.2 %)	22 (16.8%)	18 (12.1%)	0.51
Alcohol Status (Current)	123 (43.9 %)	57 (43.5%)	66 (44.3%)	0.56
Diabetes Status (ADA Definition)	9 (3.2%) DM 7 (2.5%) IFG	5 (3.8%) DM 6 (4.6%) IFG	4 (2.7%) DM 1 (0.7%) IFG	0.09
Hypertension Status (Yes)	9 (3.2%)	7 (5.3%)	2 (1.3%)	0.06
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	5456.6 (3582.3, 7743.9)	5152.0 (3493.0, 7695.0)	5544.0 (3604.0, 8351.0)	0.33

* p-value for comparison between males and females; All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for female offspring ≤ 18 years of age by study location are presented in Table 5.4 Statistically significant differences were noted for BMI, diastolic blood pressure, smoking and alcohol status, and pedometer steps. Of note, females from Arizona appeared to have the largest BMI, highest diastolic blood pressure, and the lowest pedometer steps as well as the lowest prevalence of current smokers and alcohol consumers compared to the female offspring from the other two study locations. In order to test for differences by study location among female offspring, post hoc comparisons were made using Kruskal-Wallis or chi-square test of proportions. Among female offspring in Arizona and the Dakotas, BMI ($p = 0.0002$), diastolic blood pressure ($p = 0.02$), smoking status ($p = 0.001$), alcohol status ($p = 0.0002$) and median pedometer steps ($p = 0.0002$) were statistically different. For female offspring in Arizona and Oklahoma, statistically significant differences were noted for age ($p = 0.05$), BMI ($p = 0.0012$), WHR ($p = 0.04$), diastolic blood pressure ($p = 0.008$), triglycerides ($p = 0.04$), and smoking status ($p = 0.05$). Lastly, for female offspring in the Dakotas and Oklahoma, only alcohol status was statistically significantly different, with a higher percentage of current alcohol users in the Dakotas (67.3% vs. 37.5%).

Table 5.4 Descriptive Characteristics for Female Offspring ≤ 18 by Study Location

	Arizona n = 65	Dakotas n = 52	Oklahoma n = 32	p
Age (years)	16.2 ± 0.87	16.5 ± 0.91	16.6 ± 0.86	0.08
BMI (kg/m^2)	32.7 ± 7.3	27.5 ± 7.5	27.7 ± 6.7	0.0001
WHR (cm)	0.86 ± 0.07	0.84 ± 0.06	0.83 ± 0.06	0.10
Diastolic BP (mmHg)	71.6 ± 9.8	67.8 ± 7.4	65.7 ± 10.7	0.007
Systolic BP (mmHg)	110.4 ± 9.1	108.0 ± 9.5	110.5 ± 10.9	0.56
Total Cholesterol (mg/dl)	156.1 ± 22.8	150.0 ± 24.8	150.6 ± 32.1	0.28
LDL (mg/dl)	86.5 ± 18.4	79.4 ± 22.7	79.1 ± 27.0	0.07
HDL (mg/dl)	45.3 ± 11.8	50.6 ± 13.7	50.8 ± 15.5	0.12
Triglycerides (mg/dl)	125.6 ± 77.4	105.3 ± 49.4	103.2 ± 58.5	0.07
Smoking Status (Current)	3 (4.6%)	9 (17.3%)	6 (18.8%)	0.005
Alcohol Status (Current)	19 (29.2%)	35 (67.3%)	12 (37.5%)	0.001
Diabetes Status (ADA Definition)	2 (3.1%) DM 1 (1.5%) IFG	2 (3.9%) DM	--	0.64
Hypertension Status (Yes)	2 (3.1%)	--	--	0.27
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4981.4 (3323.3, 5977.2)	7025.1 (4587.1, 10917.9)	5582.1 (3698.3, 8673.1)	0.0007

* p-value for comparison between locations; All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for male offspring ≤18 years of age by study location are presented in Table 5.5. Statistically significant differences were noted for BMI, WHR, total cholesterol, LDL, HDL, triglycerides, smoking and alcohol status, and pedometer steps. As with female offspring, male offspring from Arizona had the largest BMI when compared to the males from the other two study locations. In addition, males from Arizona had the largest WHR, highest total cholesterol, LDL, and triglycerides, as well as the lowest HDL, prevalence of current smokers, and pedometer steps compared to male offspring from the other two study locations. Post hoc comparisons revealed that BMI (p = < 0.0001), WHR (p = 0.0002), LDL (p = 0.005), HDL (p =0.002), total cholesterol (p = 0.001), triglycerides (p = < 0.0001), smoking status (p = 0.008), and pedometer steps (p = 0.002) were statistically different among male offspring in Arizona and the Dakotas. For male offspring in Arizona and Oklahoma, statistically significant differences were noted for BMI (p = 0.0004), WHR (p = < 0.0001), diastolic blood pressure (p = 0.05), LDL (p = 0.007), HDL (p =0.03), total cholesterol (p = 0.009), triglycerides (p = 0.003), alcohol status (p = 0.01), and pedometer steps (p = 0.006). Finally, for male offspring in the Dakotas and Oklahoma, statistically significant differences were noted for BMI (p = 0.04), diastolic blood pressure (p = 0.05), smoking status (p = 0.03) and alcohol status (p = 0.02).

Table 5.5 Descriptive Characteristics for Male Offspring ≤ 18 by Study Location

	Arizona n = 44	Dakotas n = 52	Oklahoma n = 35	p
Age (years)	16.5 ± 0.94	16.5 ± 0.96	16.5 ± 0.81	0.97
BMI (kg/m^2)	32.4 ± 9.2	23.2 ± 5.3	25.6 ± 6.6	< 0.0001
WHR (cm)	0.91 ± 0.08	0.87 ± 0.21	0.82 ± 0.08	< 0.0001
Diastolic BP (mmHg)	70.0 ± 10.0	68.5 ± 8.0	65.6 ± 9.9	0.07
Systolic BP (mmHg)	118.3 ± 11.6	113.3 ± 12.2	117.3 ± 12.3	0.18
Total Cholesterol (mg/dl)	168.4 ± 36.7	145.3 ± 28.6	147.5 ± 20.9	0.002
LDL (mg/dl)	93.4 ± 30.0	78.4 ± 24.2	76.3 ± 19.5	0.006
HDL (mg/dl)	43.2 ± 8.8	47.6 ± 9.1	49.8 ± 13.6	0.03
Triglycerides (mg/dl)	208.7 ± 289.9	95.0 ± 48.4	106.7 ± 73.6	0.0002
Smoking Status (Current)	3 (6.8%)	15 (28.9%)	4 (9.1%)	0.002
Alcohol Status (Current)	22 (50.0%)	27 (51.9%)	8 (22.9%)	0.02
Diabetes Status (ADA Definition)	3 (6.8%) DM --	1 (1.9%) DM 5 (9.6%) IFG	1 (2.9%) DM 1 (2.9%) IFG	0.15
Hypertension Status (Yes)	3 (6.8%)	1 (1.9%)	2 (8.6%)	0.35
Pedometer Steps (steps/day averaged over the week; Median, 25th, 75th)	4595.1 (2515.7, 6006.9)	6142.9 (4145.1, 8504.9)	5446.0 (4095.4, 7526.6)	0.002

* p-value for comparison between locations; All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

5.2.2 Offspring > 18-30 years of age

Of the 2062 offspring in the total cohort, 675 offspring were >18 - 30 years of age. Table 5.6 presents descriptive characteristics for these 675 offspring along with their parents stratified by gender. The mean age of offspring among this sample was 23.4 years. Pairwise comparisons between fathers and mothers, found that fathers were significantly older than mothers (50.3 vs. 47.3 years, $p<0.0001$) and had a larger WHR (0.98 vs. 0.90, $p<0.0001$). Fathers also had significantly higher diastolic (80.8 vs. 78.8 mmHg, $p = 0.01$), LDL cholesterol levels (191.1 vs. 187.6 mg/dl, $p = 0.02$), and triglyceride levels (208.9 vs. 174.3 mg/dl, $p = 0.0006$) compared to mothers. Furthermore, fathers had significantly higher percentages of current smokers (40.9% vs. 37.5%, $p<0.0001$), current drinkers (66.2% vs. 50.7%, $p<0.0001$), and diabetics (38.8% vs. 33.7%, $p<0.0001$) compared to mothers. Conversely, mothers had significantly higher HDL cholesterol levels (53.0 vs. 47.4 mg/dl, $p<0.0001$). There were no statistically significant differences noted for BMI, systolic blood pressure, total cholesterol, prevalence of hypertension, or median pedometer steps.

Table 5.6 Descriptive Characteristics for Offspring and Parents where the offspring is >18-30 years of age

	Offspring n = 675	Fathers n = 274	Mothers n = 574	p*
Age (years)	23.4 ± 3.5	50.3 ± 7.6	47.3 ± 6.4	<0.0001
BMI (kg/m^2)	31.9 ± 8.0	32.6 ± 7.1	33.6 ± 7.8	0.06
WHR (cm)	0.90 ± 0.10	0.98 ± 0.06	0.90 ± 0.07	<0.0001
Diastolic BP (mmHg)	74.7 ± 11.0	80.8 ± 10.6	78.8 ± 11.0	0.01
Systolic BP (mmHg)	117.3 ± 12.9	125.6 ± 15.9	125.5 ± 20.5	0.94
Total Cholesterol (mg/dl)	172.8 ± 33.6	191.1 ± 39.9	187.6 ± 35.1	0.22
LDL (mg/dl)	94.7 ± 27.8	106.2 ± 33.0	100.8 ± 28.4	0.02
HDL (mg/dl)	50.0 ± 13.3	47.4 ± 16.5	53.0 ± 15.2	<0.0001
Triglycerides (mg/dl)	144.5 ± 98.1	208.9 ± 198.9	174.3 ± 92.0	0.006
Smoking Status (Current)	275 (40.7%)	112 (40.9%)	215 (37.5%)	<0.0001
Alcohol Status (Current)	533 (89.3%)	180 (66.2%)	291 (50.7%)	<0.0001
Diabetes Status (ADA Definition)	36 (5.3%) DM 36 (5.3%) IFG	105 (38.8%) DM 34 (12.4%) IFG	193 (33.7%) DM 38 (6.6%) IFG	<0.0001
Hypertension Status (Yes)	83 (12.3%)	127 (46.4%)	218 (38.0%)	0.06
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	5305.0 (3237.3, 7551.9)	4773.9 (2962.9, 7189.8)	4970.9 (3034.4, 7277.7)	0.44

p* for comparison between fathers and mothers, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for offspring in the >18-30 year old cohort by gender are presented in Table 5.7. Males were found to have significantly higher waist-to-hip ratios (0.93 vs. 0.87 cm, p<0.0001), diastolic blood pressure (78.3 vs. 72.1 mmHg, p <0.0001), systolic blood pressure (123.6 vs. 112.6 mmHg, p<0.0001), total cholesterol (179.9 vs. 167.5 mg/dl, p <0.0001), LDL (100.7 vs. 90.3 mg/dl, p< 0.0001), and triglycerides (162.6 vs. 130.9 mg/dl, p = 0.0005) when compared to females. In addition, significantly more males had hypertension (19.4% vs. 7.0%, p<0.0001) compared to females and males had higher prevalence of both smoking (45.0% vs. 37.6%, p = 0.03) and alcohol consumption (84.8% vs. 74.6%, p = 0.006). Females were found to have a significantly higher HDL cholesterol levels (51.5 vs. 48.0 mg/dl, P = 0.0006) compared to males.

Table 5.7 Descriptive Characteristics of Offspring >18-30 years for the total cohort and stratified by sex

	Offspring n = 675	Males n = 289	Females n = 386	p*
Age (years)	23.4 ± 3.5	23.4 ± 3.6	23.5 ± 3.5	0.89
BMI (kg/m^2)	31.9 ± 8.0	31.5 ± 7.7	32.2 ± 8.2	0.28
WHR (cm)	0.90 ± 0.10	0.93 ± 0.1	0.87 ± 0.1	<0.0001
Diastolic BP (mmHg)	74.7 ± 11.0	78.3 ± 11.4	72.1 ± 9.9	<0.0001
Systolic BP (mmHg)	117.3 ± 12.9	123.6 ± 12.4	112.6 ± 11.0	<0.0001
Total Cholesterol (mg/dl)	172.8 ± 33.6	179.9 ± 36.7	167.5 ± 30.2	<0.0001
LDL (mg/dl)	94.7 ± 27.8	100.7 ± 29.7	90.3 ± 25.5	<0.0001
HDL (mg/dl)	50.0 ± 13.3	48.0 ± 13.1	51.5 ± 13.3	0.0006
Triglycerides (mg/dl)	144.5 ± 98.1	162.6 ± 125.1	130.9 ± 68.8	0.0005
Smoking Status (Current)	275 (40.7%)	130 (45.0%)	145 (37.6%)	0.03
Alcohol Status (Current)	533 (89.3%)	245 (84.8%)	288 (74.6%)	0.006
Diabetes Status (ADA Definition)	36 (5.3%) DM 36 (5.3%) IFG	17 (5.9%) DM 16 (5.6%) IFG	19 (4.9%) DM 20 (5.2%) IFG	0.83
Hypertension Status (Yes)	83 (12.3%)	56 (19.4%)	27 (7.0%)	<0.0001
Pedometer Steps (steps/day averaged over the week; Median, 25th, 75th)	5305.0 (3237.3, 7551.9)	5446.0 (3409.0, 7850.9)	5152.1 (3186.2, 7411.3)	0.24

* p-value for comparison between males and females, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for female offspring >18-30 years of age by study location are presented in Table 5.8. Statistically significant differences were noted for BMI, WHR, diastolic blood pressure, HDL, % current smokers, % current alcohol drinkers, diabetes prevalence, hypertension status, and pedometer steps between the females from the three study locations.

Similar to findings in the <18 cohort, female offspring from Arizona appeared to have the largest BMI, highest diastolic blood pressure, and the lowest pedometer steps as well as the lowest prevalence of current smokers compared to the female offspring from the other two locations. In order to test for location differences among female offspring, we conducted post hoc comparisons. Among female offspring in Arizona and the Dakotas, BMI ($p<0.0001$), WHR ($p = 0.005$) diastolic blood pressure ($p = 0.005$), HDL ($p = 0.007$), smoking status ($p = 0.004$), alcohol status ($p< 0.0001$), diabetes prevalence ($p = 0.03$), hypertension status ($p = 0.02$), and median pedometer steps ($p = 0.01$) were statistically different. For female offspring in Arizona and Oklahoma, statistically significant differences were noted for age ($p = 0.04$), BMI ($p<0.0001$), WHR ($p<0.0001$), diastolic blood pressure ($p = 0.02$), HDL ($p = 0.007$), smoking status ($p = 0.03$), alcohol status ($p = 0.02$), and diabetes prevalence ($p = 0.002$). For female offspring in the Dakotas and Oklahoma, statistically significantly differences were noted between smoking status ($p = 0.004$), alcohol status ($p<0.001$), diabetes prevalence ($p = 0.03$), and hypertension status ($p = 0.02$).

Table 5.8 Descriptive Characteristics for Female Offspring >18 – 30 years of age by Study Location

	Arizona n = 144	Dakotas n = 142	Oklahoma n = 100	p
Age (years)	22.9 ± 3.3	23.7 ± 3.6	23.9 ± 3.6	0.06
BMI (kg/m^2)	35.7 ± 8.4	30.4 ± 7.5	29.6 ± 7.3	<0.0001
WHR (cm)	0.89 ± 0.06	0.87 ± 0.21	0.84 ± 0.06	<0.0001
Diastolic BP (mmHg)	74.0 ± 9.6	70.8 ± 8.9	71.1± 11.2	0.009
Systolic BP (mmHg)	112.3 ± 9.8	111.0 ± 10.0	115.0 ± 13.5	0.06
Total Cholesterol (mg/dl)	164.4 ± 29.7	169.0 ± 32.2	169.9 ± 31.4	0.37
LDL (mg/dl)	87.5 ± 22.6	91.0 ± 26.6	93.2 ± 27.6	0.26
HDL (mg/dl)	49.2 ± 13.4	53.0 ± 13.6	52.8 ± 12.4	0.006
Triglycerides (mg/dl)	141.0 ± 79.3	125.0 ± 61.0	124.2 ± 61.6	0.16
Smoking Status (Current)	30 (20.8%)	80 (56.3%)	35 (35.0%)	<0.0001
Alcohol Status (Current)	106 (73.6%)	119 (83.8%)	63 (63.0%)	<0.0001
Diabetes Status (ADA Definition)	13 (9.0%) DM 11 (7.6%) IFG	3 (2.1%) DM 9 (6.3%) IFG	3 (3.0%) DM --	0.002
Hypertension Status (Yes)	15 (10.4%)	3 (2.1%)	9 (9.0%)	0.01
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4606.2 (2525.3, 7180.2)	5521.4 (3725.7, 8483.0)	4788.0 (3193.0, 7199.1)	0.03

* p-value for comparison between locations, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for male offspring >18-30 years of age by study location are presented in Table 5.9. Statistically significant differences were noted for BMI, WHR, triglycerides, prevalence of alcohol use and diabetes, and pedometer steps. As with female offspring, male offspring from Arizona had the largest BMI when compared to the males from the other two locations. In addition, males from Arizona had the largest WHR and highest triglyceride levels compared to male offspring from the other two locations. Post hoc comparisons revealed that BMI ($p < 0.0001$), WHR ($p < 0.0001$), triglycerides ($p = 0.006$), alcohol use (p = 0.05), diabetes prevalence (p = 0.03) and pedometer steps (p = 0.0008) were statistically different among male offspring in Arizona and the Dakotas. For male offspring in Arizona and Oklahoma, statistically significant differences were noted for BMI (p = 0.0003), WHR (p = 0.0002), alcohol status (p = 0.01), diabetes prevalence (p = 0.005) and pedometer steps (p = 0.006). For male offspring in the Dakotas and Oklahoma, statistically significant differences were only noted for alcohol status (p = 0.002).

Table 5.9 Descriptive Characteristics for Male Offspring >18 – 30 years of age by Study Location

	Arizona n = 94	Dakotas n = 109	Oklahoma n = 86	p*
Age (years)	23.2 ± 3.7	23.5 ± 3.5	23.6 ± 3.5	0.61
BMI (kg/m^2)	35.0 ± 7.8	29.1 ± 6.5	30.8 ± 7.8	<0.0001
WHR (cm)	0.96 ± 0.08	0.91 ± 0.10	0.92 ± 0.19	<0.0001
Diastolic BP (mmHg)	79.7 ± 12.6	78.5 ± 10.7	76.4 ± 10.9	0.35
Systolic BP (mmHg)	124.6 ± 11.5	123.3 ± 12.8	122.9 ± 13.1	0.51
Total Cholesterol (mg/dl)	178.5 ± 32.6	177.2 ± 36.0	184.9 ± 41.4	0.34
LDL (mg/dl)	97.9 ± 27.4	99.2± 29.3	105.6 ± 32.1	0.24
HDL (mg/dl)	47.2 ± 14.0	47.8 ± 13.0	49.2 ± 12.4	0.27
Triglycerides (mg/dl)	180.9 ± 142.3	156.7 ± 137.0	150.2 ± 80.5	0.02
Smoking Status (Current)	36 (38.3%)	54 (49.5%)	40 (46.5%)	0.57
Alcohol Status (Current)	78 (83.0%)	102 (93.6%)	65 (75.6%)	0.01
Diabetes Status (ADA Definition)	11 (11.7%) DM 9 (9.6%) IFG	4 (3.7%) DM 5 (4.6%) IFG	2 (2.3%) DM 2 (2.3%) IFG	0.007
Hypertension Status (Yes)	23 (24.5%)	18 (16.5%)	15 (17.4%)	0.31
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4385.3 (2736.0, 6261.8)	6024.1 (4166.1, 7705.0)	6079.1 (3341.7, 9199.1)	0.0009

* p-value for comparison between locations, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

5.2.3 Offpsring > 30 - 50 years of age

Of the 2062 offspring in the total cohort, 930 offspring were between the ages of >30-50 years of age. Table 5.10 presents descriptive characteristics of these 930 offspring along with their parents stratified by gender. The mean age of offspring among this sample was 39.1 years. In regard to parents, pairwise comparisons between fathers and mothers indicate that fathers were significantly older than mothers (66.4 vs. 64.4 years, p = 0.0004) and had a larger WHR (0.98 vs. 0.92, p<0.0001). Fathers also had significantly higher diastolic (75.9 vs. 72.5 mmHg, p = 0.01) and percentages of current smokers (22.9% vs. 22.6%, p<0.0001), current drinkers (36.3% vs. 21.3%, p<0.0001), and diabetics (53.9% vs. 40.3%, p<0.0001) compared to mothers. Conversely, mothers had significantly higher BMIs (32.0 vs. 30.5 kg/m^2, p = 0.0003), total cholesterol levels (189.3 vs. 182.4 mg/dl, p = 0.007) and HDL cholesterol levels (54.3 vs. 45.7 mg/dl, p<0.0001). There were no statistically significant differences noted for systolic blood pressure, LDL cholesterol, triglycerides, prevalence of hypertension, or median pedometer steps.

Table 5.10 Descriptive Characteristics for Offspring and Parents where the offspring is >30-50 years of age

	Offspring n = 930	Fathers n = 272	Mothers n = 709	p*
Age (years)	39.1 ± 5.3	66.4 ± 7.9	64.4 ± 7.9	0.0004
BMI (kg/m^2)	33.3 ± 8.1	30.5 ± 5.4	32.0 ± 6.7	0.0003
WHR (cm)	0.91 ± 0.08	0.98 ± 0.06	0.92 ± 0.07	<0.0001
Diastolic BP (mmHg)	79.1 ± 10.5	75.9 ± 10.1	72.5 ± 11.1	<0.0001
Systolic BP (mmHg)	121.4 ± 14.9	133.5 ± 18.6	131.4 ± 19.1	0.12
Total Cholesterol (mg/dl)	188.0 ± 38.0	182.4 ± 36.1	189.3 ± 33.7	0.007
LDL (mg/dl)	102.1 ± 28.5	101.1 ± 32.0	99.3 ± 29.3	0.42
HDL (mg/dl)	52.8 ± 15.4	45.7 ± 14.8	54.3 ± 15.3	<0.0001
Triglycerides (mg/dl)	182.4 ± 268.9	188.2 ± 142.1	181.8 ± 92.4	0.49
Smoking Status (Current)	358 (38.5%)	61 (22.9%)	159 (22.6%)	<0.0001
Alcohol Status (Current)	671 (72.2%)	95 (36.3%)	150 (21.3%)	<0.0001
Diabetes Status (ADA Definition)	184 (19.8 %) DM 73 (7.9%) IFG	146 (53.9%) DM 22 (8.1%) IFG	305 (43.0%) DM 85 (12.0%) IFG	<0.0001
Hypertension Status (Yes)	256 (27.6%)	166 (61.0%)	449 (63.3%)	0.43
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	5205.1 (3400.1, 7489.7)	4148.8 (2343.3, 6172.1)	3620.0 (1943.7, 5749.3)	0.12

p* for comparisons between fathers and mothers, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for offspring in the >30-50 year old cohort by gender are presented in Table 5.11. Similar to the findings in the >18-30 cohort, males were found to have significantly higher body mass index (32.6 vs. 29.8 kg/m^2, p = 0.01), waist-to-hip ratios (0.96 vs. 0.85 cm, p <0.0001), diastolic blood pressure (83.1 vs. 69.0 mmHg, p <0.0001), systolic blood pressure (126.6 vs. 110.0 mmHg, p<0.0001), total cholesterol (197.5 vs. 153.0 mg/dl, p <0.0001), LDL (82.8 vs. 82.4 mg/dl, p<0.0001), and triglycerides (136.0 vs. 114.0 mg/dl, p = 0.001) when compared to females; whereas females were found to have a significantly higher

HDL cholesterol levels (48.3 vs. 46.7 mg/dl, p = 0.0006) compared to males. Male offspring in the >30-50 year old sample were also found to have significantly more current alcohol drinkers (81.4% vs. 66.6%) and prevalence of hypertension (41.0% vs. 19.2%) compared to female offspring.

Table 5.11 Descriptive Characteristics of Offspring >30-50 years for the total cohort and stratified by sex

	Offspring n = 930	Males n = 356	Females n = 574	p*
Age (years)	39.1 ± 5.3	39.0 ± 5.0	16.4 ± 0.9	0.87
BMI (kg/m^2)	33.3 ± 8.1	32.6 ± 7.7	29.8 ± 7.7	0.01
WHR (cm)	0.91 ± 0.08	0.96 ± 0.1	0.85 ± 0.1	<0.0001
Diastolic BP (mmHg)	79.1 ± 10.5	83.1 ± 10.8	69.0 ± 9.5	<0.0001
Systolic BP (mmHg)	121.4 ± 14.9	126.6 ± 14.4	110.0 ± 9.7	<0.0001
Total Cholesterol (mg/dl)	188.0 ± 38.0	197.5 ± 46.7	153.0 ± 25.7	<0.0001
LDL (mg/dl)	102.1 ± 28.5	82.8 ± 26.1	82.4 ± 22.1	<0.0001
HDL (mg/dl)	52.8 ± 15.4	46.7 ± 10.7	48.3 ± 13.5	<0.0001
Triglycerides (mg/dl)	182.4 ± 268.9	136.0 ± 181.0	114.0 ± 65.3	0.001
Smoking Status (Current)	358 (38.5%)	144 (40.6%)	214 (37.3%)	0.54
Alcohol Status (Current)	671 (72.2%)	289 (81.4%)	382 (66.6%)	<0.0001
Diabetes Status (ADA Definition)	184 (19.8 %) DM 73 (7.9%) IFG	68 (19.1%) DM 34 (9.6%) IFG	116 (20.2%) DM 39 (6.8%) IFG	0.31
Hypertension Status (Yes)	256 (27.6%)	146 (41.0%)	110 (19.2%)	<0.0001
Pedometer Steps (steps/day averaged over the week; Median, 25th, 75th)	5205.1 (3400.1, 7489.7)	5152.0 (3493.0, 7695.0)	5544.0 (3604.0, 8351.0)	0.49

* p-value for comparison between males and females, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Table 5.12 presents descriptive characteristics of female offspring >30-50 years of age by study location. Statistically significant differences were noted for BMI, WHR, diastolic and systolic blood pressure, total cholesterol, LDL cholesterol, % of current smokers and alcohol users, diabetes prevalence, and pedometer steps between female offspring from the three study locations. Female offspring from Arizona had the largest BMI and WHR as well as the highest prevalence of diabetes. In addition, females from Arizona had the lowest number of current smokers and alcohol drinker and the lowest pedometer steps compared to the female offspring from the other two locations. Female offspring from Oklahoma had the highest diastolic and systolic blood pressures, compared to female offspring form the Dakotas and Arizona. In order to test for location differences among female offspring, we conducted post hoc comparisons. Among female offspring in Arizona and the Dakotas, BMI ($p<0.0001$), WHR ($p<0.0001$), total cholesterol ($p = 0.04$), LDL ($p = 0.02$), smoking status ($p<0.0001$), alcohol status ($p = 0.002$), diabetes prevalence ($p<0.0001$), and median pedometer steps ($p = 0.009$) were statistically different. For female offspring in Arizona and Oklahoma, statistically significant differences were noted for BMI ($p<0.0001$), WHR ($p<0.0001$), systolic blood pressure ($p = 0.001$), total cholesterol ($p = 0.001$), LDL ($p = 0.05$), HDL ($p = 0.0004$), diabetes prevalence ($p<0.0001$) and median pedometer steps ($p = 0.03$). For female offspring in the Dakotas and Oklahoma, statistically significantly differences were noted between age ($p = 0.04$), diastolic blood pressure ($p = 0.001$), systolic blood pressure ($p<0.0001$), HDL ($p = 0.04$), smoking status ($p<0.0001$), alcohol status ($p = 0.002$), and diabetes prevalence ($p<0.0001$).

Table 5.12 Descriptive Characteristics for Female Offspring >30-50 years of age by Study Location

	Arizona n = 168	Dakotas n = 176	Oklahoma n = 230	p
Age (years)	39.0 ± 5.2	38.5 ± 5.3	39.7 ± 5.9	0.11
BMI (kg/m^2)	38.3 ± 9.8	31.9 ± 7.1	31.7 ± 6.3	<0.0001
WHR (cm)	0.92 ± 0.06	0.87 ± 0.08	0.87 ± 0.06	<0.0001
Diastolic BP (mmHg)	76.7 ± 9.1	74.7 ± 9.3	78.0± 9.9	0.003
Systolic BP (mmHg)	117.3 ± 14.8	114.6 ± 12.5	121.4 ± 14.3	<0.0001
Total Cholesterol (mg/dl)	177.2 ± 32.0	182.2 ± 28.7	185.6 ± 28.8	0.004
LDL (mg/dl)	93.5 ± 22.3	99.2 ± 24.8	98.9 ± 25.4	0.05
HDL (mg/dl)	52.4 ± 16.7	53.4 ± 13.0	56.4 ± 14.6	0.001
Triglycerides (mg/dl)	159.0 ± 94.7	150.5 ± 89.4	154.1 ± 91.4	0.62
Smoking Status (Current)	46 (27.4%)	87 (49.4%)	81 (35.2%)	0.0004
Alcohol Status (Current)	107 (63.7%)	142 (80.7%)	133 (57.8%)	<0.0001
Diabetes Status (ADA Definition)	60 (35.7 %) DM 16 (9.5%) IFG	17 (9.7 %) DM 15 (8.5%) IFG	39 (17.0 %) DM 8 (3.5%) IFG	<0.0001
Hypertension Status (Yes)	34 (20.2%)	24 (13.6%)	52 (22.7%)	0.07
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4957.1 (3029.1, 6683.7)	5570.4 (3959.5, 7478.6)	5267.2 (3526.4, 7886.9)	0.02

* p-value for comparison between locations, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for male offspring >30-50 years age by study location are presented in Table 5.13. Statistically significant differences were noted for BMI, WHR, diastolic and systolic blood pressure, total cholesterol, LDL and HDL cholesterol, triglycerides, prevalence of current smoking, alcohol use and diabetes, hypertension status, and pedometer steps. As with female offspring, male offspring from Arizona had the largest BMI when compared to the male offspring from the other two locations. In addition, males from Arizona had the largest WHR as well as the highest percentage of current drinkers, diabetics, hypertension compared to male offspring from the other two locations. Male offspring from Oklahoma were found to have the highest diastolic and systolic blood pressure levels, as well as the highest cholesterol levels (total, LDL, and HDL) when compared to male offspring from Arizona and the Dakotas. Post hoc comparisons revealed that BMI ($p < 0.0001$), WHR ($p < 0.0001$), diastolic blood pressure ($p = 0.05$), systolic blood pressure ($p = 0.05$), LDL ($p = 0.04$), triglycerides ($p = 0.05$), current smoking prevalence ($p = 0.01$), diabetes prevalence ($p < 0.0001$) and pedometer steps ($p = 0.001$) were statistically different among male offspring in Arizona and the Dakotas. For male offspring in Arizona and Oklahoma, statistically significant differences were noted for BMI ($p = 0.001$), WHR ($p < 0.0001$), total cholesterol ($p = 0.0004$), LDL cholesterol ($p = 0.02$), current smoking prevalence ($p = 0.004$), alcohol status ($p = 0.007$), diabetes prevalence ($p = 0.0004$), hypertension status ($p = 0.01$) and median pedometer steps ($p = 0.05$). For male offspring in the Dakotas and Oklahoma, statistically significant differences were noted for age ($p = 0.04$), diastolic blood pressure ($p = 0.01$), systolic blood pressure ($p = 0.001$), triglycerides ($p = 0.04$), and current alcohol drinking ($p = 0.05$).

Table 5.13 Descriptive Characteristics for Male Offspring >30-50 years of age by Study Location

	Arizona n = 100	Dakotas n = 114	Oklahoma n = 142	p
Age (years)	39.2 ± 5.1	38.2 ± 4.9	39.6 ± 5.0	0.11
BMI (kg/m^2)	35.7 ± 8.9	30.8 ± 6.8	32.0 ± 6.9	<0.0001
WHR (cm)	0.98 ± 0.07	0.95 ± 0.08	0.95 ± 0.08	<0.0001
Diastolic BP (mmHg)	83.7 ± 11.8	81.2 ± 9.6	84.2± 10.9	0.003
Systolic BP (mmHg)	127.1± 15.5	122.9 ± 12.3	129.2 ± 14.8	<0.0001
Total Cholesterol (mg/dl)	186.4 ± 33.3	196.8 ± 53.5	205.7 ± 47.9	0.004
LDL (mg/dl)	103.3 ± 27.9	111.9 ± 33.9	112.9 ± 34.3	0.05
HDL (mg/dl)	49.9 ± 15.9	49.3 ± 15.4	51.3 ± 16.7	0.001
Triglycerides (mg/dl)	176.2 ± 94.1	239.5 ± 557.3	253.9 ± 419.7	0.62
Smoking Status (Current)	47 (47.5%)	39 (34.2%)	58 (40.9%)	0.02
Alcohol Status (Current)	88 (88.9%)	97 (85.1%)	104 (73.2%)	0.01
Diabetes Status (ADA Definition)	34 (34.0 %) DM 12 (12.0%) IFG	12 (10.5 %) DM 13 (11.4%) IFG	22 (15.5 %) DM 9 (6.3%) IFG	<0.0001
Hypertension Status (Yes)	56 (56.0%)	33 (29.0%)	57 (40.1%)	0.003
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4401.6 (2809.0, 6602.9)	5748.3 (3976.6, 8680.8)	5350.6 (3221.4, 7194.1)	0.02

* p-value for comparison between locations, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

5.2.4 Offspring > 50 years of age

Of the 2062 offspring in the total cohort, 177 offspring were between the age >50 years of age. Table 5.14 presents descriptive characteristics of these 177 offspring along with their parents stratified by gender. The mean age of offspring among this sample was 55.3 years. Pairwise comparisons between fathers and mothers found no statistically significant differences in age, BMI, diastolic or systolic blood pressure, triglyceride levels, percent currently smoking, drinking, prevalence of diabetes, hypertension status, or median step counts between fathers and mothers. However, fathers had significantly larger WHR (0.99 vs. 0.92, $p<0.0001$), whereas mothers had significantly higher total cholesterol levels (183.8 vs. 161.6 mg/dl, $p = 0.0006$) and HDL cholesterol levels (52.4 vs. 40.6 mg/dl, $p<0.0001$).

Table 5.14 Descriptive Characteristics for Offspring and Parents where the offspring is >50 years of age

	Offspring n =177	Fathers n = 32	Mothers n = 117	p*
Age (years)	55.3 ± 4.5	80.1 ± 5.4	78.5 ± 6.5	0.16
BMI (kg/m^2)	31.9 ± 6.1	32.5 ± 5.1	31.6 ± 5.7	0.39
WHR (cm)	0.93 ± 0.08	0.99 ± 0.06	0.92 ± 0.07	<0.0001
Diastolic BP (mmHg)	80.2 ± 10.7	65.9 ± 19.1	66.2 ± 10.4	0.93
Systolic BP (mmHg)	131.9 ± 20.0	135.2 ± 10.3	135.0 ± 21.8	0.94
Total Cholesterol (mg/dl)	193.0 ± 34.0	161.6 ± 29.9	183.8 ± 30.8	0.0006
LDL (mg/dl)	107.2 ± 28.5	85.8 ± 26.0	98.3 ± 27.4	0.02
HDL (mg/dl)	49.7 ± 13.7	40.6 ± 12.6	52.4 ± 14.8	<0.0001
Triglycerides (mg/dl)	182.4 ± 268.9	188.2 ± 142.1	166.7 ± 63.2	0.41
Smoking Status (Current)	69 (39.0%)	2 (6.5%)	14 (12.1%)	0.75
Alcohol Status (Current)	75 (42.4%)	2 (6.5%)	8 (6.9%)	0.07
Diabetes Status (ADA Definition)	59 (33.3 %) DM 21 (11.9%) IFG	18 (56.3%) DM 7 (21.9%) IFG	50 (42.7%) DM 9 (7.7%) IFG	0.15
Hypertension Status (Yes)	104 (58.8%)	26(81.3%)	83 (70.9%)	0.57
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4835.7 (3045.3, 7453.3)	3079.7 (2991.6, 5033.4)	2786.7 (1330.3, 5356.0)	0.72

p* for comparison of fathers and mothers, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for offspring in the >50 year old cohort by gender are presented in Table 5.15. Male offspring were found to have significantly higher waist-to-hip ratios (0.98 vs. 0.90 cm, p <0.0001), LDL (107.6 vs. 107.0 mg/dl, p = 0.04), and prevalence of current alcohol users (56.3% vs. 33.0%, p = 0.009) when compared to females; whereas females were found to have significantly higher HDL cholesterol levels (52.3 vs. 45.9 mg/dl, p = 0.0004) compared to males.

Table 5.15 Descriptive Characteristics of Offspring >50 years of age for the total cohort and stratified by sex

	Offspring n = 177	Males n = 71	Females n = 106	p*
Age (years)	55.3 ± 4.5	55.1 ± 4.1	55.6 ± 4.8	0.84
BMI (kg/m^2)	31.9 ± 6.1	31.8 ± 5.2	32.0 ± 6.6	0.30
WHR (cm)	0.93 ± 0.08	0.98 ± 0.06	0.90 ± 0.07	<0.0001
Diastolic BP (mmHg)	80.2 ± 10.7	81.9 ± 11.2	79.1± 10.3	0.16
Systolic BP (mmHg)	131.9 ± 20.0	130.5 ± 17.7	132.8 ± 21.4	0.52
Total Cholesterol (mg/dl)	193.0 ± 34.0	189.0 ± 35.5	195.7 ± 32.8	0.26
LDL (mg/dl)	107.2 ± 28.5	107.6 ± 28.6	107.0 ± 28.6	0.04
HDL (mg/dl)	49.7 ± 13.7	45.9 ± 14.3	52.3 ± 12.6	0.0004
Triglycerides (mg/dl)	182.4 ± 268.9	186.2 ± 130.0	186.6 ± 88.3	0.26
Smoking Status (Current)	69 (39.0%)	27 (38.0%)	42 (39.6%)	0.07
Alcohol Status (Current)	75 (42.4%)	40 (56.3%)	35 (33.0%)	0.009
Diabetes Status (ADA Definition)	59 (33.3 %) DM 21 (11.9%) IFG	23 (32.3 %) DM 13 (18.3%) IFG	36 (34.0 %) DM 8 (7.6%) IFG	0.09
Hypertension Status (Yes)	104 (58.8%)	40 (56.3%)	64 (60.4%)	0.59
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	4835.7 (3045.3, 7453.3)	4969.6 (3222.2, 7453.3)	4668.9 (2759.9, 7563.3)	0.73

* p-value for comparison between males and females All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for female offspring >50 years of age by study location are presented in Table 5.16. Statistically significant differences were noted for WHR, smoking and alcohol status. Of note, females from Arizona appeared to have the largest WHR as well as the lowest prevalence of current smokers and alcohol consumers compared to the female offspring from the other two locations. In order to test for location differences among female offspring, post hoc comparisons were used. Among female offspring in Arizona and the Dakotas, smoking status (p = 0.01), alcohol status (p = 0.005), and prevalence of diabetes (p = 0.05) were statistically different. For female offspring in Arizona and Oklahoma, statistically significant differences were noted for age (p = 0.04), WHR (p = 0.004), and triglycerides (p = 0.02). For female offspring in the Dakotas and Oklahoma, only alcohol status was statistically significantly different, with a higher percentage of current alcohol users in the Dakotas (20.4% vs. 15.1%).

Table 5.16 Descriptive Characteristics for Female Offspring >50 years of age by Study Location

	Arizona n = 13	Dakotas n = 39	Oklahoma n = 54	p
Age (years)	53.2 ± 2.7	56.5 ± 6.2	55.4 ± 3.9	0.16
BMI (kg/m^2)	34.8 ± 10.5	30.9 ± 5.6	32.0 ± 6.0	0.41
WHR (cm)	0.94 ± 0.06	0.90 ± 0.06	0.89 ± 0.08	0.01
Diastolic BP (mmHg)	81.6 ± 7.7	77.3 ± 11.7	79.8± 9.7	0.48
Systolic BP (mmHg)	136.2 ± 28.9	129.9 ± 18.8	134.0 ± 21.3	0.86
Total Cholesterol (mg/dl)	185.5 ± 26.1	193.5 ± 36.1	199.7 ± 31.5	0.30
LDL (mg/dl)	105.5 ± 21.8	103.7 ± 32.3	109.8 ± 27.5	0.57
HDL (mg/dl)	52.0 ± 10.6	52.3 ± 13.8	52.4 ± 12.4	0.95
Triglycerides (mg/dl)	139.9 ± 40.2	188.9 ± 88.3	196.2 ± 94.0	0.09
Smoking Status (Current)	2 (15.4%)	18 (46.2%)	22 (40.7%)	0.05
Alcohol Status (Current)	2 (15.4%)	19 (48.7%)	14 (25.9%)	0.02
Diabetes Status (ADA Definition)	8 (61.5 %) DM --	10 (25.6 %) DM 3 (7.7%) IFG	18 (33.3 %) DM 5 (9.3%) IFG	0.18
Hypertension Status (Yes)	10 (76.9%)	22 (56.4%)	32 (59.3%)	0.41
Pedometer Steps (steps/day averaged over the week; Median, 25th, 75th)	3915.3 (2087.5, 6534.9)	4005.0 (2438.7, 6844.6)	5595.6 (3300.6, 8482.0)	0.28

* p-value for comparison between locations, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

Descriptive characteristics for male offspring >50 years of age by study location are presented in Table 5.17. Statistically significant differences were noted for WHR, diastolic blood pressure, total cholesterol, smoking status, and diabetes prevalence. Male offspring from

Oklahoma had the smallest WHR and lowest prevalence of diabetes when compared to the males from the other two locations. In addition, males from the Dakotas had the lowest diastolic blood pressure, but had the highest total cholesterol level compared to male offspring from the other Arizona and Oklahoma. Lastly, male offspring from Arizona had the lowest reported number of current smokers compared to Dakotas and Oklahoma ($p = 0.02$). Post hoc comparisons revealed that age ($p = 0.03$), diastolic blood pressure ($p = 0.02$), total cholesterol ($p = 0.001$), and LDL cholesterol ($p = 0.03$) were statistically different among male offspring in Arizona and the Dakotas. For male offspring in Arizona and Oklahoma, statistically significant differences were noted for WHR ($p = 0.006$), total cholesterol ($p = 0.006$), smoking status ($p = 0.01$) and prevalence of diabetes ($p = 0.03$). For male offspring in the Dakotas and Oklahoma, statistically significant differences were noted for BMI ($p = 0.04$), WHR ($p = 0.0002$), and smoking status ($p = 0.03$).

Table 5.17 Descriptive Characteristics for Male >50 years of age by Study Location

	Arizona n = 15	Dakotas n =20	Oklahoma n =36	p
Age (years)	53.0 ± 2.1	56.5 ± 4.5	55.2 ± 4.1	0.06
BMI (kg/m^2)	32.5 ± 5.2	33.7 ± 6.3	30.5 ± 4.2	0.10
WHR (cm)	1.01 ± 0.06	1.01 ± 0.05	0.95 ± 0.06	0.0003
Diastolic BP (mmHg)	86.8 ± 12.2	76.7 ± 10.0	82.8 ± 10.5	0.05
Systolic BP (mmHg)	132.6 ± 20.6	127.5 ± 16.7	131.3 ± 17.3	0.68
Total Cholesterol (mg/dl)	164.0 ± 29.7	200.2 ± 33.3	193.3 ± 34.7	0.005
LDL (mg/dl)	94.4 ± 23.2	115.5 ± 27.4	108.6 ± 30.0	0.10
HDL (mg/dl)	41.6 ± 13.8	45.6 ± 13.9	47.9 ± 14.8	0.40
Triglycerides (mg/dl)	139.9 ± 43.8	207.1 ± 186.0	193.9 ± 114.1	0.53
Smoking Status (Current)	3 (20.0%)	7 (35.0%)	17 (47.2%)	0.02
Alcohol Status (Current)	7 (46.7%)	14 (70.0%)	19 (52.8%)	0.21
Diabetes Status (ADA Definition)	7 (46.7 %) DM 4 (26.7%) IFG	9 (45.0 %) DM 4 (20.0%) IFG	7 (19.4 %) DM 5 (13.9%) IFG	0.05
Hypertension Status (Yes)	11 (73.3%)	12 (60.0%)	17 (47.2%)	0.21
Pedometer Steps (steps/day averaged over the week; Median, 25^{th}, 75^{th})	3222.2 (1470.2, 6412.5)	5841.1 (3954.6, 7483.9)	5094.5 (3302.1, 7228.0)	0.24

* p-value for comparison between locations, All values mean ± standard deviation, unless otherwise noted. BMI = Body Mass Index, WHR = Waist-to-Hip Ratio; BP = Blood Pressure; DM = Diabetes Mellitus, IFG = Impaired Fasting Glucose

5.3 SPEARMAN RANK ORDER CORRELATIONS

5.3.1 Summary of Spearman Correlations of Physical Activity Levels between Offspring and Parents

The goal of the correlational analysis was to determine whether physical activity levels were related between offspring and their parents. Table 5.18 presents a summary of results for comparisons made between parent and their offspring, across all age groups and regardless of the sex of the offspring. Overall, fathers' physical activity levels were significantly and positively associated with their offspring's physical activity level in only the >18-30 year age group (rho = 0.16, p = 0.008). No statistically significant associations were noted between mother and offspring physical activity levels.

Table 5.18 Spearman Rank Order Correlations for the Association of Physical Activity Levels between Offspring and Parent

Offspring Physical Activity	Father Physical Activity	Mother Physical Activity
≤ 18 years of age	0.07	0.004
p	0.42	0.95
> 18-30 years of age	***0.16***	0.06
p	***0.008***	0.12
>30-50 years of age	0.10	0.02
p	0.09	0.51
> 50 years of age	-0.16	-0.16
p	0.37	0.09

Table 5.19 presents the results of Spearman Rank Order Correlations between parents and offspring stratified by sex for each age group. Statistically significant findings were noted

between father-offspring pairs. More specifically, physical activity levels between fathers and daughters ≤ 18 years of age were found to be significantly correlated (rho = 0.30, p = 0.01). In addition, physical activity levels between fathers and sons > 18-30 years of age were positively associated (rho = 0.26, p = 0.01). In contrast, no relationship was noted between mothers and their sons or daughters.

Table 5.19 Summary Table of Spearman Rank Order Correlations for the Association of Physical Activity Levels between Offspring and Parent stratified by sex

Male Offspring Physical Activity	Father Physical Activity	Mother Physical Activity	Female Offspring Physical Activity	Father Physical Activity	Mother Physical Activity
≤ 18 years of age	-0.16	-0.01	≤ 18 years of age	***0.30***	0.01
p	0.23	0.92	p	***0.01***	0.90
> 18-30 years of age	***0.26***	0.09	> 18-30 years of age	0.08	0.04
p	***0.0003***	0.14	p	0.33	0.48
>30-50 years of age	0.06	0.03	>30-50 years of age	0.13	0.02
p	0.51	0.57	p	0.11	0.72
> 50 years of age	-0.12	-0.16	> 50 years of age	-0.12	-0.19
p	0.68	0.29	p	0.64	0.11

5.3.2 Spearman Correlations of Physical Activity Levels between Offspring ≤ 18 Years of Age and Parents where both Parents are in the SHFS

Many of the studies, in the familial aggregation literature, that examined the association of physical activity levels between parent and child, required that a child enrolled in their study come from a two-parent household. This process was done in order to ensure that the child of interest had the opportunity to be exposed to both parents' physical activity patterns and levels. Although our study did not require that both parents be enrolled in the SHFS, we were able to examine the association of physical activity levels between parent and offspring in a sample of offspring ≤ 18 years of age (n =115), where both a father and a mother were enrolled in the SHFS.

Table 5.20 presents results between offspring regardless of sex and fathers and mothers. No statistically significant associations were noted between father and offspring and mother and offspring physical activity levels.

Table 5.20 Spearman Rank Order Correlations of Physical Activity Levels between Offspring ≤ 18 and Parent where both parents are enrolled in the SHFS

	Father PA (n = 115)	Mother PA (n = 115)
Offspring PA	0.12129	0.07822
p	0.1966	0.4060

Tables 5.21 present results of comparisons among male offspring and female offspring, respectively with their parents. Again, no statistically significant associations were found between physical activity levels of fathers and sons. For fathers and daughters, a significant positive association (rho = 0.37, p = 0.005) was noted. This association appeared to strengthen when compared to the results between fathers and daughters presented in Table 5.16 (page 98). Again, no association was noted between mothers and daughters.

Table 5.21 Spearman Rank Order Correlations of Physical Activity Levels between Offspring ≤ 18 stratified by sex and Parent where both parents are enrolled in the SHFS

	Father PA (n = 53)	Mother PA (n = 51)		Father PA (n = 62)	Mother PA (n = 64)
Male Offspring PA	-0.12476	0.00118	Female Offspring PA	0.35621	0.17004
p	0.3734	0.9935	p	0.0045	0.1792

5.4 2 X 2 CONTINGENCY TABLE ANALYSES FOR FAMILIAL AGGREGATION

5.4.1 Summary of 2 x 2 Contingency Table Analyses

Familial aggregation was also examined using concordance rates (Cells a and d) calculated for parent-offspring pairs using 2 x 2 contingency tables (Table 5.22). Based upon these concordance rates, familial aggregation occurred in 34.4%-57.7 % of father-offspring pairs and 42.8%-53.0% of mother-offspring pairs.

Table 5.22 2 x 2 Contingency Table results for Parent and Offspring Pairs stratified by sex and age group

	Fathers						Mothers					
Male Offspring	Cell a	Cell b	Cell c	Cell d	OR	p	Cell a	Cell b	Cell c	Cell d	OR	p
≤ 18 years of age	14 23.0%	16 26.2%	21 34.4%	10 16.4%	1.31	0.41	31 27.2%	26 22.8%	31 27.2%	26 22.8%	1.19	0.51
>18-30 years of age	37 29.4%	22 17.3%	25 19.8%	42 33.3%	1.14	0.66	61 24.4%	60 24.0%	58 23.2%	71 28.4%	0.97	0.85
>30-50 years of age	30 28.0%	21 19.6%	24 22.4%	32 29.9%	1.14	0.65	60 22.5%	54 20.2%	72 27.0%	81 30.3%	1.33	0.11
> 50 years of age	1 6.7%	5 33.3%	3 20.0%	6 40.0%	0.06	0.48	10 22.7%	7 15.9%	16 36.4%	11 25.0%	2.29	0.06
Female Offspring	Cell a	Cell b	Cell c	Cell d	OR*	p	Cell a	Cell b	Cell c	Cell d	OR*	p
≤ 18 years of age	19 28.4%	13 19.4%	10 14.9%	25 37.3%	0.77	0.53	27 20.3%	37 27.8%	34 25.6%	35 26.3%	0.92	0.72
>18-30 years of age	41 27.7%	37 25.0%	33 22.3%	37 25.0%	0.89	0.63	86 26.5%	73 22.5%	82 25.3%	83 25.6%	1.12	0.47
>30-50 years of age	44 26.7%	40 24.2%	35 21.2%	46 27.9%	0.88	0.56	107 24.2%	103 23.3%	114 25.8%	118 26.7%	0.10	0.46
> 50 years of age	2 11.8%	3 17.6%	10 58.8%	2 11.8%	3.33	0.05	9 12.3%	22 30.1%	22 30.1%	20 27.4%	1.00	1.00

Cell a = both parent and offspring low active, Cell b = parent high active/offspring low active; Cell c = parent low active/offspring high active; Cell d = both parent and offspring high active; Odds Ratio = cell c/cell b; p-value based on McNemar's Test

5.5 VARIANCE COMPONENTS ANALYSES

From data collected during Phase IV, we were able to estimate the familial aggregation of physical activity levels by modeling the effects of physical activity as a covariate and household effect and genetic heritability for the entire SHFS cohort and separately for the three study locations. A copy of the SOLAR for all four models is contained in Appendix B.

Tables 5.23 and 5.24 present descriptive data for the 3665 individuals in the SHFS cohort utilized in the variance component analyses. The mean age of the cohort was 39.9 years with a range of 14.1 to 93.3 years. Approximately 60% of the cohort was female (data not shown) and the average BMI was 32.2 kg/m^2. Mean pedometer step counts for the cohort were 5664.4 steps. In regard to smoking and alcohol consumption, approximately 35.7% of the cohort were current smokers and 60.0% were current alcohol drinkers. In addition, 32.5 % of the cohort reported having diabetes or impaired fasting glucose levels and approximately 20.0% of the cohort was considered disabled in some manner.

Table 5.23 Basic descriptive data for continuous variables in SHFS cohort (n= 3665) utilized in the variance component analyses

	TOTAL SHFS COHORT			
	Mean ± Standard Deviation	Count	Minimum	Maximum
Age (years)	39.9 ± 17.0	3665	14.1	93.3
BMI (kg/m^2)	32.3 ± 7.9	3625	15.6	91.4
WHR (cm)	0.91± 0.09	3628	0.34	2.71
Diastolic BP (mmHg)	76.2 ± 11.2	3648	39.0	140.0
Systolic BP (mmHg)	122.6 ± 17.1	3649	82.0	246.0
Total Cholesterol (mg/dl)	180.6 ± 37.1	3639	92.0	630.0
LDL (mg/dl)	98.1 ± 29.3	3615	9.0	288.0
HDL (mg/dl)	50.8 ± 14.5	3620	12.0	138.0
Triglycerides (mg/dl)	167.6 ± 170.1	3637	28.0	5323.0
% Body Fat	37.4 ± 10.3	3594	5.4%	83.7%
Pedometer Steps (steps/day averaged over the week)	5664.4 ± 3915.9	3269	141.6	38730.2

All statistics presented as mean ± standard deviation, unless otherwise noted.

Table 5.24 Basic descriptive data of categorical variables for the SHFS cohort (n= 3665) utilized in the variance component analyses

Smoking Status (Current smoking)	Alcohol Status (Current drinking)	Diabetes Status – ADA definition	Hypertension Status	Disabled
1307 (35.7%)	2200 (60.0%)	1192 (32.5%)	1248 (34.1%)	738 (20.1%)

All statistics are presented as: n (% of total cohort reporting yes)

Table 5.25 presents the variance component estimates of familial aggregation of physical activity levels in the SHFS. Model 1 was conducted in the total SHFS cohort (n = 3375) regardless of study location. In this model 1225 pedigrees were merged into 974 pedigree-household groups using the household ID number. Of the 19 covariates placed in the model, only age (p = 0.004), age^2 (p = 0.005), smoking status (p = 0.06), systolic blood pressure (p = 0.08), percent body fat (p = 0.004), and study location (p<0.0001) remained in the final model. The proportion of variance due to all final covariates was 0.05. The familial effects for physical activity were stronger when included in the model as a heritability than when included as a household effect. As a heritable effect, physical activity achieved statistical significance (p = 0.007) explaining approximately 9% of the trait variance.

Table 5.25 Proportion of variation in physical activity levels accounted for by SOLAR

	Physical Activity modeled as				
	Household effect		Heritability (h^2)		Covariate effect
Model 1: Total Cohort (n = 3375)	0.01 ± 0.02	p = 0.30	0.09 ± 0.04	p = 0.007	r^2 = 0.05
Model 2: Arizona (n = 1061)	0.04 ± 0.05	p = 0.21	0.08 ± 0.08	p = 0.15	r^2 < 0.01
Model 3: Dakotas (n = 1170)	0.02 ± 0.04	p = 0.31	0.09 ± 0.06	p = 0.06	r^2 = 0.08
Model 4: Oklahoma (n=1163)	0.00 ± 0.00	— —	0.05 ± 0.05	p = 0.17	r^2 = 0.05
Model 5: Total Cohort minus individuals with BMI > 40, or age > 70, or disabled (n=2259)	0.004 ± 0.03	p = 0.44	0.09 ± 0.05	p = 0.003	r^2 = 0.04

Models adjusted for the following covariates: age, sex, age*sex, age^2, age^2*sex, smoking (current vs. never/ever), alcohol consumption (current vs. never/ever), waist-to-hip ratio, BMI, BMI*sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), SBP*DBP, % body fat, hypertension status (yes/no), diabetes status (yes/no), years of education, study location, and disabled (yes/no).

Model 2 was conducted in the Arizona subsample (n =1061) which included 453 pedigrees that were merged into 347 pedigree-household groups. As with Model 1, all 19 covariates, with the exception of study location, were placed in the model, of which only the bmi*sex interaction (p = 0.04) remained in the final model. The proportion of variance explained due to all final covariates was 0.00009. As in Model 1, the familial effects of physical activity were stronger when included in the model as a heritability explaining 8% of the model variance compared to 4% when measured as a household effect, however neither effect achieved statistical significance. This finding may be due to the small sample size of the subsample, since SOLAR requires the use of larger populations.

Model 3 was conducted in the Dakotas subsample (n = 1170) which included 419 pedigrees which were merged into 320 pedigree-household groups. As with the previous two models, 18 covariates were forced into the model. For the Dakotas subsample, the covariates that remained in the final model were age*sex interaction (p = 0.0004), age^2 (p = 0.003), and percent body fat (p = 0.05). The proportion of variance explained due to these covariates was approximately 8%. Physical activity modeled as a heritable effect explained approximately 9% of the model variance, which was borderline significance (p = 0.06). However as a shared household effect, the familial effects of physical activity explained approximately 2% of the model variance, but did not reach statistical significance.

Model 4 was conducted in the Oklahoma subsample (n = 1163). In this model, age (p = 0.002), smoking status (p = 0.04), systolic blood pressure (sbp, p = 0.002), diastolic blood pressure (dbp, p = 0.02), and sbp*dbp interaction (p = 0.08) remained in the final model and explained approximately 5% of the model variance. The familial effects of physical activity when modeled as a heritability explained approximately 5% of the model variance, but did not reach statistical significance. Physical activity modeled as a household effect was deleted from the model, since it was not a significant covariate.

Lastly, Model 5 was conducted in the total SHFS cohort (regardless of study location) after eliminating data on individuals who met one or more of the following criteria: BMI > 40 kg/m^2, age >70 years, or reported being disabled. A person was considered disabled if they reported having any of the following conditions that may limit their physical activity: rheumatic heart disease, renal dialysis, kidney failure, cirrhosis of the liver, emphysema, above or below knee amputation, unable to walk, or indicated that their moderate activity was limited a lot by their health. This resulted in the elimination of data on 1,116 individuals, thus model 5 includes an n of 2259. In this model, 1225 pedigrees were merged into 974 pedigree-household groups using the household ID number. Of the 19 covariates placed in the model, only age*sex ($p = 0.05$), age^2 ($p = 0.03$), systolic blood pressure ($p = 0.08$), percent body fat ($p = 0.004$), diabetes status ($p = 0.05$), and study location ($p = 0.0004$) remained in the final model. The proportion of variance due to all final covariates was 0.04. In Model 5, after eliminating these individuals from the analyses, the familial effects for physical activity modeled as a heritable effect did not change, thus the findings from Model 1 and Model 5 are considered statistically identical.

6.0 DISCUSSION

6.1 SUMMARY OF FINDINGS

We were provided with a very unique opportunity to examine physical activity levels using an objective measure of physical activity, the pedometer, and to determine if these physical activity levels aggregated in 96 Native American extended families within the Strong Heart Family Study (SHFS). Utilizing this unique dataset, we used several different approaches to examine possible aggregation of physical activity levels within the SHFS. These findings and how they relate with other studies will be presented in the following chapter.

6.1.1 Objectively Measured Physical Activity Levels in the SHFS

There is a limited body of evidence available regarding physical activity levels in Native American populations and the sparse data that is available indicates that the problem of inactivity noted nationwide is likewise also a problem in both Native Americans adults and children.[16, 28, 30-32, 67] Most of this evidence, however, is based upon physical activity data collected using subjective methods. As mentioned earlier in this report, subjective measures of physical activity do a relatively accurate job of assessing moderate and high intensity and structured activity. However, several reports have indicated that the most frequent types of activities reported among minority populations are comprised of lower intensity activities including household and care-giving activities, and walking for exercise[30-32,75] which may not be accurately accounted for by using a questionnaire. Therefore, this study provided a rare opportunity to determine physical activity levels in Native American individuals using an objective measure of physical activity.

Aggregated reference values for steps/day indicate that active adults take between 7000 and 13000 steps/day[135]. Furthermore, it has been suggested that daily steps around 7000 - 8000 may be roughly equivalent to the accumulation of 30 minutes of moderate-intensity activity on a single day.[101] In the SHFS, the median pedometer steps per day for the entire cohort was 4919.9 (2995.6, 7336.3), which would suggest that at least 50% of our sample are not meeting the current Centers for Disease Control and American College of Sports Medicine recommendations for physical activity.[136]

When comparing our findings with other studies conducted among racially or ethnically diverse free-living samples with pedometer assessed physical activity, we find similar results. For example, Bennett et al.[137] examined pedometer step counts among multiethnic (50% African American, 42% Hispanic) low-income housing residents ranging in age from 18-70+ years. In this study, mean pedometer step counts ranged from 6587±4083.6 in participants < 25 years of age to 3285 ± 2873.3 in participants > 70 years of age. Likewise, in the SHFS study, mean pedometer steps ranged from 7168.4±4356.6 in participants < 20 years of age to 2626.3 ± 2071.9 in participants > 70 years of age. Additionally, in the Cross-Cultural Activity Participation Study, Whitt et al.[75] noted median daily step counts of 4783 (3009, 6987) and 4577 (3219, 6385) among 127 American Indian and 135 African American women (mean age 53.8 ± 10.9 years), respectively. In the SHFS, female participants aged 50-60 years were found to have slightly lower median steps counts of 3447.8 (2408.1, 5496.2), compared to those reported in the Cross-

Cultural Activity Participation Study. These findings confirm that our sample of Native American adults and adolescents are at least as inactive as other populations

In regard to younger populations, there are very few studies that have been conducted among free-living adolescents and only rarely conducted in minority populations. We were able to compare our findings in 14-20 year olds in the SHFS studies with one study conducted by Wilde et al.[138] that assessed physical activity levels using a pedometer in high school aged boys and girls (14-18 years). Adolescents and young adults in the SHFS were less active based upon pedometer steps compared to the high school population in the Wilde study. In fact, mean step counts in the free-living high school population ranged from 10,717 – 9,643 in 9th - 12th graders, while mean step counts for the14-20 year olds SHFS were 6554.4. Unfortunately, no information was provided on the racial and ethnic makeup of the Wilde et al. population.

In addition, the SHFS provided us with the opportunity to examine physical activity levels across age groups, by gender, and by study location. Consistent with previous studies[16, 139-141], female participants reported lower physical activity levels based upon pedometer steps compared to men. In addition, physical activity levels declined with increasing age and BMI. Again, these findings are similar to those in other studies that have shown decreasing levels of physical activity with increasing age and BMI[75, 142]. Furthermore, when we stratified our cohort by study location, physical activity levels were consistently lowest in Arizona regardless of gender. In addition, both male and female participants in Arizona had higher BMI levels compared to participants from the Dakotas and Oklahoma, again suggesting a negative relationship between physical activity and BMI.

6.1.2 Familial Aggregation of Physical Activity Levels in the SHFS

Familial aggregation is defined as the occurrence of a trait, in this case, physical activity, in members of a family greater than that which can be readily accounted for by chance. More simply stated, familial aggregation can be defined as the combination of genetic and environmental influences that may affect a trait within a family. The study design of the SHFS provided the opportunity to examine whether physical activity levels aggregate in a sample of multi-generational genetically linked Native American family members. In order to accomplish this, we first used simple statistical methods, such as correlation analyses and 2 x 2 contingency tables followed by more complex modeling to determine if physical activity levels aggregated in families within the SHFS.

From these simple analyses, we found that, as a continuous variable, physical activity levels among father and offspring were significantly and positively related. In contrast, no relationship was found between mother and offspring physical activity level. More specifically, physical activity levels between fathers and daughters ≤18 years of age were found to be significantly correlated (rho = 0.30, p = 0.01) and this association increased in strength when examined in father-daughter pairs when both parents enrolled in the SHFS were included in the analyses (rho = 0.37, p = 0.005). In addition, physical activity level between fathers and sons >18-30 years were positively associated (rho = 0.26, p = 0.01).

We also examined familial aggregation of physical activity levels between parent-offspring pairs using concordance rates within 2 x 2 contingency tables. In these analyses, physical activity was recoded into a categorical variable where both parent and offspring were classified as high active or low active based upon their respective median step counts. Although no statistically significant findings were noted, familial aggregation of physical activity levels, based upon concordance rates, occurred in 34.4% - 57.7% of father-offspring pairs and 42.8% - 53.0% for mother-offspring pairs. With the exception of the >50 year old offspring age group, father-offspring pairs had higher levels of familial aggregation than mother-offspring pairs. These findings appear to mirror the results from the correlation analyses.

The fact that father's activity level and not mother's activity level was associated with that of their offspring, compares with findings of several previous studies. For example, Duncan et al. [49] found that father's weekly leisure time energy expenditure was significantly related to children's (mean age 12.8 years) average daily energy expenditure ($r = 0.39$, $p<0.01$). However, the average weekly leisure time energy expenditure of mothers was not significantly related to their children's average daily energy expenditure. Moreover, when examined by sex of the offspring, the findings remained statistically significant between fathers and sons ($r = 0.43$, $p<0.05$) and between fathers and daughters ($r = 0.37$, $p<0.05$). Moore et al.[43] noted that the effect of parent's activity levels on their children was stronger for active fathers than active mothers. Fuemmeler et al.[143] found that father's physical activity seems to have a greater impact on child behavior regardless of gender of the child and Freedson et al.[51] found that the relative odds ratio of being active for the children of active fathers was 3.5 compared to only 2.0 of an active mother. The possible reason for this association is not clear.

Our findings suggest the presence of familial aggregation of physical activity levels in the SHFS. It is important to note that many of the past aggregation studies of physical activity in the literature were conducted in Caucasian families and utilized strict inclusion criteria ensuring that one and/or both parents and their child resided in the same household. This criteria not only assured the presence of a common household environment but likely over represented families with relatively high socioeconomic status from non-broken homes. Parent-offspring pairs in the

SHFS were not held to such stringent inclusion criteria as they were not required to reside in the same household. This inclusion criteria likely impacted our findings.

Studies such as those by Fuemmeler et al[143], Freedson et al.,[51] and Moore et al.[43, 51, 52] utilized an objective measure such as an accelerometer to assess physical activity. The accelerometer is a more precise instrument for assessing physical activity levels compared to a pedometer and allows for the assessment of step counts as well as intensity of physical activity. Furthermore, the physical activity data recorded by accelerometers is downloaded directly to a computer and does not require participants to record activity information. This process helps to reduce reporting errors, which may have occurred in the SHFS study, since participants were required to record step counts in a diary. More importantly, by using an accelerometer, these researchers were capable of capturing a wide range of activity levels as can more accurately capture activities and movement of lower intensity.

Based upon the findings of the simple univariate analyses alone, it appeared that physical activity levels may have familial resemblance in the SHFS. However, there are genetic and environmental factors that cannot be taken into account using these simple statistical analyses that only examined one parent and one offspring. Therefore, in order to account for heritable factors, we modeled the familial effect of physical activity in the SHFS as both a household (environmental) and genetic heritability using variance components methodology in the extended family cohort.

From variance components analyses, physical activity was modeled as a household (environmental) effect. However, the familial effects (measured as a household effect) accounted for very little of the total variation in physical activity levels and our results were not statistically significant. These findings are similar to those of Mitchell et al[129], who also found no effect of household environment on familial aggregation of physical activity among Mexican-American extended families. The lack of a significant finding for a household effect in the SHFS study may be a true null finding or may result from the fact that SHFS participants were not required to reside in the same household and/or participants may have not been properly assigned a correct household ID.

Physical activity was also modeled as a heritable (genetic) effect. We found familial relationships accounted for 9% of the total variation in physical activity levels in this population of Native American extended families without inclusion criteria requiring 2 parents in a household and from three geographic locations across the United States. Furthermore, when examined separately by study location, the familial heritability of physical activity, although not statistically significant, ranged from 5-9% and was found to be strongest in the Dakotas and weakest in the Oklahoma. A finding of no statistical significance in the three locations is likely a result of a lack of power, since SOLAR requires extremely large data sets. (Even though each of the three study locations provided well over 1,000 genetically linked individuals, these numbers may not have provided adequate power to determine statistically significant findings).

Although physical activity level was defined differently, our findings are almost identical to those of Mitchell et al.[129] who found using similar methodology, that familial effects of physical activity assessed by questionnaire, accounted for 9% of the variance of the trait in the San Antonio Family Heart Study. This study was also conducted in a minority population (42 large Mexican American families), a population quite similar to our own in terms of age. Our findings are also in line with those noted in the Canada Fitness Survey. Again using similar methodology, in the Canada Fitness Survey[53], familial correlations for physical activity levels based on data from a questionnaire ranged from (0.09-0.14). However, our findings are weaker than those noted in the Quebec Family Study,[54,57] a prospective family study on the genetics of obesity and its comorbidities in Caucasian families. In this study, strong familial associations of physical activity levels (assessed using a 3 day physical activity record) accounted for 29% of the variance in habitual physical activity and 16-25% of the phenotypic variation of physical activity.[142] The findings from the San Antonio Heart Study and the Canada Fitness Survey were right inline with the current findings. However, the Quebec Family Study, had stronger results likely reflecting the fact that their cohort was both Caucasian and likely of relatively higher SES.

Finally, we wanted to reexamine our data eliminating those participants that may not have had their physical activity levels accurately assessed by pedometer in this study. As mentioned previously, pedometers may have problems assessing physical activity in persons with gait abnormalities where a person may shuffle or not have a foot strike hard enough to displace the hips causing a step to be registered. Additionally, the pedometer may not assess physical activity accurately in persons who are extremely obese where the pedometer may not remain upright in the vertical plane. Although gait speed and the proper placement of the pedometer were not directly measured in the SHFS, we are able to identify individuals who were more likely to have these issues affect their physical activity assessment. For gait speed, we identified persons whose age was greater than 70 years and those reporting a disability. For BMI, we identified those participants whose BMI was greater than 40 kg/m^2. After eliminating these participants, the heritability of physical remained at 9% and was not significantly different from our base model, thus it is difficult to comment on whether these factors truly affected physical activity assessed by pedometer in this cohort.

6.2 STRENGTHS AND LIMITATIONS

The Strong Heart Family Study provided the unique opportunity to not only to examine physical activity levels of Native Americans from 96 extended families in three geographic locations, using an objective measure. In addition, this study also allowed for the investigation of whether physical activity levels aggregate in this population. To date, only a few extended family studies exist and only one previous family study, the San Antonio Family Heart Study, has examined familial aggregation of physical activity in a minority population. In addition, the current study is the first to examine familial aggregation in a family study using an objective measure of physical activity. Previous family studies such as the San Antonio Family Heart Study and the Quebec Family Study utilized subjective measures such as a questionnaire to assess physical activity in their populations. While this method of assessment is relatively reasonable in large population studies, it relies on participant recall and may not provide an adequate assessment of lower intensity, unstructured physical activities like walking and housework. By utilizing an objective measure of physical activity in the Strong Heart Family Study, we were able to eliminate some of the problems posed by the use of subjective measures.

Although the pedometer measures physical activity objectively, there are, unfortunately, limitations with its use as an assessment tool. First, the pedometer cannot discriminate between steps accumulated in walking, running, or stair climbing; therefore, we were unable to determine intensity of activity. Intensity of activity would have allowed us to determine whether total physical activity or specific intensity levels aggregated among families. Secondly, many pedometers, such as the pedometer used in the current study, lack an internal clock and data storage capability, thus we had to rely on the SHFS participants to accurately record their step counts from the pedometer in their seven-day activity diary. This process may have resulted in reporting errors or lack of data. Finally, participant clothing or body habitus may have played a role in the accuracy of the pedometer. In order for a pedometer to accurately assess physical activity, it must be worn snug to the body and kept upright in a vertical plane, perpendicular to the ground. Although every effort was made to ensure that participants were properly instructed on how to wear the pedometer, there was no guarantee that this occurred. Therefore, if the pedometer was not worn in a correct manner, the pedometer may not have worked properly and may have resulted in an underestimation of physical activity levels for those specific individuals.

Other limitations that should be considered when interpreting these findings include the validity and completeness of household data. While every effort was made to obtain this information, there were many missing data points, thus making comparisons among those residing in the same household environment difficult. In addition, since many of the participants moved around during the study, it was difficult to determine which household the participant considered their primary residence, thus there is concern that the household of some participants were miscoded. Additionally, we had to rely on subjectively measured information regarding health status, which may not have been reported correctly and may have affected our findings. During our analyses, it was found that a few participants reported that their health was limited or that they were unable to walk, yet they had pedometer data available with relatively high step counts.

6.3 CONCLUSIONS

In the present study, the familial resemblance of physical activity levels, measured by pedometer, was examined within 3665 genetically linked individuals from 96 Native American extended families in the Strong Heart Family Study. Despite the fact that this study was conducted within three separate geographic locations, had limited household data, was not designed specifically to examine aggregation of physical activity levels, and was not limited to 2-parent families, we still detected significant, albeit modest, evidence of familial aggregation in physical activity levels. The familial relationships accounted for 9% of the total variation in physical activity levels.

Using several different approaches, we were able to determine that physical activity levels are a heritable trait in the Strong Heart Family Study. These findings may have consequences for where and how to focus lifestyle intervention efforts. For example, as an inactive parent will likely have an inactive child, family based interventions would allow researchers and health practioners to impact on the health habits of both a parent and child. Thus, helping to break the cycle of increasing levels of inactivity from generation to generation and potentially reducing the risk of chronic disease burden in the future for all.

6.4 FUTURE DIRECTIONS

6.4.1 Future Analyses

In our variance components analyses, we conducted general family models and did not examine the specific relationships between spouses, sibships, or parent-offspring. Therefore, our next step would be to conduct these analyses in order to determine the associations of physical activity levels between these specific pairs while controlling for other covariates. In addition, it was very apparent that several of our covariates, such as BMI, total cholesterol, and triglycerides, contained many extreme values. Therefore, in future analyses it would be pertinent to determine if these outliers are leverage points and if they cluster in individuals, particularly in individuals with physical activity measures. Furthermore, the goal of variance components analysis in family studies is to estimate components of total variance or covariance that result from shared unobserved factors such as genes or environment. In order to determine the causal relationship between these observed and unobserved factors, we need to use more advanced analyses such as path analysis. Path analysis (covariance structured analyses) allows for the partitioning of observed correlations into components reflecting shared causal factors. Therefore, a future step will be to use path analysis to re-examine our findings and to come up with extended models to further describe the heritable relationship of physical activity.

6.4.2 Future Studies

In the SHFS, we utilized a pedometer to assess physical activity levels. As previously mentioned, there are several limitations associated with using a pedometer, such as an inability to assess intensity and pattern of physical activity. Therefore, future studies should consider the use of more advanced monitoring techniques such as the accelerometer. Like a pedometer, an accelerometer is non-invasive. Unlike the pedometer, the accelerometer allows for the measurement of total physical activity but also how the time in physical activity is spent. For example, the use of an accelerometer will allow for us to break down total physical into time spent in low, moderate and high intensity levels. Being able to measure these specific intensity levels will allow for a better understanding of the intensity of activity that most impacts on health.

The Strong Heart Study is assessing physical activity levels again in Phase V with pedometers. It may be possible to reexamine the aggregation of physical activity in Phase V and to determine if physical activity levels aggregate consistently over time.

6.5 PUBLIC HEALTH SIGNIFICANCE

Physical inactivity is a major risk factor for complex metabolic diseases such as obesity, diabetes, and hypertension[18] . Traditionally, these morbidities have been the specific burden of adulthood, but are now being diagnosed more frequently in younger populations[144-147]. There has been some suggestion that, as is true in adults [148], children are becoming less physically active[23, 149] and that this decline in physical activity may help to explain the sudden increase in the incidence of metabolic diseases among children. Moreover, physical activity appears to track from childhood to adulthood[23, 24]. Therefore, determining if physical activity levels are related within families could provide insight into the design of future lifestyle interventions studies. Familial aggregation of physical activity levels provides the basis for establishing family based intervention studies. Similar to findings in obesity, where obese parents tend to have overweight and obese children, physical activity appears to be related between parent and offspring. Across several geographic areas and in all households (regardless of whether family members resided in or out of the household), we were able to determine that physical activity levels are a heritable trait in the Strong Heart Family Study. By designing lifestyle intervention studies that involve a family approach, it is possible to impact on the health habits of both the parent and child, therefore potentially reducing the risk of chronic disease burden.

APPENDIX A: PEDOMETER INSTRUCTIONS AND SEVEN DAY ACTIVITY DIARY

STRONG HEART – FAMILY STUDY
GENETICS OF CARDIOVASCULAR DISEASE IN AMERICAN INDIANS

DIRECTIONS TO PARTICIPANTS FOR USING THE ACTIVITY METER (PEDOMETER)

The Accusplit Activity Meter (pedometer) counts the number of steps taken while walking. You have been requested to wear this meter EVERY DAY for a seven day period from _______ to _______. The pedometer is to be clipped at the waist to your clothes, underwear, or on a belt and worn on the _______ hip and must be kept in an upright position. Please keep the pedometer firmly against your body so it does not move around freely. You can use a belt or elastic strap to keep it in place on your hip. Please DO NOT LET THE PEDOMETER GET WET by wearing it in the rain or while bathing or swimming. Please remember to reset the pedometer to "0" (zero) when you put it on in the morning and to record the pedometer number in your activity record when you take it off at night.

If you have any questions, please contact:________________ at _________________.

Specific Instructions
1. Every morning, just before you put the pedometer on, push the reset button to read "0".
2. Record the time you reset the pedometer on the activity record page.
3. **Wear the pedometer all day except for bathing, swimming or in the rain (unless you can keep it dry). If you take it off, record the length of time it was off (minutes or hours) on your activity record page.**
4. At bedtime, take off the pedometer. Record on your activity record page (a) the pedometer number (the number of steps taken), and (b) the time you removed the pedometer.
5. Please do not touch the reset button during the day or you will erase your activity numbers.
6. Wear the pedometer on your dominant hip (right hip for right handed people and left hip for left handed people), keep it upright, and make sure it fits firmly against your body so it does not move around.
7. **Keep the cover closed or it will not record your steps.**
8. The pedometer will not work correctly if it is in a pants, coat, or shirt pocket. It will not work correctly if it is sideways either.
9. Please mail the activity record to us in the self-addressed stamped envelope after you complete your week.
10. Please keep the pedometer as a token of our appreciation of your participation in the Strong Heart Family Study.

Thank you very much for your time and effort!

SHS FAMILY STUDY – CARDIOVASCULAR DISEASE IN AMERICAN INDIANS
National Heart, Lung, and Blood Institute

ACTIVITY METER SEVEN-DAY RECORD

Name:___________________________

Reminder: Reset the Activity Meter (pedometer) to "0" every morning

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date							
Day of week							
Time attached							
Meter number at bedtime							
Time removed							
Did you take off the meter for any reason?							
If yes, for how long?							

Complete the question after completing this journal.

Has your physical activity in the past seven (7) days been typical for you compared to your regular activity level? Yes_____ 1 No_____ 2

APPENDIX B: SOLAR POLYGENIC MODELING OUTPUT

This section contains a copy of the four polygenic models conducted in the SOLAR in the Strong Heart Family Study Cohort. The outputs are as follows: 1) Total SHFS Cohort, 2) Arizona Subsample, 3) Dakotas Subsample, 4) Oklahoma Subsample, 5) Total SHFS Cohort removing participants with BMI > 40 kg/m^2, age > 70, and disabled.

MODEL 1- TOTAL SHFS COHORT

Pedigree: ped.solar
Phenotypes: newpheno.solar
Trait: sqmean Individuals: 3375

H2r is 0.0887188 p = 0.0067256 (Significant)
H2r Std. Error: 0.0378397

C2 is 0.0111884 p = 0.3038254 (Not Significant)
C2 Std. Error: 0.0229081 (C2 retained because nonzero)

age p = 0.0037261 (Significant)
age^2 p = 0.0053261 (Significant)
smoke p = 0.0614149 (Significant)
sbp p = 0.0809588 (Significant)
bdfat p = 0.0042132 (Significant)
locale p = 0.0000285 (Significant)
sex p = 0.1559912 (Not Significant)
age*sex p = 0.2924305 (Not Significant)
age^2*sex p = 0.6694211 (Not Significant)
etoh p = 0.5321386 (Not Significant)
whr p = 0.8129238 (Not Significant)
dbp p = 0.2750635 (Not Significant)
bmi p = 0.2622228 (Not Significant)
ht p = 0.6142140 (Not Significant)
diab p = 0.1116654 (Not Significant)
disabled p = 0.9832267 (Not Significant)
educ p = 0.4416722 (Not Significant)
sbp*dbp p = 0.9436505 (Not Significant)
bmi*sex p = 0.9656923 (Not Significant)

1225 pedigrees merged into 974 pedigree-household groups

The following covariates were removed from final models:
sex age*sex age^2*sex etoh whr dbp bmi ht diab disabled educ sbp*dbp bmi*sex

Proportion of Variance Due to All Final Covariates Is 0.0493445

Loglikelihoods and chi's are in sqmean/polygenic.logs.out
Best model is named housepoly and null0
Final models are named housepoly, house, poly, spor, nocovar
Initial sporadic and polygenic models are s0 and p0
Initial household and household polygenic models are h0 and hp0
Constrained covariate models are named no<covariate name>

MODEL 2 ARIZONA SUBSAMPLE

Pedigree: az.ped.solar
Phenotypes: ../newpheno.solar
Trait: sqmean Individuals: 1061

H2r is 0.0778394 p = 0.1530972 (Not Significant)
H2r Std. Error: 0.0792099

C2 is 0.0395753 p = 0.2060007 (Not Significant)
C2 Std. Error: 0.0497719 (C2 retained because nonzero)

age p = 0.2588924 (Not Significant)
sex p = 0.4534459 (Not Significant)
age*sex p = 0.6803590 (Not Significant)
age^2 p = 0.2794608 (Not Significant)
age^2*sex p = 0.4374167 (Not Significant)
etoh p = 0.4951796 (Not Significant)
whr p = 0.8699570 (Not Significant)
sbp p = 0.5047152 (Not Significant)
dbp p = 0.5064523 (Not Significant)
bmi p = 0.1617304 (Not Significant)
bdfat p = 0.8580189 (Not Significant)
ht p = 0.3713578 (Not Significant)
diab p = 0.4398284 (Not Significant)
disabled p = 0.6232472 (Not Significant)
educ p = 0.8974344 (Not Significant)
sbp*dbp p = 0.4680381 (Not Significant)
bmi*sex p = 0.0416305 (Significant)

453 pedigrees merged into 347 pedigree-household groups

The following covariates were removed from final models:
age sex age*sex age^2 age^2*sex etoh whr sbp dbp bmi bdfat ht diab disabled educ sbp*dbp

Proportion of Variance Due to All Final Covariates Is 0.0000873

Loglikelihoods and chi's are in sqmean/polygenic.logs.out
Best model is named housepoly and null0
Final models are named housepoly, house, poly, spor, nocovar
Initial sporadic and polygenic models are s0 and p0
Initial household and household polygenic models are h0 and hp0
Constrained covariate models are named no<covariate name>

MODEL 3 DAKOTAS SUBSAMPLE

Pedigree: da.ped.solar

Phenotypes: ../newpheno.solar

Trait: sqmean Individuals: 1170

H2r is 0.0943158 p = 0.0610841 (Not Significant)
H2r Std. Error: 0.0641779

C2 is 0.0187247 p = 0.3082301 (Not Significant)
C2 Std. Error: 0.0402850 (C2 retained because nonzero)

age p = 0.9988716 (Not Significant)
sex p = 0.7831361 (Not Significant)
age*sex p = 0.0003656 (Significant)
age^2 p = 0.0029755 (Significant)
age^2*sex p = 0.3180006 (Not Significant)
etoh p = 0.9836494 (Not Significant)
whr p = 0.3469672 (Not Significant)
sbp p = 0.6799839 (Not Significant)
dbp p = 0.7075365 (Not Significant)
bmi p = 0.9771831 (Not Significant)
bdfat p = 0.0498018 (Significant)
ht p = 0.6690307 (Not Significant)
diab p = 0.5668782 (Not Significant)
disabled p = 0.5512447 (Not Significant)
educ p = 0.2327625 (Not Significant)
sbp*dbp p = 0.4625529 (Not Significant)
bmi*sex p = 0.7445636 (Not Significant)

419 pedigrees merged into 320 pedigree-household groups

The following covariates were removed from final models:
age sex age^2*sex etoh whr sbp dbp bmi ht diab disabled educ sbp*dbp bmi*sex

Proportion of Variance Due to All Final Covariates Is 0.0779110

Loglikelihoods and chi's are in sqmean/polygenic.logs.out
Best model is named housepoly and null0
Final models are named housepoly, house, poly, spor, nocovar
Initial sporadic and polygenic models are s0 and p0
Initial household and household polygenic models are h0 and hp0
Constrained covariate models are named no<covariate name>

MODEL 4 OKLAHOMA SUBSAMPLE

Pedigree: ok.ped.solar
Phenotypes: ../newpheno.solar
Trait: sqmean Individuals: 1163

H2r is 0.0506717 p = 0.1675714 (Not Significant)
H2r Std. Error: 0.0548407

C2 is 0.0000000

Since it was zero, the C2 parameter has been deleted.
To keep C2 parameters even when they are all zero,
use the -keephouse option.

age p = 0.0019212 (Significant)
sex p = 0.8558546 (Not Significant)
age*sex p = 0.1777890 (Not Significant)
age^2 p = 0.1566160 (Not Significant)
age^2*sex p = 0.5097696 (Not Significant)
etoh p = 0.1761016 (Not Significant)
whr p = 0.7446217 (Not Significant)
sbp p = 0.0020104 (Significant)
dbp p = 0.0160767 (Significant)
bmi p = 0.5759817 (Not Significant)
bdfat p = 0.4326706 (Not Significant)
ht p = 0.7809682 (Not Significant)
diab p = 0.1926045 (Not Significant)
disabled p = 0.6727277 (Not Significant)
educ p = 0.2927559 (Not Significant)
sbp*dbp p = 0.0790969 (Significant)
bmi*sex p = 0.2009151 (Not Significant)

The following covariates were removed from final models:
sex age*sex age^2 age^2*sex etoh whr bmi bdfat ht diab disabled educ bmi*sex

Proportion of Variance Due to All Final Covariates Is 0.0490822

Loglikelihoods and chi's are in sqmean/polygenic.logs.out
Best model is named poly and null0
Final models are named housepoly, house, poly, spor, nocovar
Initial sporadic and polygenic models are s0 and p0
Initial household and household polygenic models are h0 and hp0
Constrained covariate models are named no<covariate name>

MODEL 5 TOTAL SHFS COHORT AFTER ELIMINATION OF THOSE WITH BMI>40, AGE> 70, AND DISABILITY

Phenotypes: newpheno2.solar
Trait: sqmean Individuals: 2259

H2r is 0.0944906 p = 0.0298423 (Significant)
H2r Std. Error: 0.0524649

C2 is 0.0049924 p = 0.4385749 (Not Significant)
C2 Std. Error: 0.0328772 (C2 retained because nonzero)

age p = 0.8989061 (Not Significant)
sex p = 0.2626925 (Not Significant)
age*sex p = 0.0510144 (Significant)
age^2 p = 0.0293533 (Significant)
age^2*sex p = 0.8569521 (Not Significant)
etoh p = 0.8235931 (Not Significant)
whr p = 0.7997208 (Not Significant)
sbp p = 0.0818169 (Significant)
dbp p = 0.1277452 (Not Significant)
bmi p = 0.5773772 (Not Significant)
bdfat p = 0.0037137 (Significant)
ht p = 0.1874490 (Not Significant)
diab p = 0.0539345 (Significant)
disabled p = 1.0000000 (Not Significant)
educ p = 0.4039629 (Not Significant)
sbp*dbp p = 0.4364531 (Not Significant)
bmi*sex p = 0.5704980 (Not Significant)
locale p = 0.0003832 (Significant)

1225 pedigrees merged into 974 pedigree-household groups

The following covariates were removed from final models:age sex age^2*sex etoh whr dbp bmi ht disabled educ sbp*dbp bmi*sex

Proportion of Variance Due to All Final Covariates Is 0.0426959

Loglikelihoods and chi's are in sqmean/polygenic.logs.out
Best model is named housepoly and null0
Final models are named housepoly, house, poly, spor, nocovar
Initial sporadic and polygenic models are s0 and p0
Initial household and household polygenic models are h0 and hp0
Constrained covariate models are named no<covariate name>

BIBLIOGRAPHY

1. Williams CL, Hayman LL, Daniels SR, et al. Cardiovascular health in childhood: a statement for health professionals from the committee on atherosclerosis, hypertension, and obesity in young (AHOY) of the Council on Cardiovascular Disease in Youth, the American Heart Association. *Circulation.* 2002;106:143-160.
2. Strauss RS, Rodzilsky D, Burack G, Colin M. Psychosocial correlates of physical activity in healthy children. *Archives of Pediatric and Adolescent Medicine.* 2001;155:897-902.
3. Blair SN, Kohl HWr, Barlow CE, Paffenbarger RSJ, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *Journal of the American Medical Association.* 1995;273(13):1093-1098.
4. Hu G, Eriksson J, Barengo NC, et al. Occupational, commuting, and leisure-time physical activity in relation to total and cardiovascular mortality among Finnish subjects with type 2 diabetes. *Circulation.* 2004;110:666-673.
5. Richardson CR, Kriska AM, Lantz PM, Hayward RA. Physical activity and mortality across cardiovascular disease risk groups. *Medicine and Science in Sports and Exercise.* 2004;36:1923-1929.
6. Thompson PD, Buchner D, Pina IL, et al. Exercise and Physical Activity in the Prevention and Treatment of Atherosclerotic Cardiovascular Disease. *Circulation.* 2003;107:3109-3116.
7. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* Feb 7 2002;346(6):393-403.
8. Erikkson KF, F. L. Prevention of type 2 (non-insulin dependent) diabetes mellitus by diet and physical activity. *Diabetologia.* 1991;34:891-898.
9. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care.* Apr 1997;20(4):537-544.
10. Hagberg JM. Exercise, fitness, and hypertension. In: Shephard RJ, Stephens T, Sutton JR, eds. *Exercise, fitness, and health*. Champaign, IL: Human Kinetics; 1990:455-466.
11. Hagberg JM, Brown MD. Does exercise training play a role in the treatment of essential hypertension? *J Cardiovasc Risk.* Aug 1995;2(4):296-302.
12. Hu G, Barengo NC, Tuomilehto J, Lakka TA, Nissinen A, Jousliahti P. Relationship of physical activity and body mass index to the risk of hypertension: a prospective study in Finland. *Hypertension.* 2004;43:25-30.
13. Wing RR, Hill JO. Successful weight loss maintenance. *Annual Review of Nutrition.* 2001;21:323-341.

14. Breslow RA, Ballard-Barbash R, Munoz K, Graubard BI. Long-term recreational physical activity and breast cancer in the National Health and Nutrition Examination Survey I epidemiologic follow-up study. *Cancer Epidemiol Biomarkers Prev.* Jul 2001;10(7):805-808.

15. Slattery ML, Potter JD. Physical activity and colon cancer: confounding or interaction? *Medicine and Science in Sports and Exercise.* 2002;34:913-919.

16. USDHHS. *Leisure-time physical activity among adults: United States, 1997-98.*: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 2002.

17. Schoenborn CA, Adams PF, Barnes PM, Vickerie JL, Schiller JS. Health behaviors of adults: United States, 1999-2001. *Vital Health Stat 10.* Feb 2004(219):1-79.

18. USDHHS. *Surgeon General's report on physical activity and health.* Washington, D.C.: US Government Printing Office: Centers for Disease Control and Prevention; 1996.

19. USDHHS. Health Behaviors of Adults: United Statees, 1999-2001. *Vital Health Statistics.* 2004;10(219):39-53.

20. Chakravarthy MV, Booth FW. Inactivity and Inaction: *We Can't Afford Either. Archives of Pediatric and Adolescent Medicine.* 2003;157:731-732.

21. Aaron DJ, Storti KL, Robertson RJ, Kriska AM, LaPorte RE. Longitudinal study of the number and choice of leisure time physical activities from mid to late adolescence. *Archives of Pediatric and Adolescent Medicine.* 2002;156:1075-1080.

22. Dovey SM, Reeder AI, Chalmers DJ. Continuity and change in sporting and leisure time physical activities during adolescence. *British Journal of Sports Medicine.* 1998;32:53-57.

23. Telama R, Yang X. Decline of physical activity from youth to young adulthood in Finland. *Medicine and Science in Sports and Exercise.* 2000;32:1617-1622.

24. Telama R, Yang X, Laakso L, Viikari J. Physical activity in childhood and adolescence as predictor of physical activity in young adulthood. *Am J Prev Med.* Jul-Aug 1997;13(4):317-323.

25. Aarnio M. Leisure-Time Physical Activity in Late Adolescence: A Cohort Study of Stability, Correlates, and Familial Aggregation in Twin Boys and Girls. *Journal of Sports Science and Medicine.* 2003;2(Supplement 2):1-41.

26. van Mechelen W, Twisk JWR, Post GB, Snel J, Kemper HCG. Physical activity of young people: the Amsterdam Longitudinal Growth and Health Study. *Medicine and Science in Sports and Exercise.* 2000;32:1610-1616.

27. Kimm SY, Glynn NW, Kriska AM, et al. Decline in physical activity in black girls and white girls during adolescence. *N Engl J Med.* Sep 5 2002;347(10):709-715.

28. Welty TK, Lee ET, Yeh J, et al. Cardiovascular disease risk factors among American Indians. The Strong Heart Study. *Am J Epidemiol.* Aug 1 1995;142(3):269-287.

29. Fischer ID, Brown DR, Blanton CJ, Casper ML, Croft JB, Brownson RC. Physical activity patterns of Chippewa and Menominee Indians: the Inter-Tribal Heart Project. *Am J Prev Med.* Oct 1999;17(3):189-197.

30. Ainsworth BE, Irwin ML, Addy CL, Whitt MC, Stolarczyk LM. Moderate physical activity patterns of minority women: the Cross-Cultural Activity Participation Study. *J Womens Health Gend Based Med.* Jul-Aug 1999;8(6):805-813.

31. Stolarczyk LM, Gilliland SS, Lium DJ, et al. Knowledge, attitudes and behaviors related to physical activity among Native Americans with diabetes. *Ethn Dis.* Winter 1999;9(1):59-69.
32. Brownson RC, Eyler AA, King AC, Brown DR, Shyu YL, Sallis JF. Patterns and correlates of physical activity among US women 40 years and older. *Am J Public Health.* Feb 2000;90(2):264-270.
33. Fontvieille AM, Kriska A, Ravussin E. Decreased physical activity in Pima Indian compared with Caucasian children. *Int J Obes Relat Metab Disord.* Aug 1993;17(8):445-452.
34. Story M, Evans M, Fabsitz RR, Clay TE, Holy Rock B, Broussard B. The epidemic of obesity in American Indian communities and the need for childhood obesity-prevention programs. *Am J Clin Nutr.* Apr 1999;69(4 Suppl):747S-754S.
35. Lee ET, Howard BV, Savage PJ, et al. Diabetes and impaired glucose tolerance in three American Indian populations aged 45-74 years. The Strong Heart Study. *Diabetes Care.* May 1995;18(5):599-610.
36. NCHS. *Health, United States, 1993.* Washington, DC: US Govenrment Printing Office; 1994.
37. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *Jama.* Jun 16 2004;291(23):2847-2850.
38. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA.* Oct 9 2002;288(14):1728-1732.
39. Zephier E, Himes JH, Story M. Prevalence of overweight and obesity in American Indian School children and adolescents in the Aberdeen area: a population study. *Int J Obes Relat Metab Disord.* Mar 1999;23 Suppl 2:S28-30.
40. Flegal KM. The obesity epidemic in children and adults: current evidence and research issues. *Med Sci Sports Exerc.* Nov 1999;31(11 Suppl):S509-514.
41. Troiano RP, Flegal KM. Overweight prevalence among youth in the United States: why so many different numbers? *Int J Obes Relat Metab Disord.* Mar 1999;23 Suppl 2:S22-27.
42. Sallis JF, Prochaska JJ, Taylor WC. A review of correlates of physical activity of children and adolescents. *Medicine and Science in Sports and Exercise.* 2000;32(5):963-975.
43. Moore LL, Lombardi DA, White MJ, Campbell JL, Oliveria SA, Ellison RC. Influence of parents' physical activity on activity levels of young children. *Journal of Pediatrics.* 1991;118:215-219.
44. Anderssen N, Wold B. Parental and Peer Influences on Leisure-Time Physical Activity in Young Adolescents. *Research Quarterly for Exercise and Sport.* 1992;63(4):341-348.
45. Epstein LH, Paluch RA, Raynor HA. Sex Differences in Obese Children and Siblings in Family-based Obesity Treatment. *Obesity Research.* 2001;9(12):746-753.
46. Rossow I, Rise J. Concordance of parental and adolescent health behaviors. *Social Science & Medicine.* 1994;38:1299-1305.
47. Shropshire J, Carroll B. Family variables and children's physical activity: influence of parental exercise and socio-economic status. *Sport, Education, and Society.* 1997;1(95-116).

48. Bogaert N, Steinbeck KS, Baur LA, Brock K, Bermingham MA. Food, activity, and family-environmental vs. biochemical predictors of weight gain in children. *European Journal Clinical Nutrition.* 2003;57:1242-1249.
49. Duncan MJ, Woodfield LA, Al-Nakeeb Y, Nevill AM. The relationship between parents' and childrens' physical activity. *Journal of Sports Science.* 2002;20:35-36.
50. Fogelholm M, Nuutinen O, Pasanen M, Myohanen E, Saatela T. Parent-child relationship of physical activity patterns and obesity. *International Journal of Obesity.* 1999;23:1262-1268.
51. Freedson PS, Evenson S. Familial Aggregation in Physical Activity. *Research Quarterly for Exercise and Sport.* 1991;62(4):384-389.
52. Kalkanis LE, Goldfield GS, Paluch RA, Epstein LH. Parental Activity as a Determinant of Activity Level and Patterns of Activity in Obese Children. *Research Quarterly for Exercise and Sport.* 2001;72(3):202-209.
53. Perusse L, LeBlanc C, Bouchard C. Familial Resemblance in Lifestyle Components: Results from the Canada Fitness Survey. *Canadian Journal of Public Health.* 1988;79:201-205.
54. Perusse L, Tremblay A, LeBlanc C, Bouchard C. Genetic and Environmental Influences on Level of Habitual Physical Activity and Exercise Participation. *American Journal of Epidemiology.* 1989;129(5):1012-1022.
55. Raudsepp L, Viira R. Influence of parents' and siblings' physical activity on activity levels of adolescents. *European Journal of Physical Education.* 2000;5:169-178.
56. Sallis JF, Patterson TL, Buono MJ, Atkins CJ, Nader PR. Aggregation of Physical Activity Habits in Mexican-American and Anglo Families. *Journal of Behavioral Medicine.* 1988;11(1):31-41.
57. Simonen RL, Perusse L, Rankinen T, Rice T, Rao DC, Bouchard C. Familial aggregation of physical activity levels in the Quebec family study. *Medicine and Science in Sports and Exercise.* 2002;34(7):1137-1142.
58. Wagner A, Klein-Platat C, Arveiler D, Haan MC, Schlienger JL, Simon C. Parent-child physical activity relationships in 12-year old French students do not depend on family socioeconomic status. *Diabetes Metabolism.* 2004;30(359-366.).
59. Welk GJ, Wood K, Morss G. Parental Influences on Physical Activity in Children: An Exploration of Potential Mechanisms. *Pediatric Exercise Science.* 2003;15:19-33.
60. Godin G, Shephard RJ, Colantonio A. Children's Perception of Parental Exercise: Influence of Sex and Age. *Perceptual and Motor Skills.* 1986;62:511-516.
61. McGuire MT, Hannan PJ, Neumark-Sztainer D, Falkner-Cossrow NH, Story M. Parental Correlates of Physical Activity in a Racially Ethnically Diverse Adolescent Sample. *Journal of Adolescent Health.* 2002;30:253-261.
62. Trost SG, Sallis JF, Pate RR, Freedson PS, Taylor WC, Dowda M. Evaluating a Model of Parental Influence on Youth Physical Activity. *American Journal of Preventive Medicine.* 2003;25(4):277-282.
63. Aarnio M, Winter T, Kujala UM, Kaprio J. Familial Aggregation of Leisure-Time Physical Activity- a Three Generation Study. *International Journal of Sports Medicine.* 1997;18:549-556.
64. Kimiecik JC, Horn TS. Parental Beliefs and Children's Moderate-to-Vigorous Physical Activity. *Research Quarterly for Exercise and Sport.* 1998;69(2):163-175.

65. Lee ET, Cowan LD, Welty TK, et al. All-cause mortality and cardiovascular disease mortality in three American Indian populations, aged 45-74 years, 1984-1988. The Strong Heart Study. *Am J Epidemiol.* Jun 1 1998;147(11):995-1008.

66. North KE, Williams JT, Welty TK, et al. Evidence for joint action of genes on diabetes status and CVD risk factors in American Indians: the Strong Heart Family Study. *International Journal of Obesity.* 2003;27:491-497.

67. Coble JD, Rhodes RE. Physical activity and Native Americans: a review. *Am J Prev Med.* Jul 2006;31(1):36-46.

68. Caspersen CJ. Physical activity epidemiology: concepts, methods, and applications to exercise science. *Exerc Sport Sci Rev.* 1989;17:423-473.

69. Ravussin E, Bogardus C. A brief overview of human energy metabolism and it's relationship to essential obesity. *American Journal of Clinical Nutrition.* 1992;55(Supplement 1):242S-245S.

70. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Reports.* 1985;100(2):126-131.

71. Kriska AM. Ethnic and cultural issues in assessing physical activity. *Research Quarterly for Exercise and Sport.* 2000;71:47-53.

72. Kriska AM, Caspersen CJ. Introduction to the Collection of Physical Activity Questionnaires. *Medicine and Science in Sports and Exercise.* 1997;29 (Supplement):S5-S9.

73. Bailey RC, Olson J, Pepper SL, Porszasz J, Barstow TJ, Cooper DM. The level and tempo of children's physical activities: an observational study. *Med Sci Sports Exerc.* Jul 1995;27(7):1033-1041.

74. Papadopoulou SK, Papadopoulou SD, Zerva A, et al. Health status and socioeconomic factors as determinants of physical activity level in the elderly. *Med Sci Monit.* Feb 2003;9(2):CR79-83.

75. Whitt MC, DuBose KD, Ainsworth BE, Tudor-Locke C. Walking patterns in a sample of African American, Native American, and Caucasian women: the cross-cultural activity participation study. *Health Educ Behav.* Aug 2004;31(4 Suppl):45S-56S.

76. Crespo CJ, Smit E, Andersen RE, Carter-Pokras O, Ainsworth BE. Race/Ethnicity, Social Class and Their Relation to Physical Inactivity During Leisure Time: Results from the Third National Health and Nutrition Examination Survey, 1988-1994. *American Journal of Preventive Medicine.* 2000;18(1):46-53.

77. Meijer GA, Westerterp KR, Verhoeven FM, Koper HB, ten Hoor F. Methods to assess physical activity with special reference to motion sensors and accelerometers. *IEEE Trans Biomed Eng.* Mar 1991;38(3):221-229.

78. Trost SG, Saunders R, Ward DS. Determinants of physical activity in middle school children. *Am J Health Behav.* Mar-Apr 2002;26(2):95-102.

79. Eston RG, Rowlands AV, Ingledew DK. Validity of heart rate, pedometry, and accelerometry for predicting the energy cost of children's activities. *J Appl Physiol.* Jan 1998;84(1):362-371.

80. Rodriguez G, Beghin L, Michaud L, Moreno LA, Turck D, Gottrand F. Comparison of the TriTrac-R3D accelerometer and a self-report activity diary with heart-rate monitoring for the assessment of energy expenditure in children. *Br J Nutr.* Jun 2002;87(6):623-631.

81. Leenders N, Sherman WM, Nagaraja HN. Comparisons of four methods of estimating physical activity in adult women. *Med Sci Sports Exerc.* Jul 2000;32(7):1320-1326.

82. Le Masurier GC, Tudor-Locke C. Comparison of pedometer and accelerometer accuracy under controlled conditions. *Med Sci Sports Exerc.* May 2003;35(5):867-871.

83. Campbell KL, Crocker PR, McKenzie DC. Field evaluation of energy expenditure in women using Tritrac accelerometers. *Med Sci Sports Exerc.* Oct 2002;34(10):1667-1674.

84. Kochersberger G, McConnell E, Kuchibhatla MN, Pieper C. The reliability, validity, and stability of a measure of physical activity in the elderly. *Arch Phys Med Rehabil.* Aug 1996;77(8):793-795.

85. Lemmer JT, Ivey FM, Ryan AS, et al. Effect of strength training on resting metabolic rate and physical activity: age and gender comparisons. *Med Sci Sports Exerc.* Apr 2001;33(4):532-541.

86. Masse LC, Fulton JE, Watson KL, et al. Detecting bouts of physical activity in a field setting. *Res Q Exerc Sport.* Sep 1999;70(3):212-219.

87. Matthews CE, Ainsworth BE, Hanby C, et al. Development and testing of a short physical activity recall questionnaire. *Med Sci Sports Exerc.* Jun 2005;37(6):986-994.

88. Matthews CE, Freedson PS. Field trial of a three-dimensional activity monitor: comparison with self report. *Med Sci Sports Exerc.* Jul 1995;27(7):1071-1078.

89. Strath SJ, Bassett DR, Jr., Ham SA, Swartz AM. Assessment of physical activity by telephone interview versus objective monitoring. *Med Sci Sports Exerc.* Dec 2003;35(12):2112-2118.

90. Matthews CE, Freedson PS, Hebert JR, Stanek EJ, 3rd, Merriam PA, Ockene IS. Comparing physical activity assessment methods in the Seasonal Variation of Blood Cholesterol Study. *Med Sci Sports Exerc.* May 2000;32(5):976-984.

91. Bassett DR, Jr., Ainsworth BE, Leggett SR, et al. Accuracy of five electronic pedometers for measuring distance walked. *Med Sci Sports Exerc.* Aug 1996;28(8):1071-1077.

92. Crouter SE, Schneider PL, Karabulut M, Bassett DR, Jr. Validity of 10 electronic pedometers for measuring steps, distance, and energy cost. *Med Sci Sports Exerc.* Aug 2003;35(8):1455-1460.

93. Schneider PL, Crouter SE, Lukajic O, Bassett DR, Jr. Accuracy and reliability of 10 pedometers for measuring steps over a 400-m walk. *Med Sci Sports Exerc.* Oct 2003;35(10):1779-1784.

94. Welk GJ, Differding JA, Thompson RW, Blair SN, Dziura J, Hart P. The utility of the Digi-walker step counter to assess daily physical activity patterns. *Med Sci Sports Exerc.* Sep 2000;32(9 Suppl):S481-488.

95. Singh PN, Fraser GE, Knutsen SF, Lindsted KD, Bennett HW. Validity of a physical activity questionnaire among African-American Seventh-day Adventists. *Med Sci Sports Exerc.* Mar 2001;33(3):468-475.

96. Bassett DR, Jr., Cureton AL, Ainsworth BE. Measurement of daily walking distance-questionnaire versus pedometer. *Med Sci Sports Exerc.* May 2000;32(5):1018-1023.

97. Motl RW, McAuley E, Snook EM, Scott JA. Accuracy of two electronic pedometers for measuring steps taken under controlled conditions among ambulatory individuals with multiple sclerosis. *Mult Scler.* Jun 2005;11(3):343-345.

98. Kilanowski CK, Consalvi AR, Epstein LH. Validation of an electronic pedometer for measurement of physical activity in children. *Pediatric Exercise Science.* 1999;11:63-68.

99. Bassett DR, Jr., Ainsworth BE, Swartz AM, Strath SJ, O'Brien WL, King GA. Validity of four motion sensors in measuring moderate intensity physical activity. *Med Sci Sports Exerc.* Sep 2000;32(9 Suppl):S471-480.

100. Leenders NY, Sherman WM, Nagaraja HN, Kien CL. Evaluation of methods to assess physical activity in free-living conditions. *Med Sci Sports Exerc.* Jul 2001;33(7):1233-1240.

101. Tudor-Locke C, Ainsworth BE, Thompson RW, Matthews CE. Comparison of pedometer and accelerometer measures of free-living physical activity. *Med Sci Sports Exerc.* Dec 2002;34(12):2045-2051.

102. Kashiwazaki H, Inaoka T, Suzuki T, Kondo Y. Correlations of pedometer readings with energy expenditure in workers during free-living daily activities. *Eur J Appl Physiol Occup Physiol.* 1986;54(6):585-590.

103. 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.* Sep 2000;32(9 Suppl):S442-449.

104. *A dictionary of epidemiology.* 4th ed. New York: Oxford University Press; 2001.

105. Caspersen CJ, Merritt RK, Stephens T. International activity patterns: a methodological perspective. In: Dishman RK, ed. *Advances in Exercise Adherence*. Champaign, IL: Human Kinetics; 1994:73-110.

106. Barnes PM, Schoenborn CA. Physical activity among adults: United States, 2000. Advance data from vital and health statistics; no.333.: National Center for Health Statistics; 2003.

107. Kimm SY, Glynn NW, Obarzanek E, et al. Relation between the changes in physical activity and body-mass index during adolescence: a multicentre longitudinal study. *Lancet.* Jul 23-29 2005;366(9482):301-307.

108. Shepherd EF, Toloza E, McClung CD, Schmalzried TP. Step activity monitor: increased accuracy in quantifying ambulatory activity. *J Orthop Res.* Sep 1999;17(5):703-708.

109. Swartz AM, Bassett DR, Jr., Moore JB, Thompson DL, Strath SJ. Effects of body mass index on the accuracy of an electronic pedometer. *Int J Sports Med.* Nov 2003;24(8):588-592.

110. Elsenbaumer KM, Tudor-Locke C. Accuracy of pedometer in adults stratified by body mass index category. *Med Sci Sports Exerc.* 2005 2003;35:S282.

111. Crouter SE, Schneider PL, Bassett DR, Jr. Spring-levered versus piezo-electric pedometer accuracy in overweight and obese adults. *Med Sci Sports Exerc.* Oct 2005;37(10):1673-1679.

112. Hoodless DJ, Stainer K, Savic N, Batin P, Hawkins M, Cowley AJ. Reduced customary activity in chronic heart failure: assessment with a new shoe-mounted pedometer. *Int J Cardiol.* Jan 1994;43(1):39-42.

113. Macko RF, Haeuber E, Shaughnessy M, et al. Microprocessor-based ambulatory activity monitoring in stroke patients. *Med Sci Sports Exerc.* Mar 2002;34(3):394-399.

114. Cyarto EV, Myers AM, Tudor-Locke C. Pedometer accuracy in nursing home and community-dwelling older adults. *Med Sci Sports Exerc.* Feb 2004;36(2):205-209.

115. Storti KL, Pettee KK, Brach JS, Richardson CR, Brown VL, Kriska AM. Accuracy of three commonly used objective activity monitors in community dwelling older adults. *Med Sci Sports Exerc.* 2005;37:S1116 (Abstract).

116. *The American Heritage Stedman's Medical Dictionary*. 2nd ed: Houghton Mifflin Company; 2004.
117. Daniels PR, Kardia SL, Hanis CL, et al. Familial aggregation of hypertension treatment and control in the Genetic Epidemiology Network of Arteriopathy (GENOA) study. *Am J Med.* May 15 2004;116(10):676-681.
118. Williams MA, Qiu C, Dempsey JC, Luthy DA. Familial aggregation of type 2 diabetes and chronic hypertension in women with gestational diabetes mellitus. *J Reprod Med.* Dec 2003;48(12):955-962.
119. Lee KE, Klein BE, Klein R. Familial aggregation of components of the multiple metabolic syndrome in the Framingham Heart and Offspring Cohorts: Genetic Analysis Workshop Problem 1. *BMC Genet.* 2003;4 Suppl 1:S94.
120. Rice T, Despres JP, Perusse L, et al. Familial aggregation of blood lipid response to exercise training in the health, risk factors, exercise training, and genetics (HERITAGE) Family Study. *Circulation.* Apr 23 2002;105(16):1904-1908.
121. Peros E, Geroldi D, D'Angelo A, et al. Apolipoprotein(a) phenotypes are reliable biomarkers for familial aggregation of coronary heart disease. *Int J Mol Med.* Feb 2004;13(2):243-247.
122. Wagenknecht LE, Bowden DW, Carr JJ, Langefeld CD, Freedman BI, Rich SS. Familial aggregation of coronary artery calcium in families with type 2 diabetes. *Diabetes.* Apr 2001;50(4):861-866.
123. Berenson GS, Srinivasan SR, Hunter SM, et al. Risk factors in early life as predictors of adult heart disease: the Bogalusa Heart Study. *Am J Med Sci.* Sep 1989;298(3):141-151.
124. Bouchard C. Genetics of human obesity: recent results from linkage studies. *J Nutr.* Sep 1997;127(9):1887S-1890S.
125. Rice T, Perusse L, Bouchard C, Rao DC. Familial aggregation of body mass index and subcutaneous fat measures in the longitudinal Quebec family study. *Genet Epidemiol.* 1999;16(3):316-334.
126. Simonen RL, Rankinen T, Perusse L, et al. Genome-Wide Linkage Scan for Physical Activity Levels in the Quebec Family Study. *Medicine and Science in Sports and Exercise.* 2003;35(8):1355-1359.
127. Welsman JR, Armstrong N. Physical activity patterns of 5 to 7-year-old children and their mothers. *European Journal of Physical Education.* 1998;3:145-155.
128. Sallis JF, Prochaska JJ, Taylor WC, Hill JO, Geraci JC. Correlates of Physical Activity in a National Sample of Girls and Boys in Grades 4 Through 12. *Health Psychology.* 1999;18(4):410-415.
129. Mitchell BD, Rainwater DL, Hsueh WC, Kennedy AJ, Stern MP, MacCluer JW. Familial Aggregation of Nutrient Intake and Physical Activity: Results from the San Antonio Family Heart Study. *Annals of Epidemiology.* 2003;13:128-135.
130. Aaron DJ, Kriska AM, Dearwater SR, Cauley JA, Metz KF, LaPorte RE. Reproducibility and validity of an epidemiologic questionnaire to assess past year physical activity in adolescents. *Am J Epidemiol.* Jul 15 1995;142(2):191-201.
131. Ramakrishnan V, Goldberg J, Henderson WG, et al. Elementary methods for the analysis of dichotomous outcomes in unselected samples of twins. *Genet Epidemiol.* 1992;9(4):273-287.

132. Tudor-Locke C, Burkett L, Reis JP, Ainsworth BE, Macera CA, Wilson DK. How many days of pedometer monitoring predict weekly physical activity in adults? *Prev Med.* Mar 2005;40(3):293-298.

133. Khoury MJ, Beaty TH, Cohen BH. *Fundamentals of Genetic Epidemiology.* Vol 22. New York: Oxford University Press; 1993.

134. *Sequential oligogenic linkage analysis routines. SOLAR*
[computer program]. Version Version 1.4.1; 1999.

135. Tudor-Locke CE, Myers AM. Methodological considerations for researchers and practitioners using pedometers to measure physical (ambulatory) activity. *Res Q Exerc Sport.* Mar 2001;72(1):1-12.

136. 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.* Feb 1 1995;273(5):402-407.

137. Bennett GG, Wolin KY, Puleo E, Emmons KM. Pedometer-determined physical activity among multiethnic low-income housing residents. *Med Sci Sports Exerc.* Apr 2006;38(4):768-773.

138. Wilde BE, Corbin CB, LeMasurier GC. Free-Living Pedometer Step Counts of High School Students. *Pediatric Exercise Science.* 2004;16:44-53.

139. Sequeira MM, Rickenbach M, Wietlisbach V, Tullen B, Schutz Y. Physical activity assessment using a pedometer and its comparison with a questionnaire in a large population survey. *Am J Epidemiol.* Nov 1 1995;142(9):989-999.

140. Tudor-Locke C, Bassett DR, Jr. How many steps/day are enough? Preliminary pedometer indices for public health. *Sports Med.* 2004;34(1):1-8.

141. Tudor-Locke C, Ham SA, Macera CA, et al. Descriptive epidemiology of pedometer-determined physical activity. *Med Sci Sports Exerc.* Sep 2004;36(9):1567-1573.

142. Sternfeld B, Ainsworth BE, Quesenberry CP. Physical activity patterns in a diverse population of women. *Prev Med.* Mar 1999;28(3):313-323.

143. Fuemmeler B, Anderson C, Masse L. Gender differences in familial aggregation of objectively measured physical activity. *Med Sci Sports Exerc.* 2006;38(Suppl 5):S23.

144. Moran A, Jacobs DR, Jr., Steinberger J, et al. Insulin resistance during puberty: results from clamp studies in 357 children. *Diabetes.* Oct 1999;48(10):2039-2044.

145. Sinaiko A. Measurement of blood pressure in children. *Am J Hypertens.* Sep 2001;14(9 Pt 1):976-977.

146. Bao W, Srinivasan SR, Wattigney WA, Berenson GS. Persistence of multiple cardiovascular risk clustering related to syndrome X from childhood to young adulthood. The Bogalusa Heart Study. *Arch Intern Med.* Aug 22 1994;154(16):1842-1847.

147. Fagot-Campagna A, Pettitt DJ, Engelgau MM, et al. Type 2 diabetes among North American children and adolescents: an epidemiologic review and a public health perspective. *J Pediatr.* May 2000;136(5):664-672.

148. Caspersen CJ, Pereira MA, Curran KM. Changes in physical activity patterns in the United States, by sex and cross-sectional age. *Med Sci Sports Exerc.* Sep 2000;32(9):1601-1609.

149. Pratt M, Macera CA, Blanton C. Levels of physical activity and inactivity in children and adults in the United States: current evidence and research issues. *Med Sci Sports Exerc.* Nov 1999;31(11 Suppl):S526-533.

150. Bouchard C, Malina RM, Perusse L. *Genetics of fitness and physical performance.* Champaign, IL: Human Kinetics; 1997.