PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN POPULATIONS WITH IMPAIRED GLUCOSE METABOLISM AND TYPE 2 DIABETES MELLITUS

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ABSTRACT

INTRODUCTION: The high physical and economic burden of type 2 diabetes mellitus is an important public health concern. The impact of various intensities of physical activity (PA) and sedentary behavior on the development of type 2 diabetes is not well understood. Additionally, more insight into how measurement methodologies for PA and sedentary behavior affect the values of activity-related outcome variables is needed.

METHODS: PA and sedentary behavior levels were assessed as part of a multi-center clinic trial of youth with type 2 diabetes from 15 U.S. centers; the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study. Agreement between the results of a subjective and objective measure of PA and sedentary behavior were examined. Also, accelerometer processing algorithms were examined, using data on adults in the National Health Examination and Nutrition Survey (NHANES) 2005-06, to determine how changing the definition of accelerometer non-wear impacts on important PA outcome variables. PA and sedentary behavior levels from accelerometers were also described in 1609 adults with impaired glucose tolerance or type 2 diabetes, in the multi-center Diabetes Prevention Program Outcomes Study (DPPOS). These results were compared to similarly assessed activity data for a nationally representative sample of adults.

RESULTS: In TODAY youth, agreement was low between the Three Day Physical Activity Recall (3DPAR) questionnaire and accelerometer results; suggesting that the 3DPAR may not provide an accurate measure of time spent in PA or sedentary behavior in overweight/obese youth with type 2 diabetes. For NHANES adults, changing the definition of accelerometer non-wear time resulted in clinically significant differences in estimates of time spent sedentary, especially in older individuals. Compared to a nationally representative sample of adults, the DPPOS participants performed more moderate-vigorous intensity (MV) PA, but not more light intensity PA. These results likely reflect the effects of a successful lifestyle intervention on MVPA.

PUBLIC HEALTH SIGNIFICANCE: The current effort advances the understanding of PA and sedentary behavior assessment methods in populations with impaired glucose tolerance and type 2 diabetes and provides estimates for the average amount of time individuals in these populations spend physically active and sedentary.

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> "We plan our lives according to a dream that came to us in our childhood, and we find that life alters our plans. And yet, at the end, from a rare height, we also see that our dream was our fate. It's just that providence had other ideas as to how we would get there. Destiny plans a different route, or turns the dream around, as if it were a riddle, and fulfills the dream in ways we couldn't have expected."
>
> - Ben Okri

Earning my PhD was always my childhood dream. I am eternally grateful that the route was at times more challenging and definitely more remarkable than the "expected" route would have been.

I would like to thank my family for their constant support and unwavering faith.

I would also like to thank my advisor, Dr. Andrea Kriska, and my committee members for their encouragement and guidance.

1.0 INTRODUCTION

1.1 DIABETES RISK AND PHYSICAL ACTIVITY

Diabetes is the most common disease involving impairment of glucose metabolism. Type 2 diabetes is a sub-classification of diabetes that typically results from insulin resistance and/or β cell dysfunction and is characterized by poor glucose regulation that often does not require insulin therapy.[1] Levels of blood glucose diagnostic of diabetes are 126 mg/dl or greater after fasting at least 8 hours and 200 mg/dl or greater 2 hours after a 75 gram glucose solution is administered (post-load test). A common precursor of type 2 diabetes, impaired glucose tolerance, is a chronic state of glucose metabolism dysfunction marked by blood glucose levels that are above normal, but lower than those diagnostic of type 2 diabetes.[2]

Currently, the World Health Organization (WHO) estimates that 90% of the 346 million diabetic individuals worldwide have type 2 diabetes.[3] This represents an increase in the prevalence of type 2 diabetes of over 50% during the past seventeen years.[4,5] It is projected that as many as 380 million people around the globe will have type 2 diabetes by 2025 and another 418 million people will have impaired glucose tolerance.[6,7] In 2010 about 8.3% of adults in the United States had diabetes, but the prevalence rate is expected to more than triple by 2050.[8] Rates among children and adolescents (< 20 years of age) in the United States are expected to increase by 178 percent by 2050 (from .27 per 1,000 to .75 per 1,000).[9]

The most common complications of diabetes include macrovasular complications related to cardiovascular disease (CVD), such as angina, myocardial infarction, stroke, peripheral artery disease, and congestive heart failure.[7] CVD is the leading cause of death among patients with type 2 diabetes and accounts for nearly 50% of all deaths among individuals with diabetes. Other common complications of diabetes are blindness, renal failure, and lower limb amputations;[7,10] all of which are caused by microvascular complications that include nephropathy, retinopathy, neuropathy, and small vessel vasculopathy. It has been suggested that individuals with diabetes are 1.80 (95% CI 1.71, 1.90) times more likely to die of any cause and 2.32 (95% CI 2.11, 2.56) times more likely to die of vascular causes when compared to individuals without diabetes.[11] Additionally, the economic costs of diabetes in the United States increased over 75% between 1997 and 2007 and in 2010 cost projections indicate that 12% of all global health expenditures were put toward diabetes.[12-14] The cost of treating diabetes, worldwide, is expected to increase over the coming decades, as the number of diagnosed cases increases.

The development of type 2 diabetes usually takes place over a period of years and is thought to be the product of a combination of personal risk factors that involve both inherited susceptibility and environmental/lifestyle related factors. The primary risk factors for the development of type 2 diabetes include impaired glucose tolerance, physical inactivity, overweight/obesity, older age, race/ethnicity and genetics, and previous gestational diabetes.[15] Some risk factors for type 2 diabetes, such as age, race/ethnicity, and genetics, are unavoidable. However, other risk factors such as overweight/obesity and physical inactivity are modifiable and can therefore be targeted in prevention and intervention efforts to reduce the risk of developing diabetes, slow down the disease progression, and/or reduce risk for complications in patients with diabetes.[15]

Overweight/obesity and physical inactivity are often referred to as lifestyle factors because they often result from personal choices related to diet and participation in activities that require lower energy expenditure. The results of several clinical trials aimed at reducing or delaying incident type 2 diabetes showed that lifestyle changes involving improvements in diet and physical activity were able to significantly improve measures of body composition and decrease incidence of type 2 diabetes in high risk individuals.[16-19] In particular the results of the Diabetes Prevention Program (DPP) showed that incident diabetes was reduced by 58% in the lifestyle intervention group compared to placebo, over an average follow-up of 3.2 years in adults that were at high risk for developing the disease. [16] Additionally, lifestyle interventions have been shown to improve control of blood glucose levels in people with type 2 diabetes and reduce the incidence of complications.[20-22]

Most lifestyle interventions for type 2 diabetes incorporate dietary modification with increases in moderate-vigorous intensity physical activity that are aimed at reducing measures of body composition.[23,24] Currently, there is evidence that increasing physical activity is related to reductions in diabetes development both through weight loss[25] and independent of weight loss.[26,27] First, there is biological evidence that physical activity can improve insulin uptake, even when there is a dysfunction in the signaling pathway related to insulin induced uptake.[28-31] Additionally, prolonged periods of inactivity may influence diabetes development by affecting the body's ability to regulate the enzyme, lipoprotein lipase, which is involved in the hydrolysis of triglycerides.[32,33] Also, inactivity may affect diabetes development through involvement in the regulation of β cell function.[34-37]

Supporting this, is evidence from clinical trials and epidemiologic studies for an independent effect of physical activity on diabetes development. More specifically, analysis from the DPP showed that individuals who reported meeting their exercise goal (150 minutes/week of moderate-vigorous activity) at year one, but did not report meeting their weight loss or fat goals at year one still had a 46% reduction in risk of developing diabetes during the remainder of the 3.2 year follow-up when compared to individuals who reported meeting none of the goals.[38] Also, the Da Qing clinical trial tested the individual effects of diet and exercise by creating separate intervention arms for exercise and dietary modification. The results showed that over a six year follow-up in individuals at high risk for the disease, there was a 46% risk reduction for diabetes in the exercise group when compared to the placebo group.[26] Finally, an analysis of eight previously published longitudinal studies concluded that there was evidence for a joint effect and for independent effects of both obesity and inactivity on incident type 2 diabetes.[39] Therefore, the results indicated that improvements to physical activity could reduce the risk associated with activity alone, as well as, some of the joint risk associated with both inactivity and obesity.

So far, much of the focus on the relationship between physical activity and diabetes has focused on moderate to vigorous intensity physical activities, such as brisk walking or jogging. However, in addition to the effects of moderate and vigorous activity, there is growing evidence that increasing light intensity activity, such as slow walking or light housework, and reducing sedentary behavior, such as sitting watching television, may exert an added benefit toward diabetes prevention. [40-44] In relation to this, the results of several studies have suggested that there is an effect of sedentary behavior on outcomes related to type 2 diabetes that is independent of the effects of moderate-vigorous activity.[45-48] For example, a study of accelerometer data from NHANES 2003-06 reported that, in adults, the amount of time spent sedentary (controlling for time spent in moderate-vigorous activity) was positively associated with diabetes related outcomes including insulin, and markers of β cell function and insulin sensitivity.[48]

It is also important to consider the fact that based on current health surveys, adults in the United States and elsewhere, spend about two-thirds of their waking hours in sedentary pursuits.[49,50] Accelerometer data collected on youth in the United States and Europe indicate that youth aged 6-11, 12-15 and 16-19 years spent about 6.44, 7.39, and 7.89 hours/day (on average) in sedentary pursuits, respectively.[51] Furthermore, reports of physical activity and sedentary behavior levels in the United States and Worldwide indicate that, in general, current populations are spending more of their time performing activities that require lower levels of energy expenditure than people did in the past. [52-54] As a result, there is an increasing need to consider the effects of activities from all parts of the physical activity spectrum (from light to vigorous intensity) on impaired glucose tolerance and type 2 diabetes.

1.2 MEASURING ACTIVITY

Most evidence regarding the effect of activity/inactivity on diabetes development has been collected using subjective questionnaires. This type of assessment is popular due to design flexibility and low participant/ investigator burden.[55,56] Furthermore, many questionnaires have been shown to be valid and reliable measures of habitual moderate-vigorous intensity physical activity and specific domains of sedentary behaviors, such as si tting watching television.[57,58] However, self-report has been shown to be less valid and reliable for measuring unplanned activities, light intensity activities, and total sedentary behavior.[55,57] Most questionnaires do not or cannot attempt to collect this information.

Compared to subjective measures, an objective measure of physical activity and sedentary behavior, the accelerometer, has been shown to be more accurate and reliable for determining all levels of total physical activity (which includes light, moderate, and vigorous activity) and sedentary behavior. More specifically, accelerometers are generally better at capturing unplanned activities and can provide a more accurate picture of behaviors that occur at the lower intensity end of the physical activity spectrum.[59] Also, objective measures are less influenced by bias because they are not subject to personal opinions and perceptions, or other types of reporting bias that can affect the results of subjective measures.[60] Therefore, a major advantage of accelerometry, is the ability to capture physical activity that takes place across the spectrum of intensity levels.

Originally, accelerometer derived physical activity data processing was focused on the reporting of moderate-vigorous intensity physical activity. Many of the methods currently used to process accelerometer data were developed and validated for the assessment of moderate-vigorous physical activity, specifically. Now that the research focus has expanded to include lower intensity activities, not all methods used in the processing and interpretation of physical activity from accelerometers have been shown to be equally valid for reporting sedentary behavior. [61-69] Some examples of this are monitor calibration and recording, identification of wear time, and number of days required to report "typical" behavior. Therefore, indicating that as we move forward with physical activity assessment that includes sedentary behavior, there is a need to reassess aspects of data processing, such as the determination of wear time, that have been previously validated for reporting physical activity, but not sedentary behavior.

To conclude, although type 2 diabetes rates are rising at an alarming pace in both the United States and World Wide, it is a highly preventable disease. The modification of lifestyle related factors including inactivity and obesity have been shown to greatly reduce the incidence of type 2 diabetes in a wide diversity of populations and to improve health outcomes for people with diagnosed diabetes. However, based on our current understanding of the importance of all intensities of activity to diabetes related outcomes, there is a need for capturing all components of activity, as well as, sedentary behavior. Therefore, additional studies are still needed to determine the levels of physical activity and sedentary behavior in populations with diabetes and/or impaired glucose tolerance and to determine if there are differences in activity and sedentary behavior between individuals with and without impaired glucose metabolism. As part of this effort, it will also be important to assure that measurement methods previously validated for physical activity are also shown to be accurate and reliable for measuring sedentary behaviors.

1.3 STUDY GOALS

The purpose of this effort is to characterize physical activity and sedentary behavior levels across a diverse range of individuals with type 2 diabetes and/or impaired glucose tolerance and to examine some of the aspects of measuring physical activity and sedentary behavior that could affect the values of activity-related outcome variables in the study populations. More specifically, this study will meet the following objectives:

1. Report physical activity and sedentary behavior levels in youth with type 2 diabetes using both a subjective and objective measure and determine the level of agreement between the results of the two measurement instruments, for this population.

Manuscript 1 will present estimates of baseline physical activity and sedentary behavior levels for youth aged 10-18 years, with newly diagnosed type 2 diabetes mellitus, that were enrolled in the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study. The TODAY trial was a multicenter clinical trial designed to evaluate the relative efficacy and safety of three treatments for type 2 diabetes in a demographically diverse cohort of youth.[70] Mean minutes per day of sedentary behavior, light intensity, and moderate-vigorous intensity physical activity from both a subjective recall questionnaire, the 3 Day Physical Activity Recall (3DPAR) and an objective measure (the ActiGraph AM7164 accelerometer) will be presented and compared. Relative and absolute comparisons of activity data from the 3DPAR and the accelerometer, using baseline results from the TODAY study cohort, will be made within gender categories. The effect of other variables, including age, race/ethnicity, and age/gender adjusted body mass index (BMIz-score), on the degree of reporting bias will also be considered. This will be part of a larger research effort, that goes beyond the scope of this dissertation by comparing physical activity and sedentary behavior levels of the TODAY youth to similar age/ gender youth without reported diabetes in NHANES 2005-06.

2. Determine and report differences in the identification of valid wear time and mean daily time in various physical activity intensities and sedentary behavior resulting from minor changes in the definition of non-wear used in accelerometer data processing in an adult population.

During the examination of the youth population outlined above a small coding error in the SAS programming was discovered, related to the identification of accelerometer non-wear. Non-wear is defined as time when the monitor is recording, but is not actually being worn.

Identifying non-wear for accelerometer data is important because otherwise time when the monitor was not worn can be confused with inactivity.

Small changes to the code, which effectively changed the definition of non-wear, were found to be capable of causing larger than expected differences in the results of the analyses both in (a) the number of participants whose data was included in the final reporting of activity-related outcome variables and (b) in the actual reported values for time spent in different intensities of activity, and in sedentary behavior. As a result, prior to conducting the analysis of data for the adult population (outlined in aim 3), it was decided that an assessment of the effects of non-wear equations should be conducted in an adult population to determine how this may impact on the original second aim of this dissertation.

Therefore, analyses were designed to examine the effects of making small changes to the definition of non-wear used in accelerometer processing on the resulting assessments of physical activity and sedentary behavior. Activity-related outcomes, including average total counts per day, average counts per minute, and mean minutes per day of wear time, sedentary behavior, light intensity activity, and moderate-vigorous intensity activity, were reported from the results of three different data processing algorithms. All three algorithms utilized the same basic definition of non-wear; 60 consecutive minutes with zero accelerometer counts. However, each data processing algorithm utilized a different variation of the 60 minute definition. The most common variations were used, in order to assess how minor changes to the definition of non-wear affect differences in the reporting of activity and sedentary behavior for a given population. This effort utilized data from adults aged 20 years and older in the National Health and Nutrition Examination Survey (NHANES) 2005-06 data collection cycle. NHANES is a cross-sectional observational study of the United States population conducted by the National Center for Health and Statistics (NCHS) of the Centers for Disease Control (CDC). The NHANES dataset was chosen for this effort because it is a large, publically available data set with accelerometer data and provides a representative sample of the United States population provided that elements of the complex survey design are accounted for in the analyses. Examinations of the direct effects of the differences in classification of non-wear on the identification of valid minutes and valid days were conducted. Differences between the resulting values for activity variables produced by the three variations of the non-wear definition were compared, both in relative and absolute terms. Additionally, these differences were examined for the population as a whole as well as by age, gender, and body mass index (BMI) groups.

3. Report physical activity and sedentary behavior levels in adults with impaired glucose tolerance and type 2 diabetes using an objective measure of physical activity capable of capturing all intensity levels of physical activity and sedentary behavior and compare the results to a nationally representative sample of adults.

Cross-sectional physical activity and sedentary behavior levels for a cohort of adults with impaired glucose metabolism and type 2 diabetes mellitus will be presented in manuscript 3. The data for this effort is from the Diabetes Prevention Program Outcomes Study (DPPOS); a multicenter study conducted at sites throughout the United States. The DPPOS is a follow-up study of the original Diabetes Prevention Program (DPP) cohort. The DPPOS was designed to assess the long-term effects of interventions used in the DPP on the development of type 2 diabetes and its complications. More specifically the data for the analyses was collected as part of an ancillary study, within the DPPOS, to collect accelerometer data on DPPOS participants in an effort to better define the relationship between physical activity and type 2 diabetes.

In this effort accelerometers were used to objectively measure physical activity and sedentary behavior levels in the DPPOS cohort. Additionally, comparisons of activity and sedentary behavior levels between the DPPOS cohort and a representative sample of the US population, from the combined NHANES 2003-04 and 2005-06 data collection cycles, were performed to provide a context for the results from the DPPOS cohort. Comparisons to individuals in NHANES grouped by diabetes status were also included.

This research effort will help to characterize physical activity and sedentary behavior levels in populations with impaired glucose tolerance and type 2 diabetes mellitus by reporting objective activity data from accelerometers for two demographically diverse populations of both youth and adults. Additionally, comparisons to population weighted estimates of physical activity and sedentary behavior from NHANES will provide additional insight into how levels of physical activity and sedentary behavior differ between groups of individuals with and without diabetes. Finally, assessing the validity of measurement methods used to collect data on physical activity and sedentary behavior will help to guide future research efforts aimed at examining the associations between diabetes development and physical activity of all intensities, as well as, sedentary behavior.

2.0 GLUCOSE METABOLISM & TYPE 2 DIABETES

2.1 OVERVIEW OF GLUCOSE METABOLISM

Glucose is an important biomolecule that is utilized by the cells of the body as a major source of energy and as a metabolic intermediary in the production of starches, cellulose, and glycogen.[71] Biomolecules are defined as chemical molecules that occur naturally in the body. All biomolecules can be classified according to four general categories: Carbohydrates (sacchrarides), lipids (fats), proteins, and nucleic acids.[72] Glucose is considered to be the most commonly occurring carbohydrate and has a chemical structure of $C_6H_{12}O_6$.[73] Along with galactose and fructose, glucose is considered a "si mple carbohydrate" or monosaccharide because it represents the smallest possible unit of a saccharide.[72]

Glucose is taken into the human body through food consumption and then processed by the cells utilizing either anaerobic or aerobic respiration.[73] Normal glucose metabolism can follow several pathways.[74] Among these are glycolysis, which results in the release of energy, glycogenesis, which results in the storage of energy, glucogenolysis, which results in the conversion of stored energy into glucose and glucogeneogenisis, which results in the breakdown of simple organic compounds, such as amino acids, into glucose. After compounds are broken down into glucose they are then made available for glucose-dependent tissues such as the brain, muscles, and red blood cells.

Proper glucose metabolism requires a process of regulation to ensure a steady level of glucose within the body.[71] The hormone, insulin, is the primary regulator signal for glucose uptake in animals and therefore is a key component in the regulation process. Insulin first originates in the pancreatic β cells as proinsulin, and is created during proinsulin cleavage. Most insulin is metabolized by the liver. Insulin secretion occurs when a g lucose molecule is transferred into the pancreatic β cells. In normal glucose metabolism, insulin secretion will occur when there is any increase in the concentration of β cell glucose above the fasting level.[71] During this process the β cells will first release stored insulin. However, if the amount of glucose is large enough the β cells will increase production of new insulin. The magnitude of production will depend largely on the quantity of glucose. The inability of the β cells to secrete enough insulin is referred to as β cell dysfunction. Insufficient secretion by the β cells will cause a dysfunction in glucose metabolism that will ultimately result in higher blood glucose levels.

During times of non-fasting most glucose metabolism takes place in the peripheral insulin-sensitive tissues, such as the muscles and adipose tissue.[71] However, glucose metabolism during fasting takes place primarily in the non-insulin sensitive tissues like the brain.[74] This is due to a decrease in basal insulin levels in the peripheral insulin-sensitive tissue that results in a decreased uptake of glucose. The steady state of glucose essential to brain function is provided by the slow release of glucose by the liver (and the kidneys), at a rate of about 7-10 g/hour which is consistent with the amount required by the consuming tissue.[74] This hepatic metabolism involves the breakdown of other compounds to release glucose through the processes of glycogenolysis and gluconeogenesis. Glucose metabolism that does take place in the muscles and fat during fasting is anaerobic and utilizes lactic acid and free fatty acid in the processes of glycogenolysis and glycogeogenesis.

2.2 INSULIN RESISTANCE

Insulin resistance is a condition in which the normal response of insulin to glucose is decreased causing a dysfunction in glucose metabolism.[71] This will result in an increase in circulating blood glucose. Insulin resistance in the liver leads to reduced production and storage of glycogen. If there is little or no glycogen the cells will secrete more glucose leading to the over-secretion of glucose by the liver. Insulin resistance in the muscles and adipose tissue will reduce glucose uptake in these cells.[71] As with the liver, it will also cause a loss of stored energy. Insulin resistance in the adipose tissue can also affect the ability of the cells to uptake lipids. This will result in an increase of free fatty acids (triglycerides) into the blood stream. As the condition of insulin resistance worsens, the bodies need for insulin increases. Eventually, the pancreas will lack the ability to produce enough insulin to ensure that an adequate level of glucose metabolism is occurring. This often leads to a chronic state of glucose metabolism dysfunction.

Proper function of glucose metabolism in typically identified through direct testing of blood glucose levels.[75] Because normal blood glucose levels vary in relation to the pattern of glucose intake, different measures of normal blood glucose have been devised for tests conducted during fasting and non-fasting hours. Normal blood glucose levels during fasting are considered to be 65 mg/dl- 99 mg/dl.[75] Non-fasting levels are usually taken 2 hours after a 75 gram glucose solution is administered to a patient orally. The glucose solution is designed to be a controlled simulation of a meal. Normal blood glucose levels for this type of post-load test are considered to be 65 mg/dl -139 mg/dl.[75] Higher or lower levels are thought to indicate impairment in the metabolic process. Both low blood sugar levels (hypoglycemia) and high blood sugar levels (hyperglycemia) are typically considered to be indicators of an underlying condition that is responsible for the metabolic impairment. A more thorough evaluation of the definition of type 2 diabetes mellitus is provided in the following section.

2.3 TYPE 2 DIABETES MELLITUS

Worldwide, the most common condition involving an impairment of glucose metabolism is type 2 diabetes mellitus. In general, diabetes is a condition of chronic hyperglycemia that is caused by defects in insulin secretion, and/or insulin action. Type 2 diabetes is a sub-classification of the disease that typically results from insulin resistance and/or β-cell dysfunction. This classification of diabetes is marked by relative insulin deficiencies that often do not require insulin therapy initially.[1]

Table 2.1 Criteria for the diagnosis of diabetes mellitus (American Diabetes Association Criteria)

A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h plasma glucose ≥200mg/dl (11.1mmol/l) during an OGTT. The test should be performed as described by theWorld HealthOrganization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l).

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.
NGSP:National glycohemoglobin standardization program, DCCT: Diabetes control & complications trial,
OGGT: Oral glucose tolerance test

Type 2 diabetes is typically diagnosed through examination of blood glucose levels using one of three basic blood tests: fasting plasma glucose (FPG), 2-hour post-load plasma glucose (OGTT), or hemoglobin A1C (A1C). The current American Diabetes Association criteria for the diagnosis of diabetes mellitus can be found in Table 2.1.

Because β cell dysfunction and insulin resistance are typically progressive disorders, individuals with blood glucose levels above the normal range, but below the diagnostic level for diabetes are considered to be at high risk for future development of diabetes. Individuals in this category are considered to have impaired glucose tolerance and are often referred to as pre-diabetic.

A staggering increase in the number of diabetes cases has occurred since international attention was brought to the epidemic in the late 1980's.[4-6] Currently, the World Health Organization (WHO) estimates that 346 million people worldwide have diabetes with 90% of the estimated total being attributable to type 2 diabetes.[3] This represents an increase of more than 50% since 1995 when the number of estimated cases of type 2 diabetes worldwide was estimated to be 135 million.[4,5] Current projections now estimate that as many as 380 million people will have type 2 diabetes and another 418 million people will have impaired glucose tolerance by 2025.[6,7] Cost projections indicate that global spending on diabetes was 12% of all health expenditures in 2010 at a price of more than 376 billion dollars (US). This spending is expected to increase to 490 billion dollars (US) by 2030.[14]

Estimates based on data collected in 2010 indicate that about 8.3% of the total US population has diabetes.(CDC FACT SHEET). This is up from 6.3% in 2002 and 5.1% in the early 1990's when reported rates began to rise.[76,77] Approximately, 90-95% of diabetes cases among adults in the US are attributed to type 2 diabetes. The American Diabetes Association

(ADA) estimated that the economic cost of diabetes in 2007 was 174 billion dollars (US).[12] This represents a marked increase from economic cost analysis of diabetes expenditures for 1997 (98 billion US)[13] and 2002 (134 billion US).[78]

The development of type 2 diabetes usually takes place over a period of years and is thought to be the product of a combination of personal risk factors that involve both inherited susceptibility and environmental/lifestyle related factors. The primary risk factors for the development of type 2 diabetes included impaired fasting glucose, physical inactivity, overweight/obesity, age, race/ethnicity and genetics, and previous gestational diabetes. [15]Some risk factors for type 2 diabetes are unavoidable. However, other risk factors such as overweight/obesity and physical inactivity are considered to be modifiable and can therefore be targeted in prevention and intervention efforts to reduce the risk of developing diabetes, slow down the disease progression, and/or reduce risk for complications in patients with diabetes.[15]

Currently, there is strong evidence that weight reduction in overweight/obese individuals can reduce the risk of developing diabetes. Several clinical trials, including The Diabetes Prevention Program (DPP), have shown that even moderate weight loss of 5-10% of body weight can prevent or delay the onset of type 2 diabetes in individuals that are considered at high risk.[16-18,79,80] Additionally, studies of bariatric surgery have also shown a significant improvement in blood glucose levels following the substantial weight loss associated with bariatric surgical procedures.[81-83]

It is also likely that physical activity has a direct effect on diabetes development that is independent of weight loss. Evidence for the association between physical activity, sedentary behavior, and type 2 diabetes are presented in chapter 4.

Individuals that do develop diabetes are known to be at higher risk for certain complications. The most common complications of diabetes are macrovasular complications related to cardiovascular disease (CVD), such as angina, myocardial infarction, stroke, peripheral artery disease, and congestive heart failure.[7] The relative risk of developing cardiovascular disease has been shown to be twice as high in women, and more than 1.5 times as high in men with diabetes compared to those without diabetes.[84,85] Other common complications of diabetes are blindness, renal failure, and lower limb amputations all of which are caused by microvascular complications that include nephropathy, retinopathy, neuropathy, and small vessel vasculopathy.[7,10]

As a result of the many complications associated with diabetes, the mortality statistics for individuals with diabetes are somewhat different than the general population. CVD is still the leading cause of death among patients with type 2 diabetes. However, CVD death rates are higher in individuals with diabetes, accounting for more than 50% of all deaths.[76] It has been suggested that individuals with diabetes are 1.80 (95% CI 1.71, 1.90) times more likely to die of any cause and 2.32 (95% CI 2.11, 2.56) times more likely to die of vascular causes when compared to individuals without diabetes.[11] It has been estimated that middle-aged adults with diabetes have a reduction in life expectancy of between 5 and 10 years.[86]

3.0 MEASUREMENT OF PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN EPIDEMIOLOGICAL STUDIES

Physical activity is defined as any bodily movement that results in energy expenditure, including those that are planned and those that are unplanned.[87] For studies conducted in free living individuals, physical activity is typically identified as occurring in one of several domains: leisure, occupational, transportation, and activities of daily living.[88] Epidemiological studies that measure physical activity will attempt to capture information on physical activity that is performed in one or more of these domains.

In addition to domain, other important aspects of physical activity are duration, frequency and intensity. Duration refers to the length of time spent physically active within a single unit of time. In activity research, duration can be used to refer to the amount of time spent in any one continuous episode or bout of activity, or the amount of total time spent active during a longer time block, such as a day or week. Frequency refers to the amount of times that physical activities are performed in a recorded time frame. The recording time frame is an import aspect of physical activity measurement and should be long enough to capture an adequate representation of an individual's physical activity for a given period of time. The time period being represented can be longer than the recording time frame and should be determined a priori by the parameters of the disease outcome being examined. Finally, intensity of activity is a measure of how much physical effort is required to perform an activity.[60] Because intensity is a measure of physiological demand it is more directly related to energy expenditure than the frequency or duration of physical activity and therefore is often reported in metabolic equivalent units (METs). The metabolic equivalent is defined as the ratio of the metabolic rate during a given activity to a known metabolic rate; where 1 MET is equivalent to the resting metabolic rate (RMR).[89] It is possible to convert values in METs to energy expenditure.[90] However, this can be problematic due to the fact that assigned MET values for intensity of activity are based on population averages and may not be applicable for a given individual. Therefore, physical activity intensity is usually reported in METs per minute, METs per hour, or as a relative measure that is based on assigned MET values.[91] Table 3.1 illustrates the most commonly utilized MET-based intensity categorization scales for adults and children. Other scales, such as those based on an individual's maximum aerobic capacity (instead of age) have been proposed, but are not as widely used.[90,92]

Table 3.1 Activity Intensity Categories for Adults, Children and Adolescents

	Intensity category			
	Sedentary	Light	Moderate	Vigorous
Adults (age 18+) [91]	1-1.59 METs	1.6-2.99 METs	3-5.99 METs	≥6 METs
Children & Adolescents [93]	1-1.59 METs	1.6-3.99 METs	4-6.99 METs	≥7 METs

METs: Metabolic equivalent units

Most sedentary behaviors involve sitting or lying down, while light housework or slow walking would be consistent with light intensity activity. Brisk walking would be considered a moderate intensity activity and running would be equivalent to vigorous intensity activity.

In public health recommendations, physical inactivity is often used to refer to a broader pattern of behavior that is marked by low levels of physical activity and/or has an excess of time spent sitting, or sedentary. In epidemiological research, the term " physical inactivity" refers to a state in which body movement is minimized.[94] This would include sleeping, as well as, activities performed during waking hours that result in lower levels of energy expenditure. Physical inactivity that takes place during waking hours is typically referred to as sedentary behavior.[40] Understanding the roles of both physical activity and sedentary behavior in disease pathways requires methods that can accurately report low intensity activities in addition to moderate and high intensity activities. Therefore, intensity of activity can have important implications on which method of assessment is the most appropriate for a given research design. In general, measurement methods that do not adequately capture information on frequency, duration, and intensity will result in less precise or inaccurate assessments of both physical activity and sedentary behavior.

3.1 SUBJECTIVE MEASURES- SELF-REPORT

Measurement methods that can be affected by the opinions or perceptions of the participants, proxy reporters, interviewers, or investigators are called subjective measures.

Questionnaires, interviews, activity diaries, and direct observation are all, commonly used, subjective measures of physical activity.

Self-reported questionnaires are the most frequently used method of measuring physical activity and sedentary behavior in epidemiological studies.[55,95,96] The popularity of the questionnaire is due mainly to design flexibility and a low degree of burden for both the participants and the investigators.[55,56] Additionally, questionnaires have been shown to be a valid and reliable tool for measuring moderate-vigorous physical activity across a wide range of populations.[95] However, because questionnaires are dependent on self-report they can be influenced by response bias (participant opinions, perceptions, and issue of social desirability). Questionnaires that inquire about past activity may also be subject to recall bias. In general, problems with poor recall seem to be more of a problem in specific populations, such as children or older adults and therefore may have less of an effect on the general adult population.[97,98] Also, poor recall can have a differentially greater effect on less structured activity, which can result in a decreased ability of questionnaires to capture low intensity activities, which are more likely to be unstructured.[55,58,99]

Three important design elements of questionnaires are complexity, time frame, and activity type. The complexity of a questionnaire will be affected by the number of questions and the level of detail/length of questions. Questionnaires can vary in complexity from single item, global, questionnaires that attempt to provide a very basic understanding of physical activity to more complex quantitative questionnaires that attempt to provide a high degree of detail about activity. Although global questionnaires are very simple they can be used in a wide variety of situations where detailed information about activity is not needed. For example, global questionnaires have been used to provide relative assessments of activity by asking participants how active they are compared to others their age and sex or by asking participants how much they watched television during a given time period (the past day, week, month, etc.) and then ranking the population or assigning them to ordinal categories based on their reported activity.[41,100,101]

Global questionnaires can be very useful when activity variables are not the main variables of interest and may be useful when the goal is to control for the confounding influence of physical activity in other predictor/disease relationships.[88] Therefore, global questionnaires are often incorporated within health surveillance systems. Examples of this are the physical activity questionnaires used in the BRFSS and YBRFSS (Behavioral Risk Factor Surveillance Systems for adults and youth), the G-PAQ used by the WHO (World Health Organization) health surveillance system, and the NHANES (National Health and Nutrition Examination Survey) physical activity questionnaire. Finally, global questionnaires can be useful for telephone interviews and other situations where a more complex survey may not be feasible.[102,103] Despite their simplicity global questionnaires have been shown to be a valid and reliable method of assessing physical activity and sedentary behavior.[57,101,104-106] However, fewer questions can lead to a greater incident of misclassification, and lack of detail regarding physical activity may limit the scope of the analysis and results.[102,106]

More complex questionnaires provide a greater level of detail about the physical activity and sedentary behavior of individuals. This enables researchers to explore questions that require information on intensity levels, frequency, and duration over longer time frames. Therefore, complex questionnaires can provide a better quantitative assessment of activity. Complex recall questionnaires that ask participants to report past activity and include details about intensity, duration, and frequency for a given period of time are often referred to as quantitative activity histories.[55,107-109] Quantitative histories can be used to examine patterns of activity over a long period of time. This is useful in epidemiological research because regular patterns of physical activity and sedentary behavior assessed by questionnaire have been associated with many chronic disease outcomes, such as type 2 diabetes and cardiovascular diseases.[45,110-112] Additionally, complex questionnaires are useful for their ability to provide details on the types of activities performed, and the context in which activities may have been performed.[55,56,113-116]

The recording time frame utilized in a complex questionnaire should be long enough to capture an adequate representation of an individual's physical activity and/or sedentary behavior for a given period of time. The time period being represented can be longer than the recording time frame and should be determined a priori by the parameters of the disease outcome being examined. Because many chronic diseases have been linked to long term patterns of physical activity the goal of many physical activity questionnaires in chronic disease epidemiology studies is to assess "usual" activity. Therefore, the recording time frame will typically be shorter than the recording period that it represents. This is important because shortening the time frames of assessment can add bias to estimates of "usual" physical activity if external factors such as seasonal change and illness are not considered in the research design.[55] Therefore, obtaining more precise estimates of physical activity and sedentary behavior may require the inclusion of questions that can assess the potential for confounding factors or that report activity over both shorter and longer periods of time.

However, some research questions only require an assessment of physical activity and sedentary behavior over a shorter period of time such as a day, week, or month. In these cases, it may be possible to utilize a question with a recording time frame that is closer or even identical to the time period of interest. Examples of this would be hypotheses involving the short-term effects of physical activity and/or sedentary behavior on biomarkers, such as cholesterol, insulin, or inflammation markers.

Activity type is often used to refer to categories of activity based on either domain or intensity of activity. In studies that are designed to assess the quantity of physical activity performed, it is necessary to capture an accurate assessment of all types of activities that elicit the greatest energy expenditure in the target population. In heterogeneous populations, like the United States population, it is usually necessary to capture information from more than one domain. Assessing activity in more than one domain can also be important when comparing two different populations. One example of this was a study of the relationship between serum insulin levels and physical activity in two ethnically and culturally disparate populations; the Pima Indians in Arizona and the occupants of Mauritius, an island nation in the Southwest Indian Ocean.[117] Both leisure and occupational activity were essential in this comparison because the Pima accumulated most of their physical activity from leisure time activities while the inhabitants of Maritius accumulate over 90% of their physical activity from occupational activity. If activity had been assessed in only the leisure or the occupational category alone, the results of the study may not have revealed the true relationships between activity and serum insulin levels in both populations. On the other hand, in a population that is very homogeneous for a specific domain on activity (work, leisure, etc.), it may not be necessary to capture activity in that domain if the goal of the analysis is to provide a valid ranking of individuals, based on their physical activity levels.

Intensity level provides another means by which to categorize different types of activities. While some questionnaires have shown to be valid for measuring moderate-vigorous activity and planned sedentary behavior (such as watching TV, work sitting, and leisure screen time) they are less accurate at providing assessments of light intensity activities and unplanned sedentary behavior.[55,57,58] Although many surveys do not attempt to provide quantitative assessments of light intensity activity and unplanned sedentary behavior, some questionnaires have attempted to provide this information. Based on the current literature, it is not clear that questionnaires can provide valid estimates for the quantity of unstructured low intensity activities. Nor has it been established that adding these categories of activity/inactivity improves quantitative assessments of total physical activity or total sedentary behavior from questionnaires.[40,41,55,58,99] However, questionnaires can provide valid qualitative information about the types of light intensity and sedentary activities performed by participants.[40,116] Qualitative data on the specific activities performed and the context of activity is also one of the advantages that subjective measures have over most of the currently available objective measures of activity.

Reliability and validity are two criteria that provide statistical evidence for the efficacy of a physical activity measurement tool. Reliability is the ability of a measurement tool to produce consistent results.[118,119] Reliability of physical activity and sedentary behavior questionnaires is usually established on the basis of test-retest reliability coefficients or intra-class correlation coefficients.[60,95,97,120,121] Test-retest reliability is particularly important for studies that attempt to identify “usual” behavior or studies in which the assessment time frame is shorter than the time period of interest.

Validity is the degree to which a questionnaire is able to measure what is was intended to measure.[118,119] Validity of questionnaires is often established by comparing the results of the questionnaire to the comparable results of other measurement methods (validated questionnaires, diaries, objective measures, or direct observation). This can be done within a subset of the study population prior to the assessment of the full population or previously completed in a similar population.[95,97,120-122] The comparison method used for validation should already be validated to assess activity in a similar population and for the same time period of interest (past month, past year, lifetime).

Questionnaires designed to report total activity and activity specific to several different domains or intensity categories, would have to be proven valid for measuring total activity and activity in each category. Validity for one question or one category of activity does not prove that the questionnaire is valid for all the variables it reported. On the other hand, some variables can be shown to be valid proxy measures for other variables that are not collected. For example, calculating total sedentary behavior would require data on both planned and unplanned sedentary behavior. Questionnaires have not proven to be a valid measure of non-planned sedentary activity and therefore a direct, accurate measure of total sedentary is difficult to assess v ia questionnaire.[58] However, validation studies have shown that questions designed to elicit the total amount of time spent watching television or the total amount of screen time per day are valid proxy measures for total time spent sedentary, in some populations.[40,58,123] Also, a questionnaire found to be valid in one population may not be valid in another population due to differences in cognitive function, types of activities performed, or other differences between populations that may affect reporting.[97,124,125] Therefore, it is important to carefully consider the study population when choosing an assessment method.

3.2 OBJECTIVE MEASURES- ACCELEROMETRY

Objective measures of physical activity and sedentary behavior are used to estimate activity-related variables, like total physical activity, using measurements taken from physiological or biomechanical parameters. Although objectively-assessed physical activity can be biased by issues related to monitor wear compliance these methods are not subject to personal opinions, perceptions, or the other types of reporting bias that can affect the results of subjective measures of physical activity and sedentary behavior.[60] As a result, objective measures are generally better at capturing unplanned activities and can provide a more accurate picture of behaviors that occur at the lower intensity end of the physical activity spectrum.[59] This also makes it possible to produce a better quantitative assessment of total physical activity. Objective measures to assess physical activity include physiological monitors, such as heart rate monitors, and motion detectors, such as pedometers, accelerometer, and GPS (Global Positioning System) devices.[90,126,127] These monitors can be used individually or data from several devices may be combined.

Currently, the most commonly utilized objective measure of physical activity is the accelerometer. Accelerometers are a type of motion detector that is capable of recording both movement and speed over a period of time.[128,129] The earliest accelerometers used in physical activity research measured movement only in the horizontal plane, but currently there are accelerometers available that can monitor movement in up to three planes: horizontal, vertical, and diagonal. Many of these devices are also equipped with an inclinometer that can record whether or not a participant is lying, sitting, or standing.

Accelerometers operate by calculating the acceleration along a given axis.[128] The information necessary to calculate the acceleration is typically provided by a piezo-electric, micro-mechanical spring, or an electrical capacitance system.[129,130] All monitor types convert movement into an electrical signal which is output by the monitor as a count. The greater the amount of movement within a given period of time, the greater the number of counts that are output for that time period.

Previous research has compared the number of counts accumulated during various activities to measured oxygen uptake. Prediction equations were then developed from regression models to create cut-points in accelerometer counts that correlated with known MET-based intensity cut-points used in physical activity research (sedentary, light, moderate, and vigorous).[131] The number of counts from the monitor for each recording period (e.g. a minute or second) can therefore be calibrated to match pre-existing MET-based intensity scales for activity. As a result, the accelerometer readings can be utilized either as raw counts or as time spent in different intensity levels of activity.

Figure 3.1 provides the resulting values from an accelerometer calibration study by Freedson et al.[131] The Freedson established cut-points for light intensity (1-3 METS), moderate intensity (3-6 METS), and vigorous intensity (>6 METS) physical activity are associated with accelerometer cut-points of 100-1951, 1952-5723, and greater than 5724 counts.[131]

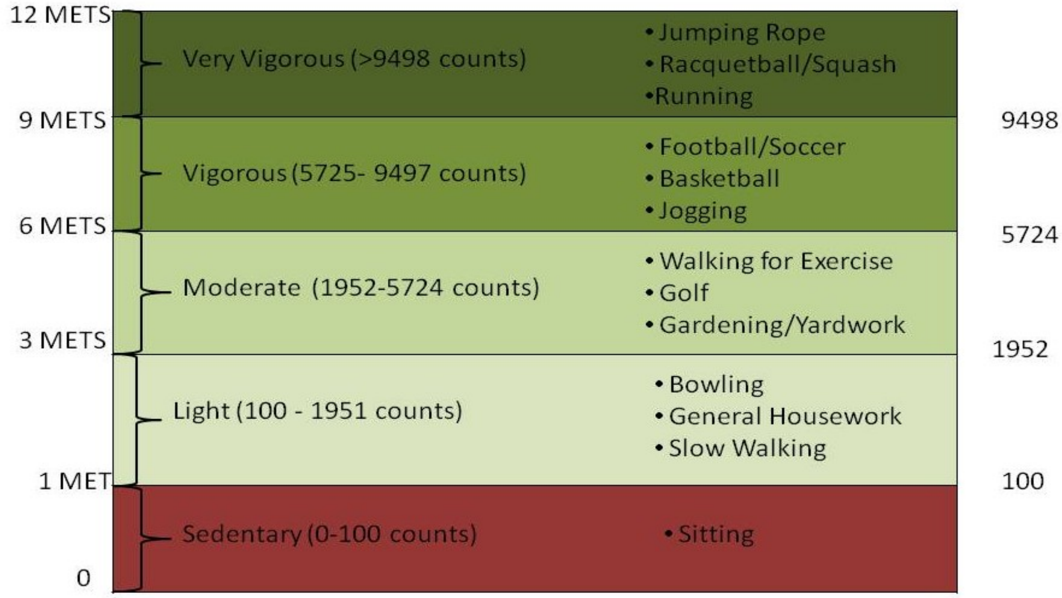


Figure 3.1 Freedson cut-points for accelerometry & the corresponding MET-based physical activity intensities

Currently, there are many types of accelerometers on the market for use in physical activity research.[132] Different monitors may have different mechanisms of measurement, record different variables, and have different body placement.[129,130,132] Also researchers may use calibration data from different regression models for converting data from the monitor to a variety of MET-based intensity scales.[131,133-136] For consistency, most research studies require that the accelerometers be worn on the same part of the body for all study participants. This is because the placement of the monitor will affect which types of movement it will record. The monitors are typically attached to a person's waist, in line with their armpit or at the small of the back, with a clip or belt.[137] However, some monitors are worn on the upper arm, wrist, thigh, ankle, or shoe. Monitors attached at the waist will record truncal movement well, but may not accurately report all upper body movement. Likewise, monitors placed at the wrist, ankle, or foot will pick-up more of the smaller movement that occurs in the extremities, but may not differentiate well between these movements and truncal movements that represent greater energy expenditure. Physical limitations of the population should be considered when choosing a monitor location. For example, some monitors may not provide an accurate assessment of activity for individuals with impaired ambulation and therefore may not be appropriate for some individuals or populations.

Also most monitors are not waterproof and therefore cannot be worn during aquatic activities such as swimming and water aerobics. Even those monitors that can be worn in water have difficulty adjusting for the uneven forces exerted by the water and may not provide an accurate reading of movement or intensity. Other general limitations of accelerometers include participant burden, cost, equipment malfunction/ noncompliance, and the possibility that wearing the monitor may cause the participant to alter their physical activity patterns.

Monitors that may be removed during the recording timeframe need to have estimates of physical activity and sedentary behavior adjusted for the time when the monitor was actively recording, but was not worn by the participant (non-wear time). Most research efforts utilize monitor specific, automated computer algorithms developed to identify and remove monitor non-wear.

Although using an automated process to remove non-wear has been shown to reduce bias in reported non-wear time, the algorithms themselves have also been shown to be a source of bias.[61,64,66,67,138,139] Validation studies have suggested that there may be more than one appropriate algorithm for a given monitor.[61,138] However, it is not clear whether all algorithms produce comparable results. Additionally, little effort has been put toward validating non-wear algorithms for use in different population sub-groups.[64] Therefore, it is not clear if the currently used algorithms are valid for all sub-groups.

Despite the limitations of accelerometers they are currently considered to be one of the best methods for assessing free living physical activity. Accelerometers have been proven to be a reliable and valid measurement of physical activity and sedentary behavior in many different types of populations including children[140-144], adults[145-148], and older adults[149-152]. Currently, there is no measure of physical activity considered to be a "gold standard" in free living conditions. However, accelerometers are the device that is most frequently used to validate other physical activity measures, including pedometers and questionnaires.[153-157]

3.3 PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR ASSESSMENT IN CHILD AND ADOLESCENT POPULATIONS

The following section is not meant to serve as a complete outline of assessment in children and adolescents, but as a guide to specific issues that must be considered in addition to the issues for the general population already discussed above.

Choosing a proper assessment tool in children and adolescents requires an understanding and consideration of the cognitive, physiological, and behavioral differences between adult populations and child and adolescent populations. Although some differences in children and adolescents only affect specific measurement methods, other issues, such as the higher drop-out rates and poorer compliance typically reported in younger populations are factors that can affect all types of measurement methods. Furthermore, changes that occur throughout childhood and adolescents must be considered when choosing a measurement method, deciding how that method with be implemented, and interpreting the results, for a given youth population.

For self-report measures, reliability and validity studies for youth populations have provided widely varying results for both reliability (0.56-0.93) and validity (0.03-0.89) coefficients.[97,120,158,159] Problems that are amplified in youth populations that may contribute to the wide range of coefficients values are poor compliance and cognitive difficulties, such as poor recall and missing values.[121,160] Also, over-reporting of physical activity and under-reporting of sedentary behavior on self-report measures is thought to be a larger problem in youth when compared to reporting in adults.[161-165] This increase in misreporting may be due in part to the fact that physical activity in youth populations tends to be more unplanned and sporadic, occurring in shorter bouts.[166] This is particularly true in pre-adolescent populations and can make it difficult to accurately assess physical activity and sedentary behavior with questionnaires.

Due to cognitive and behavioral factors, the specific age range of the population being assessed is particularly important in youth. The reliability and validity of self-report measures of activity and sedentary behavior for children under 11 y ears of age is generally lower when compared to older children.[158] Proxy reporting of physical activity and sedentary behavior by an adult, such as a parent or caregiver, has been used in an attempt to improve reporting for younger children.

However, the results of reliability and validity studies for proxy reporting measures have been mixed.[120,163,167] Therefore, the effectiveness of these methods is not clear. Interviewer administration, on the other hand, has been shown to improve the reliability and validity of recall questionnaires in older children and adolescents.[121,159] However, this method may still not be feasible for younger children and adds additional burden to the investigators.[159]

Finally, analysis that requires converting activities into MET-based intensity categories must consider the fact that children and adolescents are physiologically different than adults. Previous research indicates that resting energy expenditure is higher in youth when compared to adults.[168,169] Additionally, studies of youth and adults suggest that the energy cost of activity is higher in youth when compared to adults.[170-172] Therefore, MET-based conversion tables designed for children and adolescents, such as the compendium of physical activity for youth, should be utilized when converting reported activities into MET-based categories of physical activity.[93]

Currently, accelerometers are the most widely used measurement tool for capturing physical activity and sedentary behavior in child and adolescent populations. Advantages of the accelerometers over self-report are the smaller recording epochs that can capture the sporadic nature of children's activity and the fact that they are not as affected by the amplified cognitive difficulties reported in child and adolescent populations.

However, there are several issues that should be considered when assessing physical activity and sedentary behavior in child and adolescent populations, using accelerometry. The first issue is that the activity of children and adolescents tends to be more varied, when compared to adult activity.[163,173] This is true for the types of activities performed, the directions of movements, as well as, the patterns of behavior over the recording time frame. Although there is no consensus at this time, there is some evidence that monitors with more axis and shorter epoch times may be better at capturing the varied activity of child and adolescent populations.[132,174,175] It has also been suggested that to capture an accurate representation of "typical behavior" from activity monitors, 4 or more 10 hour days of data are required from youth, as opposed to 3 or more 10 hour days, as is required in adults.[121,132,176] However, this finding is based on data from generally healthy youth populations and is rooted in the fact that youth in the examined populations vary their activity more from one day to another than adults. Finally, different accelerometer count based cut-points have been derived for youth, based on the premise that there are physiologically based differences in how movement relates to MET-based intensity categories of physical activity and energy expenditure that shift throughout childhood and adolescents.[69,177-180]

3.4 PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR ASSESSMENT IN POPULATIONS WITH DIABETES

Few studies have attempted to identify methodological issues specifically related to the measurement of physical activity and sedentary behavior in populations with type 2 diabetes.[181,182] The results of these studies do not specifically indicate a need for a consideration of type 2 diabetes diagnosis when considering, interpreting, or assessing methods of measurement for physical activity and sedentary behavior. However, there are specific risk factors and complications associated with type 2 diabetes that have been previously linked to biased estimates of physical activity and sedentary behavior that should be addressed. The most important of these include overweight and obesity, poor ambulation and/or gait abnormality, and differences in activity patterns (when compared to non-disease populations).

Overweight and obesity are among the most important risk factors for type 2 diabetes. Studies of subjective measures of physical activity and sedentary behavior have shown that reporting bias on questionnaires may be more pronounced in overweight and obese individuals than it is in normal weight individuals.[162,183-185] This was found to be true in both adult and adolescent populations. Studies of objectively measured physical activity in overweight and obese populations reported that central adiposity can cause a tilt in waist and hip worn monitors that can hinder the ability of spring-levered pedometers to work properly and therefore cause an underestimation of activity.[186-188] However, studies in accelerometers and accelerometer based step-counters have shown that for most monitor types the effect of tilt angle is not significant.[188-192] Also, analyses that attempt to convert accelerometer results into energy expenditure should consider the fact that body mass effects energy expenditure. Although the current conversion equations take weight into account, there is evidence that these equations may not provide accurate estimates for overweight and obese individuals.[189,193-195] In relation to this, Ainsworth et al.[91] originally suggested that the MET-based values associated with each intensity level were not intended to produce accurate assessments of energy expenditure for individuals. The compendium values were designed to represent population averages that could be used to standardize survey data and may not be applicable to certain individuals without adjustments for personal factors, such as obesity.

Neuropathy, a common complication in type 2 diabetics, can lead to gait abnormalities and poor ambulation. Poor ambulation and gait abnormalities can affect the types of activities performed by individuals in a population. Furthermore, monitoring devices that are designed to record ambulatory activities do no t provide meaningful results for individuals who are non-ambulatory. Additionally, it has been shown that some monitoring devices do not accurately record activity in individuals with gait abnormalities.[196-198] Therefore, the disability of the specific study population being examined should be considered when designing questionnaires or determining monitor type and placement.

Currently, population based studies have suggested that adults, children, and adolescents with type 2 diabetes are more sedentary and spend less time in high intensity activities than their non-diabetic counterparts.[199-203] Therefore, research efforts designed to capture physical activity and sedentary behavior in populations with type 2 diabetes should consider methods that can capture all intensities of physical activities well. As a result, it may be necessary to examine differences in physical activity and sedentary behavior variables to determine if there are additionally considerations in the reporting of physical activity and sedentary behavior that need to be addressed within these populations specifically. As part of this analysis effort, we will attempt to expand the understanding of methodological issues in physical activity measurement that may be important for populations of individuals with impaired glucose metabolism or type 2 diabetes mellitus.

4.0 TYPE 2 DIABETES MELLITUS, PHYSICAL ACTIVITY, AND SEDENTARY BEHAVIOR

4.1 BIOLOGICAL CONNECTION

The biological role of physical activity on maintaining healthy glucose metabolism is not completely understood. However, there are physiologic processes involving physical activity that are thought to play a role in maintaining normal glucose metabolism. First of all, it has been shown that exercise increases insulin uptake in the muscles. This may be due in part to the increased availability of GLUT4, a transporter carrier proteins utilized by hum ans and other mammals.[30] The greater availability of this protein allows for an increase in the rate of glucose metabolism. The increase in blood flow during exercise may also increase the rate at which insulin is delivered to the working muscles. Both insulin and exercise cause translocation of GLUT4 from an intercellular compartment to the surface of the cell which is a necessary step in glucose uptake.[30] Because the signaling pathways are different for the insulin and exercise induced uptake of glucose it is possible to increase insulin uptake via exercise even if there is a dysfunction in the signally pathway related to insulin induced uptake.[28,29,31,204]

In addition to the evidence for the positive, exercise induced, effects of physical activity on the body, there is evidence that prolonged periods of inactivity, may have a negative effect on normal biological processes in the body.[33-35,40,205] In relation to impaired glucose tolerance and type 2 diabetes mellitus, the results of several studies suggest that inactivity has a strong influence on lipoprotein lipase (LPL) activity in skeletal muscles.[33-35] LPL is an enzyme that is necessary for hydrolysis of the triglyceride contained in lipoproteins. LPL binds to circulating lipoproteins when present on the vascular endothelium. Higher circulating levels of LPL in skeletal muscle have been linked with higher plasma glucose levels.[206,207] More specifically, higher levels of circulating LPL has been shown to cause preferential use of lipids as an energy source which can lead to insulin resistance.[206,27] One study in mice and rats showed that both acute and chronic inactivity lead to a decrease in LPL activity in weight-bearing skeletal muscle. It has also been suggested that inactivity may also affect diabetes development through its influence on gene activation and deactivation [32], and on the regulation of β cell function.[36]

4.2 PHYSICAL ACTIVITY, SEDENTARY BEHAVIOR, AND TYPE 2 DIABETES MELLITUS

There is substantial evidence from both clinical trials and epidemiologic studies for the effect of physical activity on the development of impaired glucose tolerance and type 2 diabetes mellitus. The most compelling evidence comes from clinical trials that were designed to test the efficacy of lifestyle interventions for reducing the incidence of type 2 diabetes. The most well-known, of these studies, was the Diabetes Prevention Program (DPP). The DPP was a multicenter clinical trial that examined the efficacy of metformin and of a lifestyle intervention to delay or prevent the onset of type 2 diabetes mellitus in adults at high risk for developing the disease. Although both lifestyle intervention and metformin were successful for reducing the incidence of diabetes in the DPP, the lifestyle intervention, which included a physical activity goal of 150 minutes/week of moderate-vigorous exercise, was more successful with a 58 % reduction in diabetes incidence when compared with placebo over an average follow-up of 2.8 years.[16] A post-hoc analysis of the DPP that attempted to separate the effects of physical activity, weight loss, and dietary improvement on the incidence of diabetes showed that those individuals who did not meet the weight loss goal or the fat goal, but did report making the activity goal had a 46% reduction in incident diabetes compared to those individuals that did not make any of the goals.[38]

Other large clinical studies, including the Diabetes Prevention Study (DPS) in Finland,[18] the Da Qing study in China,[26] and the Indian Diabetes Prevention Program[17] have confirmed the findings of the DPP in a wide diversity of populations around the world. In particular, the Da Qing clinical trial tested the individual effects of diet and exercise by creating separate intervention arms for exercise and dietary modification. The results showed that over a six year follow-up in individuals at high risk for the disease, the reduction in risk of diabetes was 46% lower in the exercise group.[26] A report of follow-up evidence from the DPP, DPS, and the Da Qing study showed that even after follow-up periods of 10,7, and 20 years , respectively, there was still a substantial reduction in the risk of developing diabetes for individuals who participated in a lifestyle intervention that included physical activity.[22]

Additionally, there are many epidemiologic studies that show the positive effects of physical activity on diabetes related outcomes. A review of twenty prospective studies performed in large cohorts reported, that in all studies reviewed, there was a negative association between physical activity and diabetes development.[208] Although a few of the studies reported no association in specific population subgroups, meta-analysis that involved ten of the same studies, reported that based on a total of 301,221 participants and 9,267 incident cases of diabetes, the summary risk reduction of type 2 diabetes was 0.69 (95% CI 0.58-0.83) for regular participation in moderate intensity activity when compared to *being sedentary* and 0.70 (0.58-0.84) for regular walking compared to almost no walking.[209] The risk reduction in this study was found to be significant, even after adjusting for BMI. In relation to this, a study in the Pima Indians of Arizona showed that there was a negative relationship between incident diabetes assessed by the OGTT and total physical activity for both men and women.[210] Although the results were attenuated by BMI, when the analysis was performed stratified by tertiles of BMI, the diabetes incidence rate remained lower in more active than in less active individuals from all BMI groups, for all but males in the middle BMI group. Finally, another analysis that utilized the results of eight previously published longitudinal studies concluded that there was evidence for a joint effect and for independent effects of both obesity and inactivity on incident type 2 diabetes.[39] Therefore, these results indicate that improvements to physical activity can reduce the risk associated with activity alone, as well as, some of the joint risk associated with both inactivity and obesity.

Although, most studies of physical activity and diabetes have focused on activities that are at least moderate intensity, there is also evidence for a connection between lower intensity activity and type 2 diabetes. First of all, there is evidence that walking, an activity that can fall into both the light and moderate intensity categories, can have a positive effect on diabetes related outcomes and can reduce the risk of diabetes development.[209,211-214] Additionally, objectively reported light activity was found to be negatively associated with post-prandial glucose levels in Australian adults without diagnosed diabetes.[44] Finally, a study in older adults found that reported performance of light activity, at least once a week, was associated with a reduced risk of diabetes for those aged 70 years and greater. However, the results were attenuated by adjusting for important covariates.[215]

In addition to the effects of physical activity on the development of diabetes, there has been growing evidence that reducing the amount of time spent sedentary may also have an effect on the development of diabetes. Currently, there are numerous studies that have linked the amount of time spent watching television to diabetes related outcomes and increased risk for diabetes development.[45,216-221] Additionally, total sedentary behavior, obtained from accelerometer output has also been linked to diabetes related outcomes and the development of diabetes in several studies.[36,46-48,222] Specifically, one study that examined the cross-sectional relationship between average total sedentary minutes per day from the accelerometer and cardio-metabolic biomarkers in a representative sample of U.S. adults found that total sedentary was positively associated with insulin, HOMA-%B, and HOMA-%S ($p < 0.05$).[48] Therefore, it is now recognized that capturing all intensities levels of physical activity, as well, as sedentary behavior is important to understanding the effect of activity on diabetes development.[35,40,41,214,223]

4.3 PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR LEVELS IN INDIVIDUALS WITH TYPE 2 DIABETES

The current American College of Sports Medicine (ACSM) recommendations for physical activity, approved by the American Diabetes Association (ADA), suggest that in order to reduce the risk of diabetes, adults should perform 150 minutes or more of moderate-vigorous physical activity per week. In general, it has been reported that most adults in the United States are not meeting these recommendations.[224,225] Recent data on physical activity levels, specifically in adults with type 2 diabetes or impaired glucose tolerance from large population surveys in the United States and elsewhere indicate that individuals with type 2 diabetes or impaired glucose tolerance are less active compared to individual without diabetes.[202,226-231] In general, questionnaires that identify individuals as active or inactive have reported that 50-60% of adults with impaired glucose tolerance or type 2 diabetes are inactive compared to approximately 30-38% of adults without impaired glucose metabolism.[202,227,229,230]

Most large, population representative studies do not collect objective physical activity data. However, during the 2003-04 and 2005-06 cycles of NHANES accelerometers were used to collect data on physical activity and sedentary behavior. One study that utilized accelerometer data from NHANES 2005-06 reported that average daily step counts in individuals with diabetes were 2183 +/- 189 versus 3668 +/- 89 in individuals without diabetes.[232] Currently, there are no other population representative studies of adults that report accelerometer based physical activity data by diabetes status. Additionally, there is no population representative data on sedentary behavior levels for adults.

Currently, the CDC estimates that less than 1% of the child and adolescent population in the United States have type 2 diabetes. Therefore, it should not be surprising that there are no studies, based on population representative data that report physical activity or sedentary behavior levels for children and adolescents with type 2 diabetes. In fact, the only study that reports physical activity levels in a large sample of children and adolescents with type 2 diabetes is a paper that was generated in connection with this dissertation effort. Physical activity and sedentary behavior levels were generated from baseline accelerometers data files on 242 youth ages 10-18 who participated in the treatment options for type 2 diabetes in adolescents and youth study (TODAY) and had complete accelerometer data.[233] The results of this analysis showed that for most age/gender categories the TODAY youth spent less time in moderate-vigorous activity and for all age categories they spent more time in sedentary behavior, when compared to a nationally representative sample of obese youth from NHANES 2005-06.

5.0 PAPER #1: ASSESSMENT OF PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN YOUTH WITH TYPE 2 DIABETES

Manuscript 1 will present estimates of baseline physical activity and sedentary behavior levels for youth aged 10-18 years, with newly diagnosed type 2 diabetes mellitus, that were enrolled in the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study. Mean minutes per day of sedentary behavior, moderate-vigorous intensity, and light intensity physical activity from both a subjective recall questionnaire (3DPAR) and an objective measure (accelerometer) will be presented and compared.

5.1 BRIEF OVERVIEW OF TODAY TRIAL

Baseline data from the treatment options for type 2 diabetes in adolescents and youth study (TODAY) will be used to determine the level of agreement between an objective measure of activity (accelerometer) and a subjective measure of activity (3DPAR questionnaire) for reporting time spent in physical activity and sedentary behavior in adolescents and youth with type 2 diabetes (manuscript 1).

The TODAY trial was a randomized, double-blind, parallel-group clinical trial funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). [70] TODAY was designed to evaluate the relative efficacy and safety of three treatments for type 2 diabetes in youth: metformin alone, metformin plus rosiglitazone, and metformin plus an intensive lifestyle program. The primary objective of the trial was to compare the three treatment arms on time to treatment failure, defined as loss of glycemic control.

Participants were recruited from 15 clinical centers across the United States and a total of 1211 patients were screened.[70,234] To be eligible, participants were required to be 10-17 years old, with less than two years of type 2 diabetes, a BMI ≥85th percentile at time of diagnosis or at screening, had availability and agreement of an adult caregiver to support participation, were negative for pancreatic autoimmunity (both GAD and IA2 antibodies), and had fasting C-peptide > 0.6 ng/mL. Additionally, participants with hemoglobinopathies were excluded.

After screening was completed 927 patients were entered into a 2 to 6 month run-in period.[234] The run-in period was performed to ensure that participants could tolerate therapy with metformin, accomplish mastery of a standard diabetes education curriculum, and demonstrate ability to adhere to study requirements.[70] Participants who successfully completed the run-in period were found to decrease their weight by a mean of 0.68 kg compared to a 0.71 kg weight gain in those that failed the run-in period.

5.1.1 Measures

5.1.1.1 Demographics

Demographic data was collected at the baseline visit. Participants and their caregivers were asked to report participant's age and self-identified racial/ethnic group as White non-Hispanic, Black non-Hispanic, Asian non-Hispanic, Hispanic, or Native American.

5.1.1.2 Physical Activity- Subjective

Subjective physical activity data were measured utilizing the 3DPAR. The 3DPAR is a self-administered questionnaire of physical activity for the previous three days that has been validated in similarly aged youth.[235-238] The 3DPAR was administered during the clinic visit, following the participant's use of the accelerometer and asked participants to recall activity over the time period that coincided with the final three days of accelerometer monitoring. Trained interviewers guided the process of completing the questionnaire by providing the initial instructions and clarifying the questionnaire.

Based upon a list of 77 leisure, occupation, and daily living activities, participants were asked to record the main activity that they participated in during each 30 minute block of time, from 6 AM to 12 AM, for each of the past three days. They were also instructed to estimate the intensity level the activity was performed based upon the following categorizations: *Light Activity* requires little or no movement with slow breathing; *Moderate Activity* requires some movement and normal breathing; *Hard Activity* requires a moderate amount of movement and increased breathing; and *Very Hard Activity* requires quick movements and hard breathing.

Intensity values (METS) were assigned to each of the 77 activities and their four intensity levels listed on the questionnaire and were based on the Compendium of Physical Activity.[91]

Physical activity from the 3DPAR was analyzed in terms of total hours of physical activity, total daily MET hours, and total time spent per day in the various intensity levels of physical activity (light, moderate, vigorous) and sedentary behavior.

5.1.1.3 Physical Activity- Objective

Objective physical activity data were collected using the ActiGraph AM7164 accelerometer (Pensacola, FL). This ActiGraph model is a small, uniaxial piezoelectric accelerometer that is typically worn at the waist, which measures vertical acceleration ranging in magnitude from 0.05 to 2.00 Gs with frequency response of 0.25 – 2.50 Hz. Data output from the ActiGraph accelerometer are activity counts, which quantify the amplitude and frequency of these filtered accelerations and were summed over a 1-minute time interval. The sum of the activity counts is related to activity intensity and can be categorized based on validated activity count cut-points. Previous studies have demonstrated that the ActiGraph accelerometer is a valid and reliable measure of physical activity in children and adolescents.[239]

Participants received an accelerometer prior to their clinic visit and wore the accelerometer for a period of 7 days. Participants were asked to record the time at which they put on the monitors in the morning and the time they took off the monitors at night in a physical activity diary. At the end of the 7 day period, the participant returned the accelerometer and physical activity diary at their clinic visit.

Data from the accelerometer were downloaded, processed, and screened for wear time using previously reported methods (http://riskfactor.cancer.gov/tools/nhanes). Average total activity counts per day were calculated using summed daily counts detected over wear periods. Time in minutes spent in different activity intensities was calculated using age-specific count ranges corresponding to sedentary, light (1-3.99 METs), moderate (4-6.99 METs) and vigorous intensity (≥ 7 METs). [A MET is an estimate of relative intensity such that one MET represents the energy expenditure for an individual at rest whereas a 10 MET activity requires 10 times that amount]. These intensity levels were derived from a published age specific, energy expenditure prediction equation. [140] The equation adjusts for the higher resting energy expenditure of youth. [172,240] Non-wear time was defined as intervals of at least 60 consecutive minutes of zero counts, with allowance for up to 2 minutes of observations with greater than zero counts/minute. Wear time was determined by subtracting non-wear time from the total observation time for the day. Total activity was defined as the combination of light, moderate, and vigorous activity (≥1 MET). Time spent in sedentary behavior was defined as the amount of wear time accumulated in counts below100 counts/minute. To be included in any accelerometer related analyses, participants must have had accelerometer data that included 10 hours of wear time on 3 or more valid days.

5.1.1.4 Anthropometrics

All anthropometric measures were taken with youth wearing lightweight clothing and without shoes by trained and certified research staff. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. BMI was calculated as kg/m2 and BMI z-score was derived from the sex-and age-specific standards published by the National Center for Health Statistics.

5.1.2 Baseline Demographic and Anthropometric Characteristics

704 youth successfully completed the run-in period, were randomized and entered the main clinical trial.[234] 699 of the 704 individuals randomized completed the baseline assessments.

At baseline the cohort had a mean age of 14 yrs., mean diabetes duration of 7.8 months, and a mean body mass index Z-score of 2.15. The baseline cohort was 64.9% female, 41.1% Hispanic, 31.5% non-Hispanic black, 19.6 % non-Hispanic white, and 7.8 % other racial/ethnic groups. 41.5% of the baseline cohort had a household annual income of less than $25,000; and 26.3% had a highest education level of parent/guardian less than a high school degree.[234]

5.2 PAPER #1 OVERVIEW

Purpose: To compare reported values of physical activity (PA) and sedentary behavior assessed by a recall questionnaire and an accelerometer in a diverse cohort of youth with type 2 diabetes.

Methods: PA data was examined in 236 participants, in the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study, who had complete accelerometer and 3 day physical activity recall (3DPAR) data. 3DPAR/accelerometer agreement for total time spent physically active (TPA), time spent in light (LPA) and moderate-vigorous (MVPA) intensity activities, and time spent sedentary was compared with Spearman's correlations and Bland-Altman plots.

Results: Spearman coefficients were not significant for MVPA, LPA, or TPA between the two measurement instruments. Sedentary time in females ($r = .19$, $p < .05$) was significantly but weakly correlated between instruments. Examining absolute differences between the two measures (absolute value of 3DPAR recorded minutes/day minus accelerometer recorded minutes/day), the median differences were large in males and females for MVPA (50 & 52 min/day), LPA (116 & 97 min/day), and sedentary time (136 & 177 min/day).

Conclusions: The relationship between the 3DPAR and accelerometer for sedentary behavior and PA intensity levels was weak, at best, in overweight/obese youth with type 2 diabetes. Reported mean minutes/day of MVPA and LPA were, in general, substantially higher and sedentary time much lower on the subjective 3DPAR when compared to recorded values from the accelerometer for both gender groups. The differences between instruments appear to be driven by reported values from the 3DPAR. These results suggest that the 3DPAR may not provide an accurate measure of the quantity of time spent in either PA or sedentary behavior in overweight/obese youth with type 2 diabetes.

In summary this manuscript provides an assessment of the levels of physical activity and sedentary behavior in a demographically diverse cohort of youth with type 2 diabetes. Additionally, this effort assesses the validity of the 3DPAR questionnaire for measuring both time spent in different intensities of physical activity and total time spent sedentary. The results of these analyses suggest that measurement methods for physical activity and sedentary behavior should be validated in populations with type 2 diabetes, even if the methods in question have been previously validated in the general population.

6.0 PAPER #2: DIFFERENCES IN PHYSICAL ACTIVITY OUTCOMES DUE TO ACCELEROMETER NON-WEAR ALGORITHMS

Activity-related outcomes, including average total counts per day, average counts per minute, and mean minutes per day of wear time, sedentary behavior, moderate-vigorous intensity activity, and light intensity activity, will be reported from the results of three different data processing algorithms. Each data processing run will utilize a different variation of the 60 minute definition of accelerometer non-wear (60 consecutive minutes with zero accelerometer counts). The most common variations of this definition will be used, in order to assess how minor changes to the definition of non-wear affect real changes in reporting of activity and sedentary behavior for a given population. This analysis, will utilize data from adults aged 20 years and older in the National Health and Nutrition Examination Survey (NHANES) 2005-06 data collection cycle.

6.1 BRIEF OVERVIEW OF NHANES

Accelerometer data from the NHANES data set (2005-06 cycle) will be used to identify the differences in reported physical activity and sedentary behavior produced by three commonly used non-wear algorithms (manuscript 2). Accelerometer data from the NHANES data set (2003-04 & 2005-06 cycles) will also be used as a p opulation representative assessment of physical activity and sedentary behavior levels for comparison to the physical activity and sedentary behavior levels in the DPPOS study population (Manuscript 3).

NHANES is a cross-sectional observational study of the United States population conducted by the National Center for Health and Statistics (NCHS) of the Centers for Disease Control (CDC). The NHANES survey has been conducted for nearly 50 years. Early NHANES assessments were conducted as a s eries of surveys that focused on different population groups and health outcomes. Since 1999, the survey has become a continuous program that is organized into 2 year cycles of data collection. The continuous NHANES survey over-samples certain subgroups to ensure a population representative sample and to correspond to current public health trends. F rom 2003-2006 oversampling was conducted on a dolescents (12-19 years of age), adults $\geq$ 60 years of age, African Americans, Mexican Americans, and individuals with low income.

The NHANES continuous survey utilizes a multi-stage complex random survey design. During the first stage of sampling, primary sampling units (PSUs) are selected. These units are typically individual U.S. counties, but may be comprised of a group of counties. The PSUs are further divided into segments. Both PSUs and segments are chosen using probability proportional to measurement size (PPS) meaning that their probability of being included increases with population size. Households within each segment are selected randomly from all households in the segment. Individuals from selected households are chosen from random within designated age-sex-race/ethnicity sub-domains. Selected individuals are assigned sampling weights that correspond to the number of individuals that they represent in the general population. To ensure accurate representation of the general population, sampling weights are further adjusted for non-response and other factors. Analyses that do not consider the complex sampling design and weights may lead to biased estimates and overstated significance.

Household interviews are conducted on all selected individuals to attain demographic, socio-economic, dietary, and health related information. Health examinations are later conducted by trained clinicians and medical personnel in Mobile Examination Centers (MECs) that are sent to each selected PSU segment. Samples for laboratory assessments are collected during the examination.

6.1.1 Measures

6.1.1.1 Demographics

Demographic information including age, gender, and race were collected during the initial screening. Age in years was self-reported at the initial screening. To ensure de-identification, individuals over the age of 85 years were assigned the age of 85. Updated values for age at the time of the examination (MEC) were calculated for those individuals who were less than 85 years of age and did not have an imputed age value at the time of the household survey. Participants were asked to categorize themselves as non-Hispanic white, non-Hispanic Black, Mexican American, Other Hispanic, or Other race (including mixed race).

6.1.1.2 Physical Activity

Physical activity measures have been included in the annual NHANES survey since 1999 when a self-reported questionnaire was added. The questionnaire utilized in NHANES assesses activities of moderate and vigorous intensity performed in the last 30 days.

During the 2003-2004 and 2005-2006 cycles, physical activity data were collected using the ActiGraph AM7164 accelerometer (Pensacola, FL) which was worn at the waist and measured vertical acceleration. A ccelerometry measures were collected from all eligible NHANES participants that were included in the mobile examination (MEC) portion of the survey. Exclusionary criteria included age <6 years, walking impaired, or other limitations that preventing wearing the monitor according to the protocol.

NHANES participants were given the monitor at their MEC visit and asked to wear the device for the next 7 d ays, during their waking hours, and to remove the monitor for water related activities such as swimming or bathing. For the data presented here, only participants aged 20 years or older with accelerometer data were included in the analysis of wear/ non-wear minutes and valid/invalid days. Additionally, the comparison of physical activity-related outcomes only included participants aged 20 ye ars or older with 10 or more hours of monitor wear time on at least 3 or more valid days.

Data from the accelerometer were downloaded through the NHANES website as PAM files. The files were prescreened by the NCHS for outliers and unreasonable accelerometer count values which are flagged in the dataset. A fter downloading the data, I performed all additional screening and processing of records with SAS code that was designed for each study. All studies utilized a non-wear algorithm that defined non-wear as at least 60 consecutive minutes of zero counts with allowance for up to two minutes of observations greater than zero counts per minute. Two additional algorithms were utilized for manuscript #2.

Average total activity counts per day were calculated using summed daily counts detected over wear periods. Activity intensity thresholds were defined as light, (1-2.99 METs), moderate (3-5.99 METs) and vigorous intensity (≥ 6METs). [A MET is an estimate of relative intensity such that one MET represents the energy expenditure for an individual at rest whereas a 10 MET activity requires 10 times that amount]. NCI cut-point for NHANES were used in manuscript #2 and Freedson cut-point were utilized in manuscript #3. The corresponding NCI count ranges are 100 < = Light < 2200 < = Moderate-vigorous. The corresponding Freedson cut-points for adults were light intensity (100- 1751 cts/min), moderate intensity (1752- 5724 cts/min), and vigorous intensity (≥ 5725 cts/min) activity. Time spent in sedentary behavior was defined as the amount of time accumulated in counts that were < 100 counts per minute. Wear time was determined by subtracting non-wear time from the total observation time for that day.

6.1.1.3 Laboratory Data

Fasting plasma glucose was assessed only on those participants in the AM session who were at least 12 years of age. Participants were instructed to fast for ≥ 9 hours prior to the laboratory procedures. Glucose concentrations were assessed by measuring the concentrations of nicotinanide adenine dinucleotide (NADH) spectrophotometrically at 340 mm. In additional to individuals who self-reported having diabetes, or use of insulin, those individuals with a fasting glucose level above 125 mg/dl were classified as having diabetes. Individuals with a fasting glucose level between 100 and 125 mg/dl were considered as having impaired fasting glucose, but not diabetes.

6.1.1.4 Anthropometrics

Body composition measures were also collected during the MEC portion of the survey by trained health technicians. Initially, weight was measured in pounds on a Toledo digital scale and then converted into kilograms using standard procedures. For height measurements, participants were asked to stand straight with their feet flat on the floor and the back of their head against a vertical measurement board, aligned in the Frankfurt horizontal plane. All height measurements were taken in centimeters. Body Mass Index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m^2).

6.2 OVERVIEW PAPER #2

Purpose: To determine how changes to accelerometer algorithms that differentiate between wearing the monitor during sedentary activities (such as sitting) versus not wearing the monitor, impacts on overall accelerometer results, as demonstrated in a national data set.

Methods: 2005-06 National Health and Nutrition Examination Survey accelerometer data for adults, age ≥ 20 yrs. (N=4016) was processed using 3 different algorithms for identifying recorded periods of monitor non-wear. Each algorithm defined non-wear as a minimum of 60 minutes of continuous inactivity, but varied by different parameters for the allowance of incidental movement during a non-wear period. Agreement between the results of the 3 algorithms for estimates of daily average wear time, sedentary behavior, and physical activity outcome variables were tested using Kendall's W correlation coefficients and by examining differences in weighted population mean values between each pair of algorithms; overall and stratified by gender, older adults (≥ 65 years) vs. all other adults, and obesity status, respectively.

Results: Kendall's W coefficients for daily average wear time, sedentary time, and activity-related variables were very high between all 3 non-wear algorithms (W >.90, p<0.0001). Absolute mean differences between algorithms, for sedentary behavior, were clinically significant; ranging from 16.6-30.9 minutes/day in adults 20-64 yrs. and from 29.3-56.1

minutes/day in older adults. The differences in mean sedentary values between algorithms did not appear to vary by gender or obese status.

Conclusion: Changing the parameters for movement allowances during monitor recorded non-wear time resulted in clinically significant differences in estimates of time spent sedentary, especially in older adults. These results argue for standardization across studies in the non-wear algorithms used in accelerometer processing for reporting sedentary behavior.

In summary, this manuscript contributes to the overall goals of this dissertation effort by providing an evaluation of the algorithms used in processing physical activity and sedentary behavior data collected by accelerometers. This is relevant because accelerometers are the most widely accepted method for measuring both time spent in physical activity of all intensity levels and total time spent in sedentary behavior. The results of this research effort provide insight into the impact of small changes to accelerometer processing algorithms on reported levels of physical activity and sedentary behavior. The results of this effort suggest that changes to the definition of non-wear used in accelerometer processing algorithms can have a clinically significant impact on reported values of time spent in sedentary behaviors. Therefore, these results indicate that accelerometer processing algorithms developed for use with assessments of moderate-vigorous physical activity should also be validated for sedentary behavior.

7.0 PAPER #3: PHYSICAL ACTIVITY & SEDENTARY BEHAVIOR IN THE DIABETES PREVENTION PROGRAM OUTCOMES STUDY (DPPOS)

Objectively-measured physical activity and sedentary behavior will be reported for a cohort of adults with impaired glucose tolerance and type 2 diabetes mellitus, using accelerometer data from the Diabetes Prevention Program Outcomes Study (DPPOS). Additionally, to provide a context for these findings, the results from the DPPOS cohort will be compared to the activity and sedentary behavior levels of a representative sample of the United States population, from the combined National Health and Nutrition Examination Survey (NHANES) 2003-04 and 2005-06 data collection cycles.

7.1 DPP AND DPPOS FOLLOW-UP STUDIES

The Diabetes Prevention Program Outcomes Study (DPPOS) is a follow-up study of the original Diabetes Prevention Program (DPP) cohort. The DPPOS is designed to assess the long-term effects of interventions used in the DPP on the development of type 2 diabetes and its complications. Figure 7.1 illustrates the time line and enrollment from the original DPP through the DPPOS and accelerometer ancillary study.

Briefly, The DPP was a multi-center, randomized, controlled clinical trial with a primary aim to determine if certain interventions could prevent or delay type 2 diabetes in adults at high risk for developing the disease.[16] From 1996 to 1999 the study enrolled 3,234 overweight adults aged ≥25 years with blood glucose levels that were higher than normal but not yet in the diabetic range. Major exclusionary criteria included a myocardial infarction within the past 6 months, symptoms of coronary heart disease, serious illness, or use of medications known to impair glucose tolerance,

Nearly half of all participants were from minority groups that are disproportionately affected by type 2 diabetes. Other higher risk groups targeted for recruitment included individuals age 60 and older, women with a history of gestational diabetes, and people who have a first-degree relative with type 2 diabetes. Study participants were randomized to a metformin treatment group, a lifestyle intervention group, or a placebo group. The DPP was ended after an average follow-up of 3.2 years.[16] The results of the trial indicated that the lifestyle intervention reduced the incidence of diabetes by 58% (95%CI 48%, 66%) and that Metformin reduced the incidence of diabetes by 31% (95% CI: 17%, 43%).

Of the 3150 eligible and surviving DPP participants, 2766 (88%) enrolled in the DPPOS.[241] After the results of the DPP were given to the participants there was a wash-out period of 2 w eeks for metformin and placebo participants. Following the wash-out period placebo and metformin group participants were given a 16-session group program modeled after the intervention given to lifestyle participants in the DPP.

After the lifestyle intervention materials had been given to all participants the DPPOS follow-up study was initiated in September 2002.[241] In the DPPOS, those randomly assigned to metformin continued taking 850 m g of the drug twice a day unless diabetes developed and required other types of treatment or the drug was discontinued for other reasons. However, the placebo pills were discontinued. All DPPOS participants were offered Lifestyle sessions (HELP) every 3 months. The primary outcome remained unchanged between the DPP and DPPOS and outcome assessment examinations continued on the same yearly and 6 monthly schedule as in the DPP.

The mean age of participants at the baseline of DPPOS was 55 years.[241] 68% were female, 55% Caucasian, 20% African-American, 16% Hispanic American, 4% Asian or Pacific Islander-American, and 5% American Indian.

At the time of enrollment 38.4% of DPPOS participants had a confirmed diagnosis of type 2 diabetes, based on the DPP diagnostic criteria. Currently available follow-up data on the DPPOS indicates that after 5.5 years of follow-up in the DPPOS 1301 of the 2335 individuals (55.7%) with data had been diagnosed with type 2 diabetes.[241]

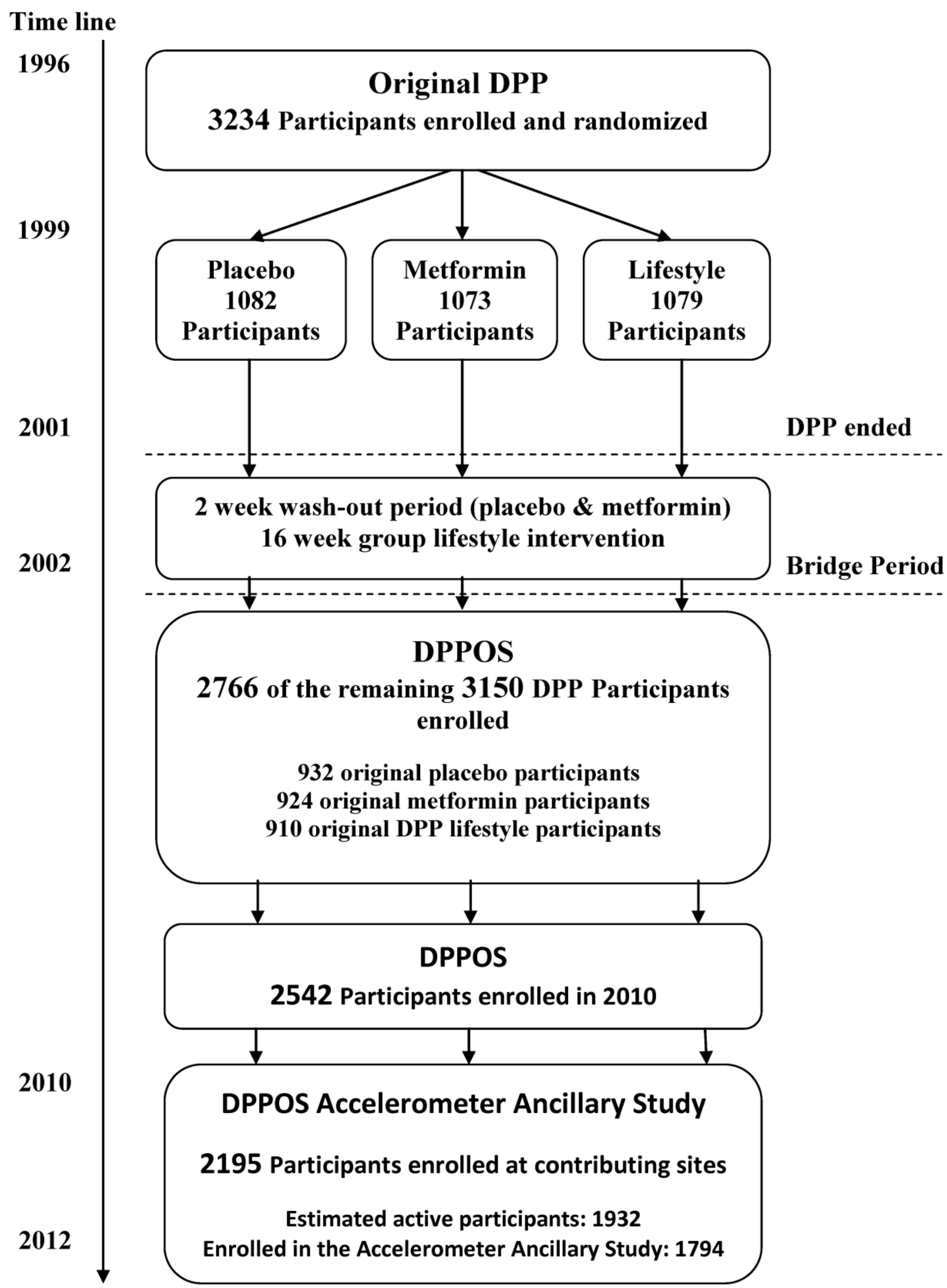


Figure 7.1 Timeline & enrollment figures for the original DPP, the DPPOS follow-up study, & the DPPOS Accelerometer Ancillary Study

7.2 MEASUREMENTS IN THE DPPOS

7.2.1 Demographics

Demographic data on age, gender, and race/ethnicity were collected in the original DPP. Participants were asked to self-identify race/ethnicity as Caucasian, African-American, Hispanic American, Asian or Pacific Islander-American, or American Indian.

7.2.2 Physical Activity

Physical activity in the original DPP and the DPPOS has been measured using an interviewer administered recall questionnaire, the Modifiable Activity Questionnaire (MAQ). The MAQ assesses past year, moderate-vigorous intensity leisure and occupational activities.[56] The version of the MAQ utilized in the DPPOS population was modified to include activities common to the study population.[242] The MAQ also assesses leisure sedentary behavior, by asking participants "On average, how many hours per day do you spend watching television". The MAQ is administered once a year, at the mid-year visit.

7.2.3 Laboratory Measures

Blood glucose levels were assessed at the midyear visit with a fasting plasma glucose test (FPG) and at the annual visit using an oral glucose tolerance test (OGTT). Participants were asked to fast for 10, but not more than 18 hours prior to their test. Testing was not performed in participants reporting alcohol consumption within 36 hours prior to the test, illness within the past 7 days, atypical diet in the last 3 days, steroid use, or exercise within the past 10 hours. For the OGTT, after a fasting blood sample is drawn participants are asked to consume a standard glucose containing solution of 75 gm glucose. Plasma for glucose is drawn at 0, 30, 120 minutes. Diabetes status is based on the ADA guidelines for blood glucose levels of ≥ 126 mg/dl FPG or ≥ 200 mg/dl 2-h plasma glucose during an OGTT.[2] Diagnosis of diabetes with either the FPG test or the OGTT at the clinic visit is confirmed within the 6 weeks following the initial diagnosis using an OGTT.

7.2.4 Anthropometrics

Weight was measured in pounds on a balance scale and then converted into kilograms using standard procedures. For height measurements, participants were asked to stand straight with their feet flat on the floor and the back of their head against a vertical measurement board, aligned in the Frankfurt horizontal plane. All height measurements were taken in centimeters. Body Mass Index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m^2).

7.3 DPPOS ACCELEROMETER ANCILLARY STUDY

The DPPOS Accelerometer Ancillary Study is a multi-center cross-sectional study that is funded by an R-01 grant through the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) as an ancillary study within the larger DPPOS follow-up study. The principle investigator of the study is Dr. Andrea Kriska, PhD of the University of Pittsburgh. This study was designed to incorporate an objective measure of physical activity and sedentary behavior into the DPPOS.

The primary aim of the DPPOS follow-up study is the same as the original DPP. Therefore, neither the DPP nor the DPPOS study was designed to assess the individual effects of physical activity on the development of diabetes. Post-hoc analysis in the original DPP, indicated that leisure time moderate-vigorous activity levels reported on the MAQ, were shown to be significantly different between randomized study arms, at the end of the DPP follow-up (average 3.2 years).[16] Furthermore, change in physical activity was significantly related to diabetes incidence, in the lifestyle arm. However, statistical significance was lost, after adjusting for weight change. Another post-hoc analysis within the lifestyle arm, that included an assessment of goal achievement and diabetes incidence, reported that for the 495 DPP lifestyle participants that did not meet the weight loss goal at year 1, but did meet the exercise goal, there was still a 46% reduction in diabetes incidence.[38]

The difficulties in achieving a clear understanding of the effect of physical activity on the incidence of diabetes in the DPP may have been due, in part, to difference in precision between the self-reported measurement of physical activity and the more precise measurement used for the covariate weight. Additionally, the original analysis did not consider the effects of light intensity physical activity or sedentary behavior, both of which have since been shown to affect blood glucose levels, controlling for the effects of moderate-vigorous activity.[44,48] This may be particularly important in this population, as populations with impaired glucose tolerance and type 2 diabetes have been shown to spent less time in moderate-vigorous activity and more time in light intensity activity and sedentary behavior than individuals with normal glucose tolerance.[202,232] In relation to this, the assessment tool used in the DPPOS to measure physical activity levels, the MAQ, does not measure light intensity activity or total time spent sedentary. Therefore, in order to assess the association between all intensities of physical activity, sedentary behavior and the development of type 2 diabetes in the DPPOS cohort it is necessary to use an additional measure; the accelerometer.

7.3.1 Study Objectives

The primary goals of the DPPOS ancillary study are to objectively assess physical activity levels in the DPPOS cohort using an accelerometer to accurately measure all intensities of physical activity and sedentary behavior and to determine if levels of physical activity differ among remaining diabetic and non-diabetic participants by or iginal randomized group. Secondary goals include using accelerometer data to determine if those individuals who are more active have better health profiles. Important outcomes are factors related to diabetes and heart disease that are already being collected in the DPPOS. This study will also seek to determine the relationship between the accelerometer output and the data collected from the physical activity questionnaire already being used in the DPPOS (the MAQ).

7.3.2 Physical Activity Data Collection and Processing

Objective physical activity data were collected using the ActiGraph GT3X accelerometer (Pensacola, FL). This ActiGraph model is a small, tri-axial accelerometer that is typically worn at the waist. The GT3X accurately and consistently measures acceleration ranging in magnitude from approximately 0.05 to 2.00 Gs with frequency response of 0.25 – 2.50 Hz. This parameter allows for the detection of normal human motion while filtering out high-frequency vibrations that occur such as riding in a car. Data are output from the ActiGraph accelerometer in the form of steps and activity counts, which quantify the amplitude and frequency of the filtered accelerations along each of the three axes. The accelerometer output is summed and outputted in time intervals of 1 second. For comparability to NHANES only counts from the horizontal axis were used in these analyses and 1 minute averages were created from the 1 second output to match the epoch length reported for NHANES. Previous studies have demonstrated that the ActiGraph accelerometer is a valid and reliable measure of physical activity in adults.

Once a participant signed the consent form for the accelerometer study, during their midyear or annual DPPOS visit, a clinic staff member initialized an accelerometer for them and showed the participant how to wear the monitor. All monitors were worn on a belt, at waist/hip height. Participants who received an accelerometer were asked to wear the monitor during waking hours (except during swimming or bathing) for a period of 7 days following their visit. Participants were asked to record the time at which they put on the monitors and the time they took off the monitors in a physical activity (PA) diary. At the end of the 7 day period, the participant returned the accelerometer and PA diary by returning the monitor in person or mailing it back to the clinic.

Data was then downloaded by the clinic staff onto a local, designated computer(s) using software provided by ActiGraph, the makers of the GT3X accelerometer. The data was transferred to the University of Pittsburgh Accelerometer Data Coordinating Center from the clinics via a proprietary data transfer system, known as data stream, designed by the Epidemiology Data Center (EDC) at the University of Pittsburgh. Data stream was loaded on all designated computers, at each site and was set to run automatically each day. In addition to transferring all files, the data stream program also created an archive of the transferred files on the local computer and notified a designated staff member via email, as to which files had been sent and received by the data coordinating center.

Data from the accelerometers were processed, and screened for wear time. Non-wear was defined as at least 60 consecutive minutes of zero counts with allowance for up to two minutes of observations greater than zero counts per minute. Wear time was determined by subtracting non-wear time from the total observation time for that day. Participants must have had accelerometer data that included 10 hours of wear time on 4 or more valid days to be included in the final analyses.[68] Only days with 10 or more hours of wear time were utilized to calculate mean daily physical activity and sedentary behavior.

Average total activity counts per day were calculated using summed daily counts detected over wear periods for counts recorded on the horizontal axis. The sum of the activity counts were then related to activity intensity and categorized based on validated activity count cut-points. Time in minutes spent in different activity intensities were calculated using count ranges corresponding to sedentary, light (1-2.99 METs), moderate (3-5.99 METs) and vigorous (≥ 6 METs) intensity activity. [A MET is an estimate of relative intensity such that one MET represents the energy expenditure for an individual at rest whereas a 10 MET activity requires 10 times that amount]. Freedson cut-points for adults corresponding to sedentary behavior (0-99 cts/min), light intensity (100-1751 cts/min), moderate intensity (1752-5724 cts/min), and vigorous intensity ($\geq$ 5725 cts/min) activity were used.[131]

7.3.3 Eligibility and Recruitment

Twenty-three of the remaining 26 DPP sites agreed to participate in the accelerometer study. All remaining DPPOS participants at contributing sites, that were not confined to a wheelchair and able to walk, were eligible for study inclusion. Participation in the ancillary study was optional and all recruitment, consent, and enrolling of participants was conducted by clinic staff at each site. I conducted all recruitment, consenting, and enrollment of participants at the Pittsburgh site. Enrollment was conducted from October 2010 to June 2012. A total of 1794 participants from 23 sites were enrolled in the Accelerometer Ancillary Study (Figure 7.1).

7.3.4 Enrollment and Retention

At the beginning of the enrollment period for the accelerometer ancillary study there were 2542 DPPOS participants from all 26 sites across the United States (Figure 7.2). In this cohort, an estimated 1932 participants were actively attending scheduled clinic visits at sites participating in the accelerometer ancillary study. Overall, 1794 (92.8%) of the active participants at enrolled sites consented to participate in the accelerometer study. Of the 138 participants not consented, 9 were ineligible due to either cognitive impaired or because they were non-ambulatory and the remaining 131 either declined to participate or did not come in for a clinic visit during the enrollment period.

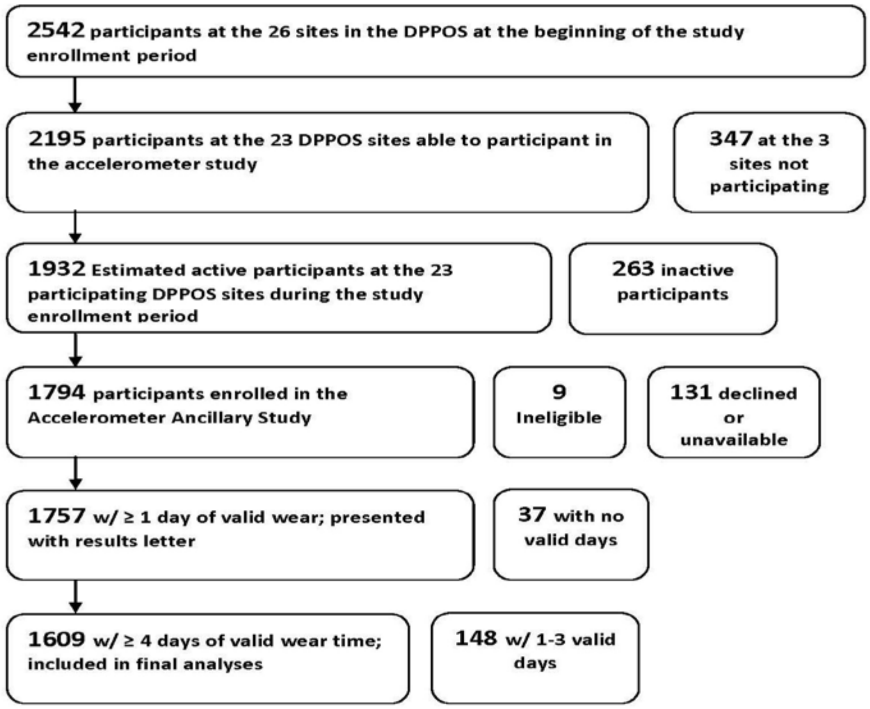


Figure 7.2 Enrollment and retention of DPPOS Accelerometer ancillary study participants

Seventeen hundred and fifty-seven of the 1794 participants (97.9%) that enrolled in the study had at least one valid day of 10 or more hours of wear time and were issued a results letter (Figure 7.2). The letters contained the participant's personal values for moderate-vigorous intensity activity, light intensity activity, total activity (light + moderate-vigorous activity), and sedentary time in both minutes and hours per day, as well as, comparison values from the combined NHANES 2003-04 and 2005-06 study cohorts. Of the participants with ≥1 valid day, 1609 (91.5% of enrolled participants) met the requirement of at least 4 days of valid monitor wear and were therefore included in all final analyses of activity-related outcome variables.

7.3.5 Participant Characteristics

Demographic data for the 1609 individuals included in the final analyses is presented in table 7.1. At the time the study was conducted, the 1794 participants who enrolled in the Accelerometer Ancillary Study had a mean age of 63.67 years and 69.57% were female. The cohort was 52.5% Caucasian, 18% African-American, 17% Hispanic American, 5% Asian or Pacific Islander-American, and 7% American Indian (table 7.1). There were no significant demographic or randomization differences between the subpopulation of individuals that completed 4 or more days and those individuals that did not. ($p < 0.05$ for all variables)

Table 7.1 Basic demographic variables and randomized arm assignment for all individuals enrolled in the DPPOS accelerometer study and for those individuals with at least 4 valid days of recorded wear time.

	All Enrolled Participants	**Participants with 4 or more valid days**
	N= 1794	**N=1609**
Mean Age	63.67 (SEM 0.26)	63.69 (SEM 0.24)
Gender	69.57 % female	69.86 % female
Race		
Caucasian	52.5 %	53 %
African-American	18 %	18 %
Hispanic-American	17 %	17 %
Asian or Pacific Islander- American	5 %	5 %
American Indian	7 %	7 %
Not given	.05 %	<.05 %
Randomized arm		
DPP Placebo	33.67 %	33.81 %
DPP Lifestyle	33 %	32.75 %
DPP Metformin	33.33 %	33.44 %

7.4 PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR LEVELS IN THE DPPOS COHORT

7.4.1 Statistical analyses

Descriptive statistics for accelerometer data are provided for all DPPOS participants with ≥ 4 valid days (10+ hours of wear time) of recording. Statistical comparisons using ANCOVA were performed to determine the effect of age, gender, race/ethnicity, and treatment group on reported values of physical activity and sedentary behavior, controlling for the effects of the other covariates, as well as, wear time. Adjusted least-square means are presented for time spent sedentary and in light, moderate-vigorous (MVPA) and total (TPA) physical activity to provide a less biased assessment of differences in sedentary behavior and physical activity between important population sub-groups. Age was included as a continuous variable in all models. However, additional models with age as a categorical variable (39-59, 60-69, and ≥ 70 years of age) were run, so that adjusted least-square means could be produced for categories of age.

7.4.2 Unadjusted estimates of physical activity and sedentary behavior

Unadjusted descriptive data for the 1609 D PPOS participants who completed the accelerometer study with ≥ 4 valid days of data is provided in table 7.2. Mean accelerometer wear time was 841.85 (SEM 2.06) minutes or about 14 hours per day. On average participants spent 556.27 (SEM 2.17) minutes per day (9.25 hours/day) in sedentary behaviors. Additionally, 285.57 (SEM 2.25) minutes per day (4.75 hrs./day), on average, were spent in total (light and moderate-vigorous intensity) physical activity. Specifically, an average of 15.33 (SEM 0.48) of the total activity minutes were spent in moderate-vigorous physical activity (MVPA). The median estimate for time spent in MVPA was 8.50 minutes/day.

Table 7.2 Unadjusted descriptive statistics for activity-related variables for the 1609 DPPOS participants with at least 4 valid days of wear time.

Activity-related variable	Mean (SEM)	Median	Lower Quartile	Upper Quartile	Range
Sedentary (min/day 0-99 ct)	556.27 (2.17)	557.71	500.86	612.60	717.43
Light activity (min/day 100-1951 ct)	270.24 (2.10)	257.86	210.83	321.67	584.54
Moderate-vigorous activity (min/day >=1952 ct)	15.33 (0.48)	8.50	2.67	20.86	246.00
Total activity (Light + MVPA)	285.57 (2.25)	273.86	223.14	342.17	605.73
Count avg (ct/min/d)	250.81 (20.11)	199.98	149.53	274.21	26751
Count total (per day)	210909 (15901)	169138	121278	238834	22108716
Estimated Wear time (min/day)	841.85 (2.06)	841.67	780.60	897.71	608.68

7.4.3 Identification of important covariates for physical activity and sedentary behavior levels in the DPPOS

Comparisons of values for wear time based on Mann Whitney-U statistics (not shown) indicated that wear time was significantly different (P<0.05) across treatment, gender, age, and race/ethnicity groups. ANCOVA analysis was then performed, to examine differences between mean values of sedentary time, time spent in light intensity, moderate-vigorous intensity, and total physical activity, across treatment arm, age, gender, and racial/ethnic groups. Several stages of model building were performed. The fully adjusted model contained data from 1605 of the total 1609 individuals; due to missing race/ethnicity information on 4 participants. All models included wear time and treatment group. Only the models for moderate-vigorous physical activity violate the assumptions of homoscedasticity (equal variance) and normality (data not shown). As a result, moderate-vigorous physical activity was transformed using the square root transformation.

For sedentary behavior, light intensity, and total physical activity there was a significant interaction between treatment group and average wear time, therefore the interaction term was included in the models for these outcome variables, but not moderate-vigorous physical activity. Based on the ANCOVA results, there were significant differences for sedentary, light intensity, and total physical activity ($P < 0.05$) across treatment groups in the model that controlled for treatment group and wear time only. Additionally, differences between age, gender, and race/ethnicity groups were also significant for all sedentary and physical activity variables (ANCOVA $P < 0.05$) when these variables were each independently added, as covariates, to the model that contained treatment group, average wear time, and the interaction term. There were no other first order interaction terms.

However, when all demographic variables were added to the model together treatment group was no longer significant in any of the full models. Additionally, the difference between gender groups was no longer significant in the full model for sedentary behavior.

7.4.4 Adjusted least square means for time spent in physical activity and sedentary behavior among DPPOS participants

Tables 7.3- 7.6 contain adjusted least square mean values for minutes per day of sedentary behavior, light intensity, square root transformed moderate-vigorous, and total physical activity for treatment group (table 7.3), gender (table 7.4), age group (table 7.5) and racial/ethnic group (table 7.6); adjusted for important covariates.

Overall, the differences between treatment groups in total physical activity were small (differences in adjusted mean values <10 minutes/day) and insignificant with a slightly lower adjusted mean value for sedentary behavior and slightly higher mean values for light intensity and transformed moderate-vigorous intensity physical activity in the DPP lifestyle group when compared to the metformin and placebo groups (table 7.3).

Table 7.3 Adjusted least-square means (95% CI) by treatment group for time (minutes/day) spent in different intensities of physical activity and sedentary behavior.[1]

Activity Variable	**DPP Placebo N=542**	**DPP Lifestyle N=526**	**DPP Metformin N=537**
Sedentary (min/day 0-99 ct)	555.78 (548.32, 563.24)	551.13 (543.64, 558.621)	556.05 (548.47, 563.64)
Light PA (min/day 100-1951 ct)	268.83 (261.83, 275.83)	272.19 (265.16, 279.22)	268.78 (261.66, 275.90)
SQRT Moderate-vigorous (MV) PA (min/day >=1952 ct)	3.51 (3.33, 3.70)	3.72 (3.53, 3.91)	3.54 (3.35, 3.73)
Total PA (Light + MV PA) min/day	286.12 (278.66, 293.58)	290.77 (283.28, 298.26)	285.85 (278.26, 293.43)

PA= Physical activity , * Significantly different than reference group: DPP Placebo, P<.05

[1] All values are adjusted for average wear time, age, race/ethnicity, and gender. Sedentary behavior and light activity are adjusted for treatment group*average wear time.

The adjusted mean value for light intensity physical activity (table 7.04) was significantly higher in females when compared to males (275.51 versus 264.36 minutes/day, p=0.005). Conversely, the adjusted mean value for the square root of moderate-vigorous physical activity was lower in females when compared to males (p< 0.001) Overall, differences in sedentary time and total physical activity between males and females was small and insignificant.

Table 7.4 Adjusted least-square means (95% CI) by gender for time (minutes/day) spent in different intensities of physical activity and sedentary behavior. [2]

Activity Variable	**Female N=1121**	**Male N=484**
Sedentary (min/day 0-99 ct)	552.99 (547.25, 558.73)	555.65 (547.91, 5563.39)
Light PA (min/day 100-1951 ct)	275.51* (270.12, 280.90)	264.36 (257.09, 271.63)
SQRT Moderate-vigorous (MV) PA (min/day >=1952 ct)	3.07* (2.93, 3.21)	4.11 (3.92, 4.30)
Total PA (Light + MV PA) min/day	288.91 (283.17, 294.65)	286.25 (278.50, 293.99)

PA= Physical activity , SQRT= square root,
* Significantly different than reference group: Males, P<.05

[2] All values are adjusted for average wear time, age, race/ethnicity, and gender. Sedentary behavior and light activity are adjusted for treatment group*average wear time.

In general, adjusted mean sedentary time increased with age while both light intensity and moderate-vigorous intensity physical activity decreased, as age increased (table 7.5). Differences in adjusted mean values for sedentary and light intensity activity were significantly different (P< 0.0001) in all age groups, when compared to the youngest age group (39-59 years). As age increased accelerometer measured sedentary behavior increased and all intensities of physical activity decreased.

Table 7.5 Adjusted least-square means (95% CI) by age group for time (minutes/day) spent in different intensities of physical activity and sedentary behavior.[3]

Activity variable	39-59 years N=569	60-69 years N=606	70+ years N=434
Sedentary (min/day 0-99 ct)	541.55 (534.03, 5449.07)	549.04* (541.82, 556.25)	576.67* (568.32, 585.02)
Light PA (min/day 100-1951 ct)	278.81 (271.75, 285.86)	274.71* (267.95, 281.47)	252.97* (245.14, 260.80)
SQRT Moderate-vigorous (MV) PA (min/day >=1952 ct)	4.19 (4.00, 4.38)	3.67* (3.48, 3.85)	2.77* (2.56, 2.98)
Total PA (Light + MV PA) min/day	300.35 (292.82, 307.87)	292.86* (285.65, 300.07)	265.23* (256.88, 273.58)

PA= Physical activity, **SQRT= square root**,
* Significantly different than reference group: 39-59 years, P< .05

[3] **All values are adjusted for average wear time, treatment group, gender, and race/ethnicity. Sedentary behavior and light activity are adjusted for treatment group*average wear time.**

Comparisons across racial/ethnic groups (table 7.6) revealed greater similarities between the Black non-Hispanic, white non-Hispanic, and Asian or Pacific Islander non-Hispanic groups for sedentary behavior and light intensity physical activity, with greater departures in values for the Hispanic and Native American groups.

Adjusted mean values for sedentary time were significantly lower for Hispanics (529.02 minutes/day, $p<0.0001$) and Native Americans (546.60 minutes/day, $p=0.04$) when compared to White non-Hispanics (563.10 minutes/day).

Table 7.6 Adjusted least-square means (95% CI) by race/ethnicity for time (minutes/day) spent in different intensities of physical activity and sedentary behavior.[4]

Activity variable	Asian N=83	Black N=285	Hispanic N=275	Native American N=109	White N=853
Sedentary (min/day 0-99 ct)	564.41 (548.02,580.79)	568.47 (559.41, 577.54)	529.02* (519.94, 538.10)	546.60* (531.90, 561.30)	563.10 (557.79, 568.43)
Light PA (min/day 100-1951 ct)	255.04 (239.66,270.41)	259.49 (250.98, 268.00)	294.10* (285.57, 302.62)	279.28* (265.48, 293.08)	261.77 (256.77, 266.77)
SQRT Moderate-vigorous (MV) PA (min/day >=1952 ct)	4.17* (3.76, 4.59)	3.14 * (2.92, 3.37)	3.80* (3.57, 4.03)	3.33 (2.96, 3.70)	3.51 (3.37, 3.64)
Total PA (Light + MV PA) min/day	277.49 (261.11, 293.88)	273.42 (264.35, 282.49)	312.88* (303.79, 321.96)	295.30* (280.60, 310.00)	278.80 (273.47, 284.12)

PA= Physical activity , **SQRT= square root**, * Significantly different than reference group: White, P<.05

[4] All values are adjusted for average wear time, treatment group, gender, and age group. Sedentary behavior and light activity are adjusted for treatment group*average wear time.

For light intensity physical activity adjusted mean values were significantly higher for Hispanics (294.10 minutes/day, $p<0.0001$) and Native Americans (279.28 minutes/day, $p= 0.02$) when compared to White non-Hispanics (261.77 minutes/day). For the square root of moderate-vigorous physical activity adjusted mean values for Asian or Pacific Islander non-Hispanics and Hispanics were significantly higher compared to non-Hispanic whites ($p=0.003$ and $p=0.03$, respectively); while the adjusted mean values for Native Americans and Black non-Hispanics were lower ($p=0.37$ and $p=0.006$, respectively).

7.4.5 Summary

Overall, when examining potential covariates, the largest differences between groups appeared to be across categories of age with increasing amounts of sedentary behavior and decreasing amounts of light and moderate-vigorous physical activity as age category increased. As a whole, there were also significant differences in adjusted means between racial/ethnic groups in the fully adjusted model for all activity-related outcome variables. Likewise, differences in gender were also significant for specific intensities of physical activity in the fully adjusted model, but not for total physical activity or sedentary behavior. Finally, although there were small differences between treatment groups in mean time spent sedentary and mean time spent in different intensities of physical activity, these differences were not statistically significant after controlling for the effects of age, gender, race/ethnicity, and wear time. Therefore, comparisons between the physical activity and sedentary behavior levels in the

DPPOS and NHANES populations should consider age and, if possible, gender and race/ethnicity in the research design, as important covariates.

7.5 NHANES 2003-06 COMPARISON POPULATION

To provide a basis for drawing conclusions about the physical activity and sedentary behavior levels reported from the DPPOS cohort, this effort compared the DPPOS cohort and a population representative cohort of similar aged adults. The National Health and Nutrition Examination Survey Population (NHANES) from 2003-04 and 2005-06 was chosen as t he comparison population for two major reasons. First of all, when weighting procedures are properly used, NHANES provides a large population representative sample for comparison. Secondly, accelerometer data, from the ActiGraph accelerometers that were used to collect data on physical activity and sedentary behavior in NHANES from 2003-2006, has been previously shown to be comparable to the data collected from the newer generations of ActiGraph GT3X accelerometers used in the DPPOS cohort; provided that the results from both accelerometer models are based on one axis (the vertical axis).[243,244]

7.5.1 Statistical analyses for NHANES descriptive statistics

To comply with the 10 year age categories utilized in the sampling design of NHANES, individuals that were 39 years of age or younger were not included from the NHANES datasets. Therefore, all presented NHANES data is for individuals aged ≥ 40 years who participated in the accelerometer study and had ≥ 4 days of 10 or more hours of wear time. Calculations of means and standard errors for NHANES data were performed utilizing weighting procedures, based on the complex sampling design. Reweighting of the population was done to adjust for unequal probabilities of selection and non-response prior to the analysis of accelerometer data and utilized modified code provided by NCI (National Cancer Institute) for NHANES. Data for both the 2003-04 and 2005-06 cycles were reweighted for age, gender, race/ethnicity, and BMI.

For the sub-sample of individuals from NHANES 2003-04 and 2005-06 that provided fasting blood samples for the fasting plasma glucose (FPG) test; the sampling weights provided for the *fasting subsample* by the CDC were used instead of the examination weights. Likewise, for the smaller sample of fasting participants that completed an oral glucose tolerance test (OGTT) the sampling weights provided for the *OGTT subsample* were used instead of the examination weights. The same reweighting procedures were used in both of these sub-samples. Fasting sub-sample weights were also converted to a four year data set (4 year weights). Because the OGTT was only given in the 2005-2006 cycle; 2 year weights were utilized.

Diabetes status was determined on the basis of glucose tolerance and included categories of normal glucose tolerance, impaired glucose tolerance, and diabetes mellitus. For the fasting subsample participants, diabetes status was determined on the basis of reported diabetes medication usage and the results of the FPG test. For the OGTT subsample participants, diabetes status was determined on the basis of reported diabetes medication usage and the results of the oral glucose tolerance test (OGTT). Identification of impaired glucose tolerance and diabetes mellitus for the FPG and OGTT tests were made in accordance with the ADA guidelines.[2]

7.5.2 NHANES participant characteristics

A total of 4376 adults age ≥ 40 years, in the general NHANES 2003-04 and 2005-06 combined cohort, had at least 4 days with ≥ 10 hours of monitor wear time. 1839 of these individuals were also randomly selected to participate in the morning blood draw and therefore were included in the *fasting subsample*. 654 of those 1839 individuals in the *fasting subsample* were also selected to participate in the oral glucose tolerance test (*OGTT subsample*).

Population weighted estimates for age, gender, race/ethnicity, and diabetes status are provided in table 7.7. The weighted mean (SEM) age of participants was 56.9 (0.43), 57.3 (0.45), and 56.9 (0.73) years for all individuals, the fasting subsample, and the *OGTT subsample* participants, respectively. Between 76% and 78% of individuals in each subgroup self-identified as non-Hispanic White and close to 53% were female. Differences in the weighted demographic variables across the three groups (all participants, *fasting subsample* participants, and *OGTT subsample* participants) were small, as w as expected, due to the weighting and reweighting procedures used for each population subgroup.

Table 7.7 Population weighted demographic data for participants age ≥40 years, with 4+ valid days of accelerometer data from NHANES 2003-06.

	All Participants N= 4376	**Fasting sample participants N= 1839***	**OGTT sample participants N= 654****
Mean(SEM) age	56.9 (0.43)	57.3 (0.45)	56.9 (0.73)
Gender (female)	52.6 %	53.3%	52.8 %
Race/ethnicity			
Mexican American	5.8 %	6.1 %	5.5 %
Other Hispanic	2.7 %	2.0 %	2.4 %
White, non-Hispanic	76.7 %	76.8 %	77.7 %
Black, non-Hispanic	10.4 %	10.0 %	9.3%
Other (including mixed race)	4.4 %	5.2 %	5.0 %
Diabetes status			
Normal glucose tolerance	NA	48.8 %	70 %
Impaired glucose tolerance	NA	34.8 %	20 %
Diabetes	NA	16.4 %	10 %

OGTT= oral glucose tolerance test SEM= standard error of the mean NA=Not available
* weighted values based on those individuals that participated in the fasting tests for 2003-04 & 2005-06.
** weighted values based on participants that took part in the oral glucose tolerance test (given only in 2005-06)

Additionally, the results on table 7.7 indicate that a higher percentage of individuals were identified as having diabetes in the *fasting subsample* group when compared to the *OGTT subsample* group (16.4% versus 10%). Likewise, a higher percentage of individuals in the *fasting subsample* were reported to have impaired glucose tolerance when compared to individuals in the *OGTT subsample* (34.8% versus 20%). It is unclear if this difference is the result of differences in population sampling or if it is the result of differences in the identification test used for diabetes status; since the FPG test was used as the primary identification tool for the *fasting subsample* and the oral glucose tolerance test was used as the primary identification tool for the *OGTT subsample*.

Therefore, to determine if the differences in diabetes status between the *OGTT subsample* and the *fasting subsample* may have resulted from the differential identification of diabetes and impaired glucose tolerance, by the FPG test and the oral glucose tolerance test (OGTT), a more detailed comparison of the FPG and OGTT results was conducted in the subsample of individuals that completed both the FPG and OGTT. Agreement between the results of the FPG and OGTT tests for the identification of impaired glucose tolerance and diabetes mellitus was assessed via a sensitivity/specificity analysis for results from the FPG when compared to the gold standard, the OGTT. Additionally, descriptive comparisons were made between the mean values for time spent in physical activity and sedentary behavior for the *fasting subsample* and *OGTT subsample* participants to examine if differences between other population characteristics of the subsamples resulted in differences in accelerometer reported physical activity or sedentary behavior.

7.5.3 Comparison of diabetes status classification between the oral glucose tolerance test and fasting plasma glucose

654 Individuals aged ≥ 40 years from the 2005-06 cycle of NHANES completed both the FPG and the OGTT. Diabetes status was determined according to the ADA guidelines for both the FPG and OGTT.[2] The 45 Individuals who report taking diabetes medications at the time of the examination and blood draw were not included in the comparison of results between the two measures. Table 7.8 contains the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the FPG when compared to the gold standard measure, the OGTT, based on population weighted estimates (using the fasting subsample weights) from the remaining 609 individuals.

The sensitivity and specificity can be defined as the proportion of actual positives which are correctly identified and the proportion of actual negatives which are correctly identified, respectively. Additionally, the PPV and the NPV can be thought of as the ratio of true positives to combined true and false positives and the ratio of true negatives to combined true and false negatives, respectively.

Table 7.8 Sensitivity, specificity, PPV, and NPV for the identification of impaired glucose tolerance and type 2 diabetes mellitus, by fasting plasma glucose (FPG); when compared to results from the oral glucose tolerance test (OGTT).[5]

	Sensitivity	Specificity	PPV	NPV
Type 2 diabetes mellitus	47.64	99.93	98.68	94.66
Impaired glucose tolerance	58.43	71.44	25.88	90.96
Impaired glucose tolerance & type 2 diabetes mellitus	74.60	63.43	45.77	85.78

PPV= positive predictive value, NPV= negative predictive value

For the diagnosis of type 2 diabetes the FPG was very good at identifying those that did not have diabetes (specificity 99.93 and NPV 94.66). Additionally, more than 98% of the diabetes cases identified in this population by the FPG were confirmed by the OGTT. However, more than 50% of true diabetes cases were missed by the FPG (sensitivity 47.64).

The OGTT confirmed negative findings for impaired glucose tolerance from the FPG test more than 90% of the time and the FPG test identified a fair proportion of all true impaired glucose tolerance cases (71.44%). Conversely, only about 25% of the cases of impaired glucose

[5] Results are based on population weighted values from the 609 individuals from NHANES 2005-06, aged ≥40 years, with 4+ days of accelerometer data, not taking diabetes medication w/ both OGTT and FPG results. ADA criteria for the FPG and OGTT results were used to identify impaired glucose tolerance and type 2 diabetes mellitus.

tolerance identified by the FPG test were confirmed positive by the OGTT and the FPG test only identified about 58% of the true impaired glucose tolerance cases. Although the sensitivity and specificity of the FPG test has been shown to vary across populations, the results of this analysis are in line with the results of other studies that reported sensitivity and specificity values for the FPG (compared to the OGTT) from adult populations in the United States,[245] Europe,[246] and Korea.[247]

These results suggest that there are important differences between the FPG and the OGTT for identifying individuals as having impaired glucose tolerance and diabetes. Therefore, when the results for activity outcomes from NHANES are examined by diabetes status groups (in addition to age and gender) it will be important to report findings from both the *OGTT subsample* and the larger *fasting subsample* for mean values of physical activity and sedentary behavior. This will be particularly important if the differences are large enough to affect the interpretation of comparisons between the NHANES and DPPOS cohorts.

7.5.3 Physical activity and sedentary behavior levels for individuals in the fasting subsample and for individuals in the OGTT subsample

Descriptive statistics, based on popul ation weighted estimates for average wear time, sedentary behavior, light intensity, moderate-vigorous intensity, and total physical activity (light + moderate-vigorous intensity) in minutes/day are presented in table 7.9 f or the *fasting subsample* and in table 7.10 for the *OGTT subsample*. Population weighted estimates for average total counts/ day and average counts/minute are also presented.

Table 7.9 Descriptive statistics based on population weighted estimates of activity-related variables for individuals aged ≥40 years in the NHANES 2003-06 fasting sample group. [6]

Activity-related variable	Mean (SEM)	Median	Lower Quartile	Upper Quartile	Range
Sedentary (min/day 0-99 ct)	503.99 (3.02)	495.60	421.47	579.71	1039.82
Light activity (min/day 100-1951 ct)	333.68 (2.68)	329.78	261.22	401.33	725.36
Moderate-vigorous activity (min/day >=1952 ct)	21.25 (0.81)	14.79	4.69	31.04	206.40
Total activity (Light + MVPA)	354.94 (3.03)	349.26	278.02	430.00	745.02
Count avg (ct/min/d)	291.10 (4.93)	269.63	187.20	369.39	1146.40
Count total (per day)	249659 (4513.18)	231265	156078	315862	966574
Estimated Wear time (min/day)	858.93 (3.05)	848.47	789.65	907.60	769.63

On average, NHANES 2003-06 participants in the *fasting subgroup*, who were age ≥40 years and had at least 4 valid days (≥10 hours of wear time), had an average monitor wear time of 858.93 minutes or about 14.3 hours/ day. Additionally, on average these participants spent 503.99 (SEM 3.02) minutes/day (8.39 hours/day) in sedentary behavior and 354.94 (SEM 3.03) minutes/day (5.91 hours/day) in total physical activity. On average, 21.25 (SEM 0.81) minutes/day of their total physical activity was spent in moderate-vigorous intensity activities.

[6] with at least 4 valid days of accelerometer wear time.

Mean values for daily sedentary behavior and physical activity variables appear to be similar between the *fasting subsample* (table 7.9) and the smaller *OGTT subsample* (table 7.10). On average, NHANES 2005-06 participants in the OGTT subgroup, who were age ≥40 years and had at least 4 valid days, spent 501.79 (SEM 5.09) minutes/day (8.36 hours/day) in sedentary behavior and 362.48 (SEM 5.66) minutes/day (6.04 hours/day) in total physical activity (Table 7.10). On average, 22.38 (SEM 1.38) minutes/day of their total physical activity was spent in moderate-vigorous intensity activities.

Table 7.10 Descriptive statistics based on population weighted estimates of activity-related variables for individuals aged ≥40 years in the NHANES 2005-06 OGTT sub-sample. [7]

Activity-related variable	Mean (SEM)	Median	Lower Quartile	Upper Quartile	Range
Sedentary (min/day 0-99 ct)	501.79 (5.99)	494.42	413.14	588.90	973.07
Light activity (min/day 100-1951 ct)	340.10 (5.17)	338.75	264.77	410.40	719.02
Moderate-vigorous activity (min/day >=1952 ct)	22.38 (1.38)	15.73	5.43	32.54	180.67
Total activity (Light + MVPA)	362.48 (5.66)	355.87	281.84	439.05	740.86
Count avg (ct/min/d)	301.18 (8.53)	274.58	196.63	386.85	1146.40
Count total (per day)	259483 (7508.03)	238647	165808	332233	301.18
Estimated Wear time (min/day)	864.27 (5.09)	850.53	793.98	915.15	769.63

[7] with at least 4 valid days of accelerometer wear time.

Based on these results, there is no evidence of population level differences between the 2005-06 NHANES *OGTT subsample* and the 2003-04 and 2005-06 *fasting subsample* that may cause differences between the values reported for physical activity and sedentary behavior related outcome variables from the two subsamples. Therefore, no additional examination for the differences in population characteristics between the two subsamples was warranted.

7.5.4 Summary

There were no important differences in mean daily values for physical activity and sedentary behavior related variables between the NHANES 2005-06 *OGTT subsample* and the NHANES 2003-04 and 2005-06 combined *fasting subsample*. Therefore, it was decided to use only the larger *fasting subsample* for comparisons between the DPPOS cohort and the NHANES population when stratifying only by gender and age. However, the results of the sensitivity/specificity analysis and the small sample size of the *OGTT subsample* support including estimates of time spent in physical activity and sedentary behaviors from both the NHANES 2005-06 *OGTT subsample* and the NHANES 2003-06 *fasting subsample* for comparisons that are stratified by diabetes status. In this way, the larger *fasting subsample* can be used for the primary comparisons and the *OGTT subsample*, which uses a better method for assigning diabetes status, can be used to confirm the findings of the comparisons between the DPPOS cohort and the NHANES *fasting subsample* (when there are enough *OGTT subsample* participants to do so).

7.6 COMPARISON OF PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR BETWEEN DPPOS AND NHANES PARTICIPANTS

The results of previous studies suggest that glucose levels are related to higher levels of sedentary behavior and lower levels of physical activity.[39,40,44,45,209] Therefore, it would be expected that physical activity levels would be lower and sedentary behavior levels would be higher in the DPPOS cohort, when compared to a nationally representative sample of similar age and gender adults from the NHANES cohort. This is based on the fact that all individuals in the DPPOS cohort have been identified as having impaired glucose tolerance or type 2 diabetes compared to the NHANES *fasting subsample* in which nearly half of all individuals included in the comparison population had normal glucose tolerance at the time of the activity monitoring and blood draw (48.8% of those w/ ≥ 4 valid days of wear time).

Based on the same premise, for the comparisons that include diabetes status, it would be expected that the physical activity and sedentary behavior levels in the DPPOS cohort would be similar to individuals with diabetes and impaired glucose tolerance in NHANES. More specifically, because a previous DPPOS report [241] indicated that several years prior to this current data collection effort, more than half of all DPPOS participants had been diagnosed with diabetes, it would be expected that participants in the DPPOS would have physical activity and sedentary behavior levels more similar to individuals with diabetes in NHANES or at least in between those individuals with impaired glucose tolerance and those individuals with diabetes from NHANES.

7.6.1 Statistical analyses

Descriptive comparisons of DPPOS data to NHANES data were stratified by important covariates that were determined from the results of the ANCOVA analysis for the DPPOS population. Comparisons between the DPPOS population and similar aged individuals in the NHANES 2003-06 data set were performed using those NHANES 2003-06 adults, age ≥ 40 years with 4 or more valid days of monitoring, whose diabetes status was determined on the basis of the FPG test results (*fasting subsample*) and separately for the subgroup of individuals whose diabetes status was determined on the basis of the OGTT (*OGTT subsample*). Tests of trend across diabetes status groups for differences in sedentary behavior, light and moderate-vigorous intensity physical activity were performed for the NHANES *fasting subsample* using the Wald F test statistic generated from generalized ordinal logistic models. Wear time was tested as a potential covariate in all models. All models were stratified by gender and age category. Subgroups represented by less than 15 people were not included in the final assessments due to the potential loss of population representativeness and tests of trend were not performed on the *OGTT subsample* due to low numbers of individuals with diabetes in most age/gender subgroups.

Statistical analyses were performed using SAS 9.3 with the exception of the generalized ordinal logistic regression models and the assessment of trend for differences in time spent in physical activity and sedentary behavior by diabetes status group; which was performed in StataSE12.

7.6.2 Descriptive comparisons of DPPOS and NHANES physical activity and sedentary behavior levels stratified by age and gender

Overall, gender and age group stratified mean and standard error (SEM) values for physical activity and sedentary behavior outcome variables for the DPPOS cohort and the population weighted NHANES *fasting subsample* participants (≥40 years), indicate that males and females in the DPPOS were more sedentary and less likely to engage in light and total (light + moderate-vigorous) physical activity when compared to similar age and gender individuals from the NHANES fasting subsample (table 7.11 for females and 7.12 for males).

For both males and females the gap in mean values for sedentary behavior, light intensity, and total physical activity was widest in the youngest age group, where the DPPOS participants averaged greater than an hour more sedentary time per day (551.02 vs. 479.33 minutes/day in females and 551.56 vs. 481.12 minutes/day in males) and greater than an hour less light intensity physical activity per day (292.23 vs. 356.56 minutes/day in females and 290.28 vs. 358.64 minutes/day in males) when compared to the population weighted NHANES *fasting subsample*. Although statistical comparisons could not be performed between the estimates for NHANES and the DPPOS cohorts (due to differences in sampling design and violations of normality and equal variance), the size of the standard errors for all estimates are very small (< 10 minutes) compared to the differences in time spent in sedentary behavior, light intensity and total physical activity. This suggests that these differences are likely to be statistically significant.

However, estimates of moderate-vigorous physical activity were more similar between the DPPOS cohort and the population representative sample from the 2003-06 combined NHANES *fasting subsample* with some age/gender groups within the DPPOS reporting higher point estimates of moderate-vigorous physical activity than the comparable age/gender group from the population weighted 2003-06 combined NHANES *fasting subsample*. Specifically, females aged 60-69 years and ≥70 years of age had slightly higher estimates of mean (SEM) minutes/day of MVPA when compared to weighted values for NHANES females in the same age group (13.31 SEM 1.01 vs. 11.75 SEM 0.86 and 7.46 SEM 0.83 vs . 6.52 SEM 0.81, respectively) and males aged 60-69 years and ≥70 years of age had slightly higher point estimates of mean minutes/day of MVPA when compared to NHANES males in the same age group (21.27 SEM 1.45 vs. 18.74 SEM 1.29 and 13.33 SEM 1.43 vs. 10.71 SEM 1.51, respectively). However, it is not known if these differences could be statistically significant.

Table 7.11 Mean values for sedentary behavior and physical activity-related variables for female participants from the DPPOS and the NHANES 2003-06 fasting subsample (≥40 years of age) by age group

	39-59 years		**60-69 years**		**≥ 70 years**	
	DPPOS N= 466	**NHANES 2003-06 N= 424***	**DPPOS N= 402**	**NHANES 2003-06 N= 241***	**DPPOS N= 256**	**NHANES 2003-06 N= 251***
Sedentary (min/day 0-99 ct)	551.02 (3.82)	479.33 (6.80)	546.58 (4.05)	506.62 (12.72)	569.00 (5.51)	550.52 (6.53)
Light PA (min/day 100-1951 ct)	292.23 (3.74)	356.56 (4.81)	277.72 (4.12)	334.60 (7.39)	244.97 (4.81)	270.50 (6.22)
Moderate-vigorous (MV) PA (min/day >=1952 ct)	16.14 (0.75)	20.70 (1.07)	13.31 (1.01)	11.75 (0.86)	7.46 (0.83)	6.52 (0.81)
Total PA (Light + MVPA)	308.37 (3.95)	377.26 (5.04)	291.03 (3.96)	346.34 (7.59)	252.43 (5.04)	277.02 (6.47)
Estimated Wear time (min/day)	859.40 (3.71)	856.59 (4.18)	837.61 (4.39)	852.97 (10.77)	821.43 (4.97)	827.54 (7.10)

PA= Physical activity , * Population size prior to weighting

Table 7.12 Mean values for sedentary behavior and physical activity-related variables for male participants from the DPPOS and the NHANES 2003-06 fasting subsample (≥40 years of age) by age group

	39-59 years		60-69 years		≥ 70 years	
	DPPOS N= 103	NHANES 2003-06 N= 432*	DPPOS N= 204	NHANES 2003-06 N= 224*	DPPOS N= 178	NHANES 2003-06 N= 294*
Sedentary (min/day 0-99 ct)	551.56 (11.17)	481.12 (5.56)	559.68 (6.30)	535.21 (11.42)	572.43 (6.50)	590.86 (8.81)
Light PA (min/day 100-1951 ct)	290.28 (9.61)	358.64 (5.24)	264.41 (5.65)	309.36 (5.28)	227.20 (5.85)	254.29 (5.57)
Moderate-vigorous (MV) PA (min/day >=1952 ct)	30.83 (2.33)	34.16 (1.35)	21.27 (1.45)	18.74 (1.29)	13.33 (1.43)	10.71 (1.51)
Total PA (Light + MVPA)	321.11 (10.56)	392.79 (5.84)	285.68 (6.12)	328.10 (5.83)	240.53 (6.31)	265.00 (6.07)
Estimated Wear time (min/day)	872.68 (8.54)	873.92 (3.59)	845.36 (6.09)	863.31 (10.56)	812.96 (5.97)	855.86 (8.75)

PA= Physical activity, * Population size prior to weighting

7.6.3 Descriptive comparisons of DPPOS and NHANES physical activity and sedentary behavior levels stratified by age, gender, and diabetes status

Based on the decision to include both the *fasting subsample* and the *OGTT subsample* in the comparisons with the DPPOS cohort, the primary comparisons between the DPPOS cohort and the larger *fasting subsample* from NHANES 2003-06 are presented first in figures 7.3 (moderate-vigorous intensity physical activity), 7.4 (light intensity physical activity), and 7.5 (sedentary behavior). The comparisons between the DPPOS cohort and the *OGTT subsample* from 2005-06 are presented afterward, in figures 7.6 (moderate-vigorous intensity physical activity) , 7.7 (light intensity physical activity), and 7.8 (sedentary behavior), to support the result of the primary comparison. For the *OGTT subsample*, some categories were represented by less than 15 individuals and were not reported in figures 7.6-7.8 due to concerns over the possible loss of population representativeness (all values are presented in appendix A). Additionally, tests of trend could not be provided for the *OGTT subsample* due to small sample size.

7.6.3.1 Comparisons for different intensities of physical activity

Figure 7.3 illustrates the differences between mean minutes/day of moderate-vigorous physical activity (MVPA) for the DPPOS cohort and individuals from the combined NHANES 2003-04 and 2005-06 *fasting subsample*. For the NHANES *fasting subsample*, although point estimates of MVPA were generally lower in individuals with diabetes and higher in normal glucose tolerant individuals, these trends were only significant in the youngest age groups of males ($p<0.004$) and females ($p<0.03$).

Point estimates for mean minutes/day spent in MVPA where higher for males in all age groups from the DPPOS cohort when compared to individuals with diabetes or impaired glucose tolerance in NHANES (30.83 vs. 23.99 & 28.54, 21.27 vs. 11.51 & 20.22, and 13.33 vs. 9.13 & 9.78, for the 39-59, 60-69, and ≥ 70 year age groups, respectively).

Additionally, DPPOS males aged 60-69 and ≥ 70 years had slightly higher point estimates for mean MVPA than similar aged normal glucose tolerant males from the NHANES *fasting subsample* (21.27 vs. 19.40 minutes/day and 13.33 vs. 13.03 minutes/day).

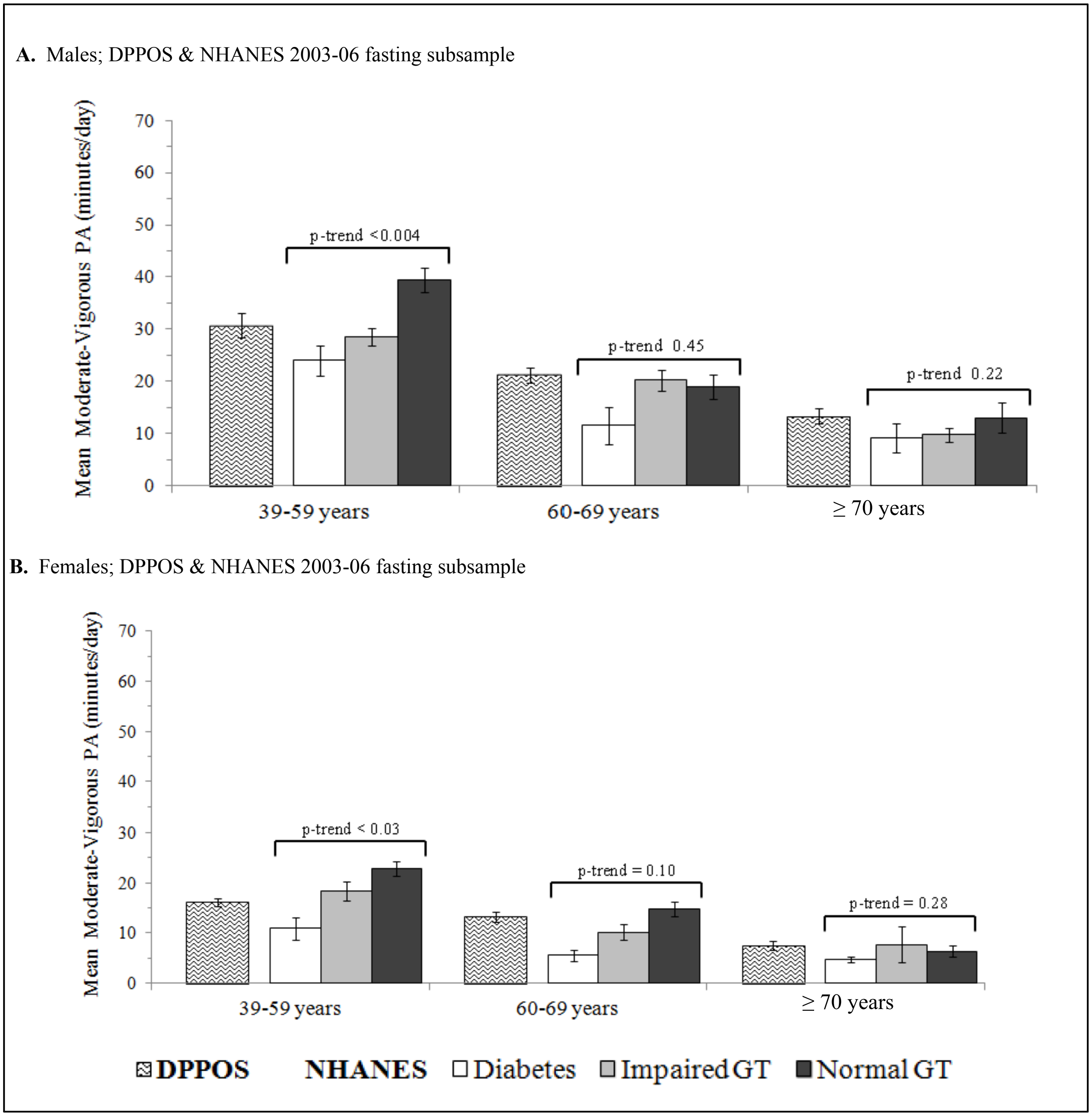


Figure 7.3 Mean minutes/day spent in moderate-vigorous activity by gender and age group for adults age ≥ 39 years (≥40 years for NHANES) with ≥ 4 valid days of monitoring. For the classification of diabetes status (NHANES participants), the fasting plasma glucose test was used. Wald f-statistic p-values were used for p-trend.

Females in all three age categories of the DPPOS cohort had higher point estimates for mean recorded MVPA when compared to similar aged females in the NHANES *fasting subsample* with diabetes (16.14 vs. 10.88, 13.31 vs . 5.99, and 7.46 vs . 4.64 minutes/day, respectively). Additionally, 60-69 year old DPPOS females had higher point estimates for reported MVPA when compared to females of similar age with impaired glucose tolerance from the *fasting subsample* (13.31 vs. 10.18 minutes/day).

DPPOS females age ≥ 70 years had similar point estimate for mean daily MVPA when compared to the females age ≥ 70 years with normal glucose tolerance from the NHANES *fasting subsample* (7.46 vs. 6.35 minutes/day). However, this finding was not confirmed by the *OGTT subsample* point estimate for the mean daily MVPA in females aged ≥ 70 years with normal glucose tolerance (10.19 minutes/day).

Figure 7.4 presents a comparison of time spent in light intensity physical activity (LPA) between the DPPOS participants and the NHANES fasting participants. All NHANES participants are presented by diabetes status group. For NHANES fasting males aged 40-59 and 60-69 years there were significant trends in mean LPA with lower recorded LPA among individuals with diabetes and higher recorded LPA among normal glucose tolerant individuals ($p<0.02$ and $p<0.01$, respectively).

A weak, non-significant trend, in the same direction, was seen in NHANES *fasting* males, aged ≥ 70 years ($p=0.44$). Although, point estimates for mean daily LPA tended to be lower in individuals with diabetes than individuals without diabetes for all age groups of NHANES fasting females, the trend in LPA across all three diabetes status group was only statistically significant in females aged 60-69 years ($p<0.03$).

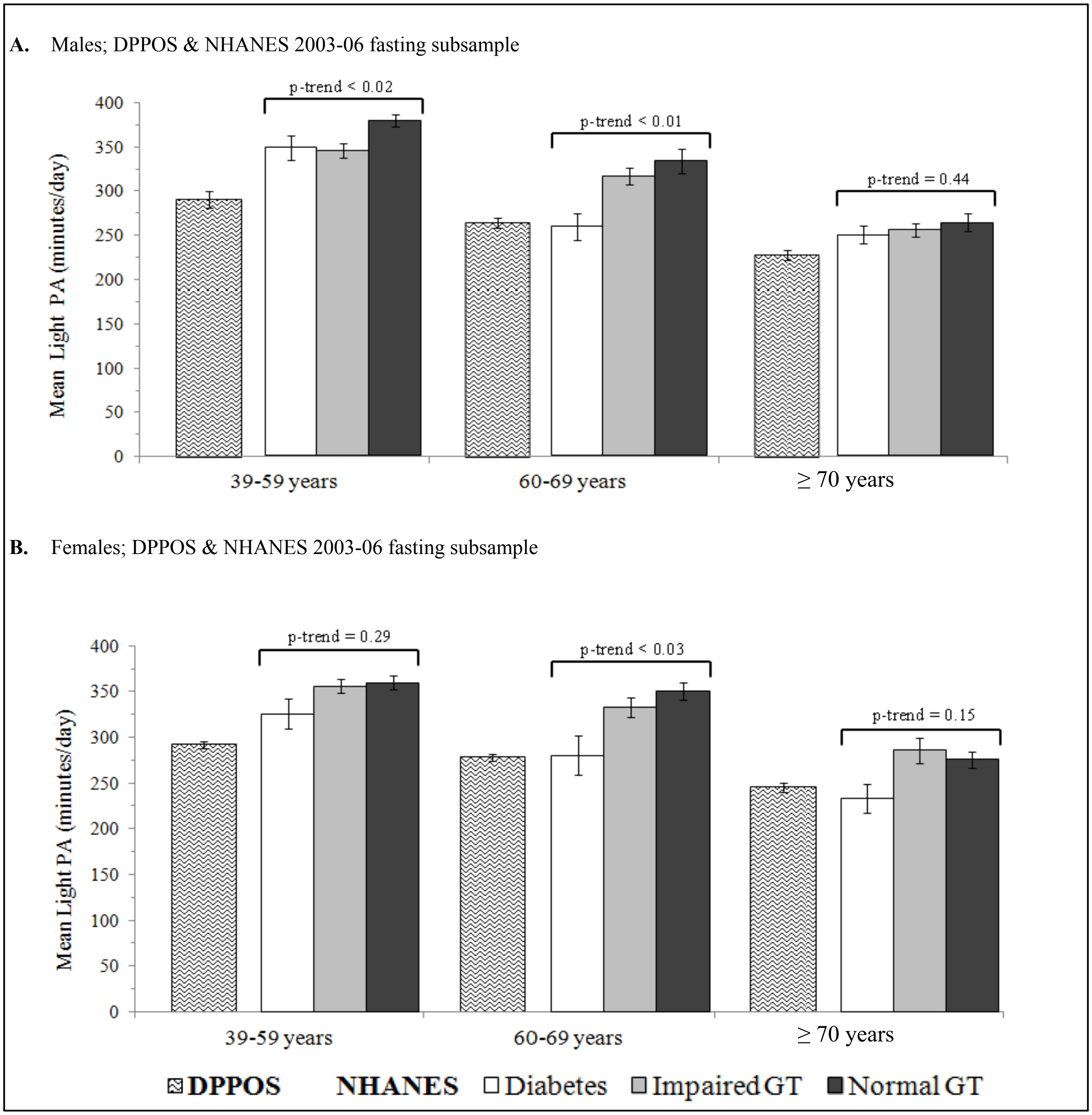


Figure 7.4 Mean minutes/day spent in light intensity physical activity by gender and age group for adults age ≥ 39 years (≥40 years for NHANES) with ≥ 4 valid days of monitoring. For the classification of diabetes status (NHANES participants), the fasting plasma glucose test was used. Wald f-statistic p-values were used for p-trend.

In general, daily averages of recorded LPA among DPPOS participants was lower than LPA among NHANES fasting sample participants with normal glucose tolerance or impaired glucose tolerance within the same age/gender group. Additionally, younger males and females (≤ 59 years of age) and older males (≥ 70 years of age) in the DPPOS had lower point estimates for mean minutes/day of LPA when compared to NHANES fasting sample participants in the same age/gender group.

However, point estimates for mean daily LPA in females aged 60-69 years were similar between the DPPOS and the NHANES fasting sample (277.72 vs. 280.14) and point estimates for daily mean LPA for 60-69 year old males and females ≥70 years of age were slightly higher in the DPPOS cohort compared to the individuals with diabetes in the NHANES fasting *subsample* (264.41 vs. 255.74 and 244.97 vs. 233.24, respectively). The trends in LPA across diabetes status groups was similar between the *fasting subsample* and the *OGTT subsample* and the levels of LPA were generally lower compared to the NHANES participants regardless of which measure of diabetes status was used.

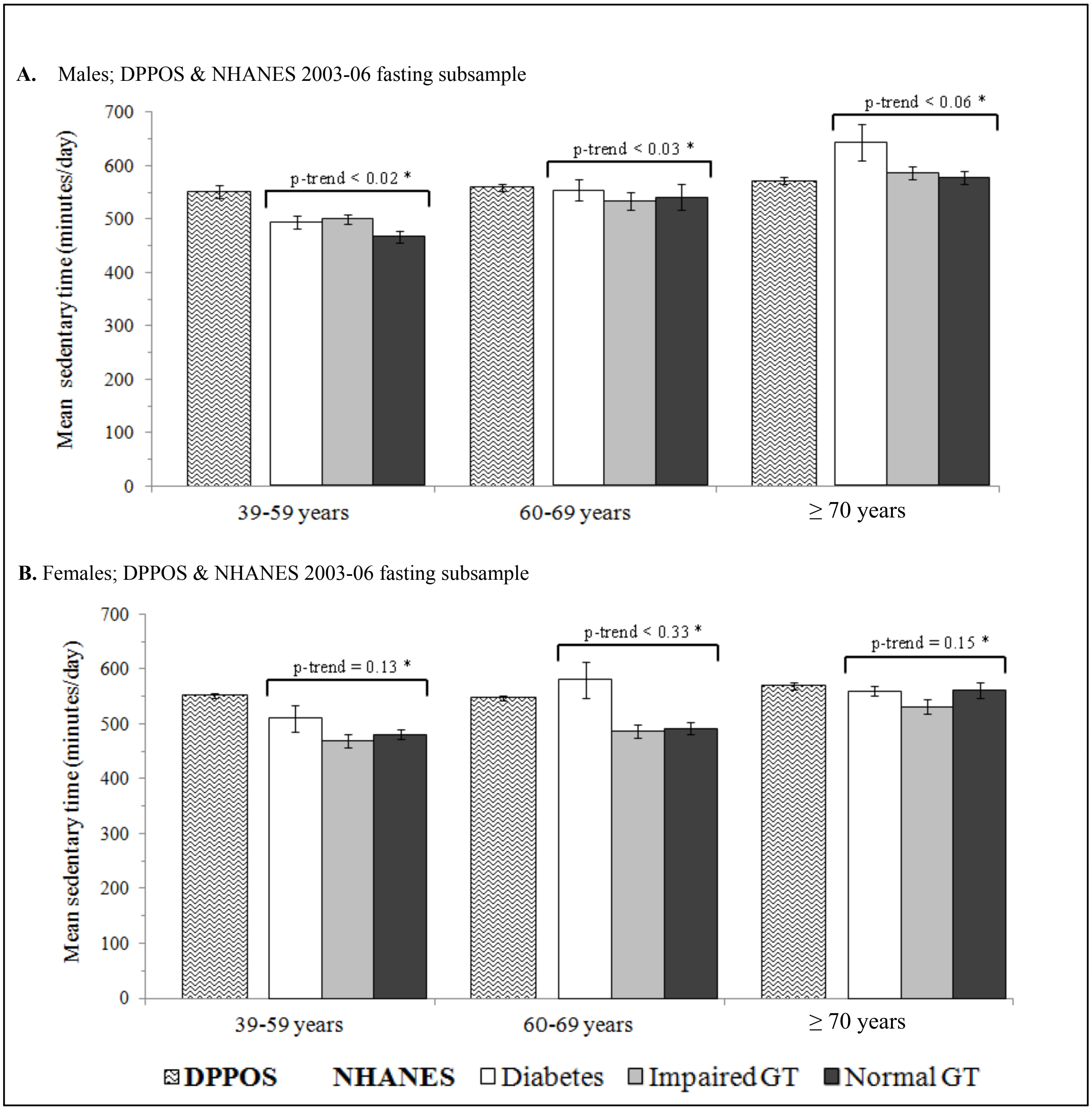
7.6.3.2 Comparisons for sedentary behavior

Figure 7.5 presents a graphical comparison of time spent sedentary in minutes/day between the DPPOS cohort and individuals from the NHANES 2003-04 and 2005-06 *fasting subsample*. All comparisons are presented by gender and age groups. For NHANES fasting males aged 40-59 and 60-69 years there were significant trends in mean sedentary time (controlling for wear time) with higher recorded sedentary time among individuals with diabetes and lower recorded sedentary time among normal glucose tolerant individuals ($p<0.02$ and p<0.03, respectively). The same trend was seen in NHANES fasting males, age ≥ 70 years, but was only borderline significant (p=0.06). Although point estimates for mean daily sedentary time were higher in individuals with diabetes than individuals without diabetes, for all age groups of females in the NHANES *fasting subsample*, the trends in sedentary time (controlling for wear time) across all three diabetes status group were not statistically significant.

Individuals in the DPPOS cohort spent more time, on average, in recorded sedentary behavior than individuals with normal glucose tolerance or individuals with impaired glucose tolerance in the same age/gender category from the NHANES *fasting subsample* (except for males aged ≥ 70 years).

Based on point estimates, DPPOS participants aged 39-59 years also typically spent more time, on average, in recorded sedentary behavior when compared to individuals with diabetes in NHANES (551.56 vs. 491.28 minutes/day in males, and 551.02 vs. 509.79 minutes/day in females). These findings are generally supported by the results from the *OGTT subsample* (figure 7.8).

The mean amount of recorded time spent sedentary was similar between 60-69 year old males from the DPPOS cohort and the NHANES *fasting subsample*. However, point estimates for time spent sedentary were lower for DPPOS participants, who were 60-69 year old females or were males ≥ 70 years old, when compared to similar gender/age individuals from NHANES (547.43 vs. 641.90, 546.58 vs. 579.98 minutes/day, respectively). Also, based on the *OGTT subsample* results females ≥ 70 years of age in the DPPOS cohort spent less time in sedentary behavior per day, on average, than similarly aged females in NHANES with diabetes (figure 7.6).



*** model includes wear time as a covariate**

Figure 7.5 Mean minutes/day spent in sedentary behaviors by gender and age group for adults age ≥ 39 years (≥40 years for NHANES) with ≥ 4 valid days of monitoring. For the classification of diabetes status (NHANES participants), the fasting plasma glucose test was used. Wald f-statistic p-values were used for p-trend.

7.6.3.3 OGTT subsample comparisons

The resulting values for time spent in different intensities of physical activity and sedentary behavior from the *OGTT subsample* support the relationships seen between different diabetes status groups within the NHANES *fasting subsample* and the DPPOS cohort. This is despite the fact that there are differences in specific values of physical activity and sedentary behavior between the *OGTT subsample* and the *fasting subsample*. For the DPPOS cohort and the NHANES *fasting and OGTT subsamples,* all values for time spent in moderate-vigorous intensity and light intensity physical activity, sedentary behavior, and other activity-related outcome variables are presented in appendices tables A.1 (males) and A.2 (females). The following section contains figures illustrating the means and standard errors for time spent in moderate-vigorous intensity physical activity (7.6), light intensity physical activity (7.7), and sedentary behavior (7.8) for the DPPOS cohort and the NHANES 2005-06 *OGTT subsample*.

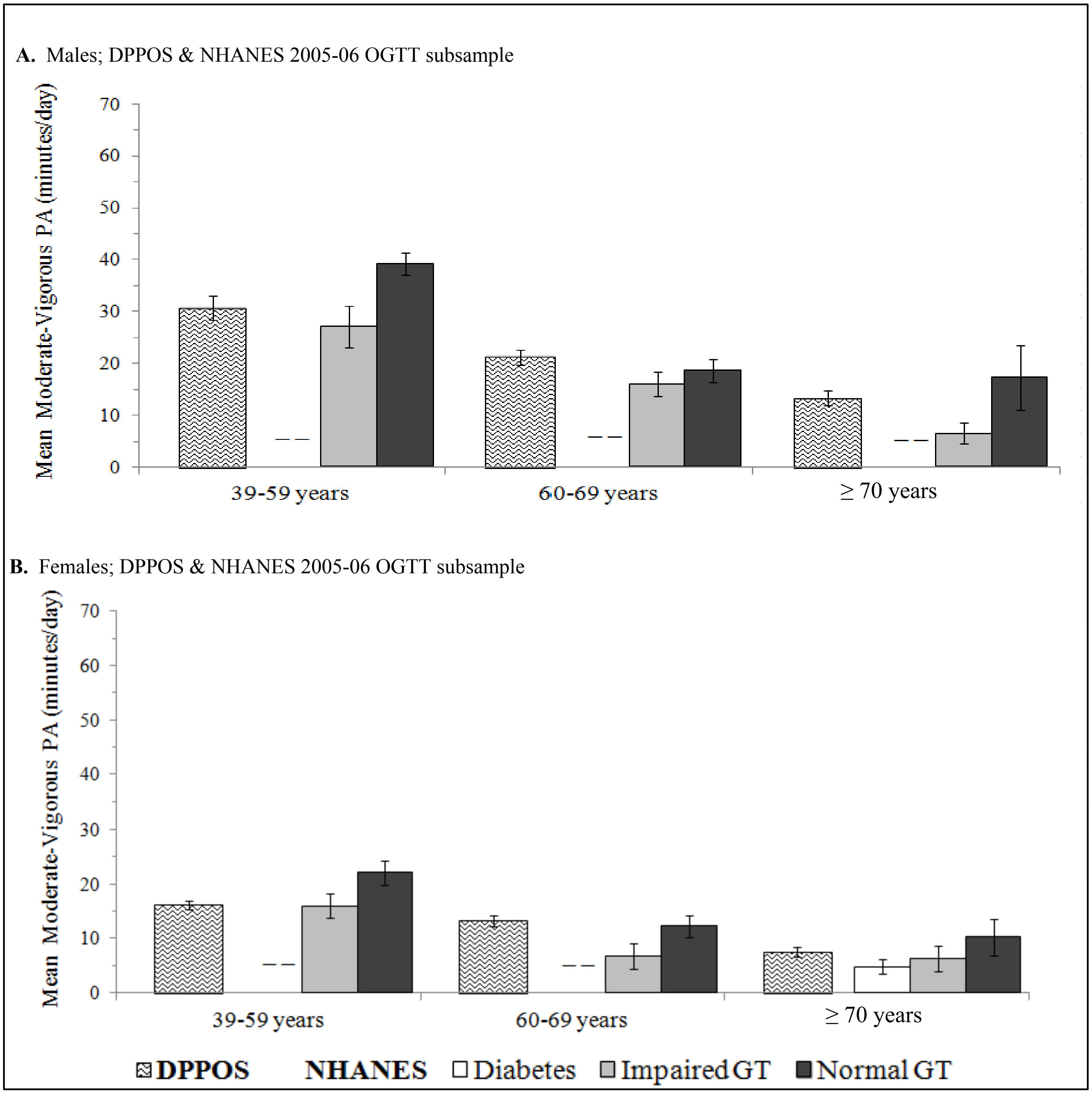


Figure 7.6 Mean minutes/day spent in moderate-vigorous activity by gender and age group for adults age ≥ 39 years (≥40 years for NHANES) with ≥ 4 valid days of monitoring. For the classification of diabetes status (NHANES participants), the oral glucose tolerance test was used. Wald f-statistic p-values were used for p-trend.

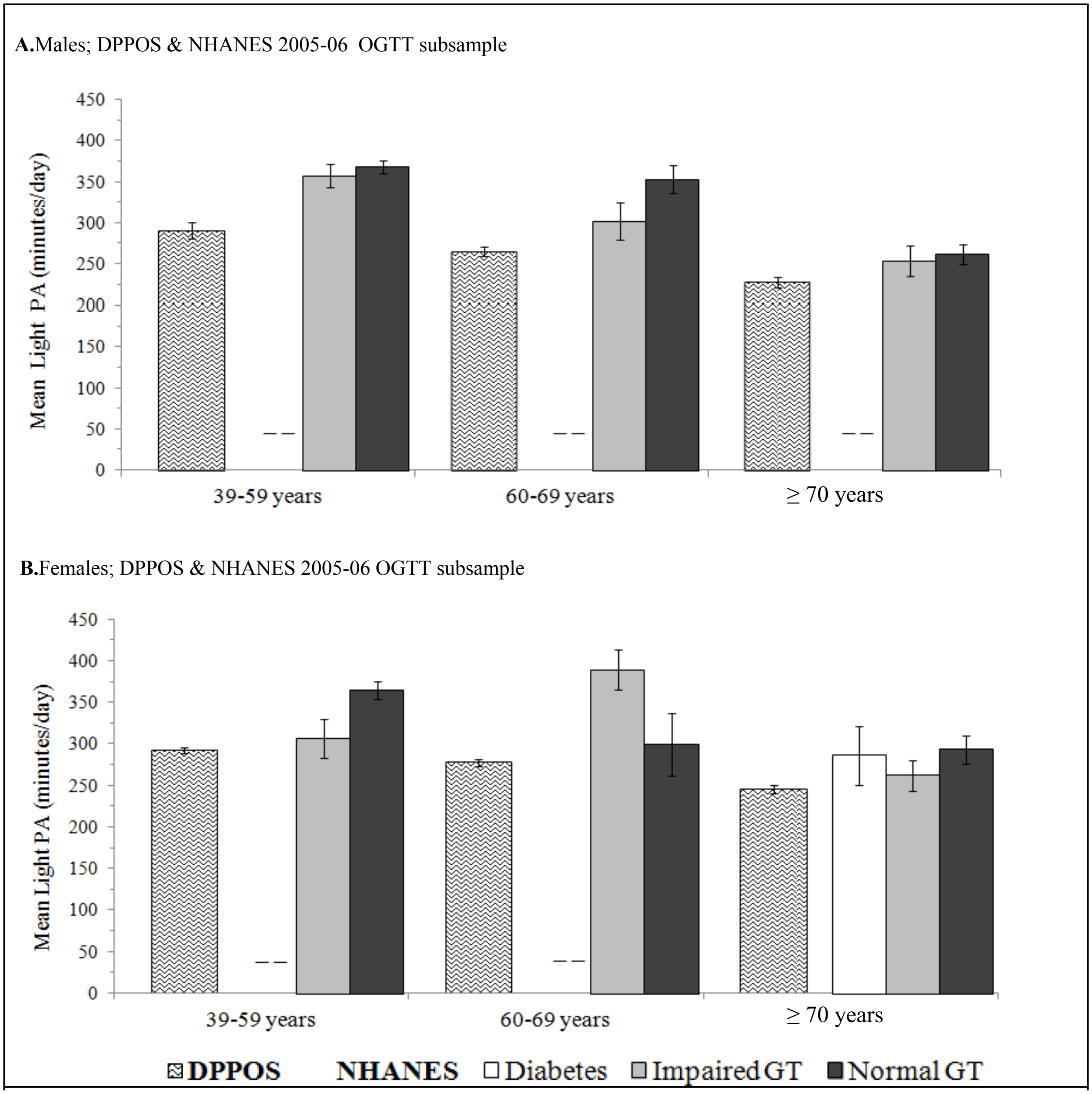
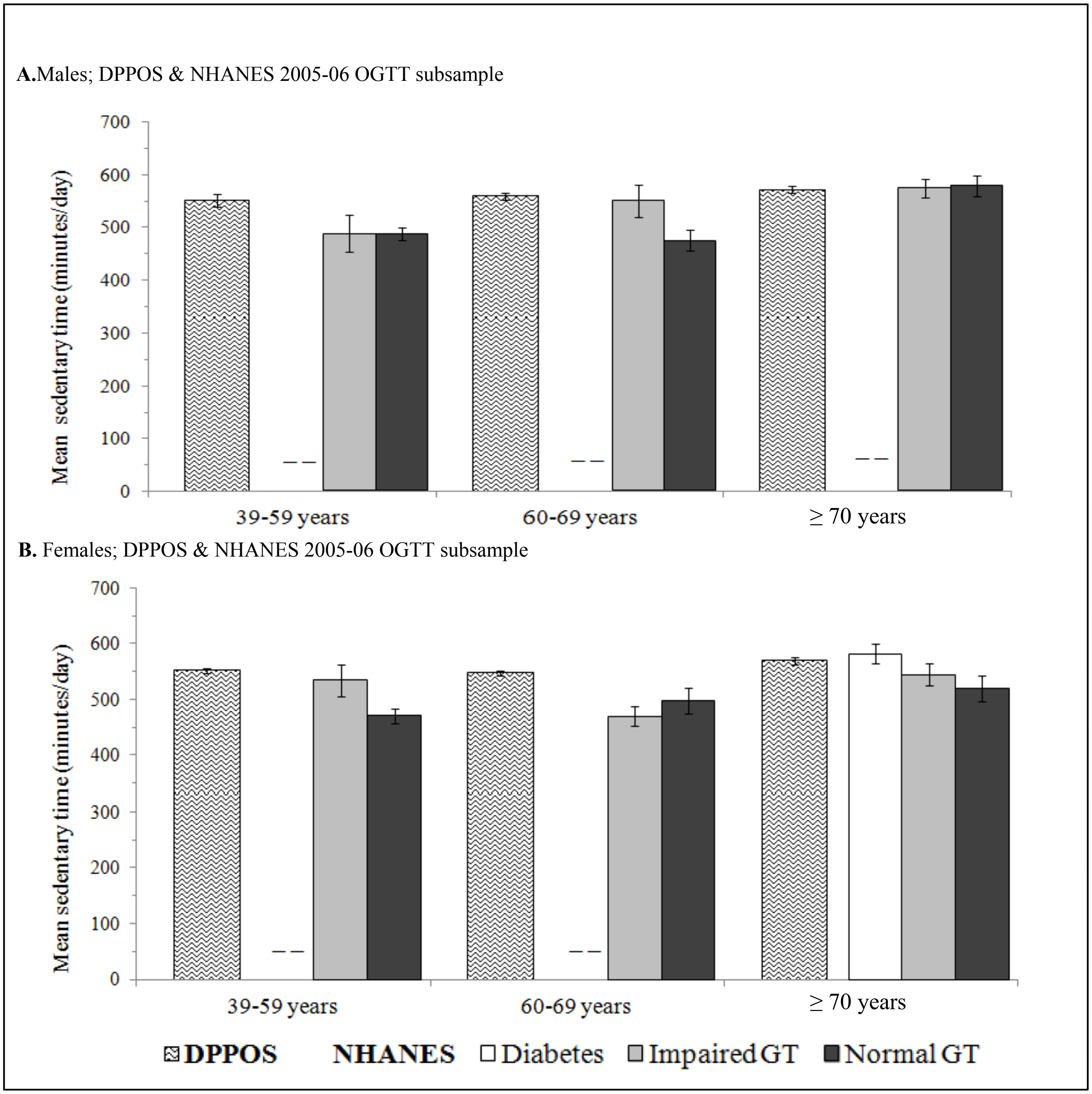


Figure 7.7 Mean minutes/day spent in light intensity physical activity by gender and age group for adults age ≥ 39 years (≥40 years for NHANES) with ≥ 4 valid days of monitoring. For the classification of diabetes status (NHANES participants), the oral glucose tolerance test was used. Wald f-statistic p-values were used for p-trend.



*** model includes wear time as a covariate**

Figure 7.8 Mean minutes/day spent in sedentary behaviors by gender and age group for adults age ≥ 39 years (≥40 years for NHANES) with ≥ 4 valid days of monitoring. For the classification of diabetes status (NHANES participants), the oral glucose tolerance test was used. Wald f-statistic p-values were used for p-trend.

7.6.3.4 Summary

Not all trends in time spent sedentary and in different intensities of physical activity were significant across the diabetes status groups in the weighted NHANES subsample. However, for most age/gender groups there was the general appearance of a trend with higher mean minutes per day of sedentary behavior and lower mean minutes per day of physical activity among NHANES participants with diabetes.

For male participants specifically, levels of moderate-vigorous physical activity (MVPA), appeared to be higher in DPPOS participants of all age groups, when compared to similar aged NHANES males with diabetes or impaired glucose tolerance. Additionally, the mean estimates of MVPA in minutes per day for DPPOS males in the 60-69 and ≥ 70 year age categories were similar, although slightly higher, than the mean MVPA estimates for normal glucose tolerant males in the same age category (based on the *fasting subsample*).

For females, estimates of MVPA in minutes/day were higher in the DPPOS cohort for all age groups when compared to similar aged individuals in NHANES with diabetes, and when compared to individuals in NHANES with impaired glucose tolerance in the 60-69 year old age category, only. As expected, DPPOS females still appeared to spend less time in MVPA than normal glucose tolerant individuals in the weighted NHANES subsample.

When compared to similar aged NHANES participants with diabetes, the DPPOS participants < 60 years of age, spent nearly an hour more per day in sedentary behaviors (for both males and females). However, in the older age groups the mean minutes per day of recorded sedentary time was more similar between the NHANES participants with diabetes and the DPPOS participants for males and slightly lower for DPPOS females in the 60-69 year old group (and possible the $\geq$ 70 year old age group based on the *OGTT subsample*) when compared to similar age/gender NHANES participants with diabetes.

7.6.4 Discussion

The DPPOS participants had higher than expected levels of moderate-vigorous physical activity (MVPA) when compared to similar individuals in the population representative NHANES *fasting and OGTT subsamples*. During the initial Diabetes Prevention Program (DPP) intervention, participants were encouraged to meet a physical activity goal of achieving 150 minutes/week of MVPA.[16] In order to achieve this goal, participants were asked to become aware of the time they spent in MVPA and to adopt behavioral changes that would lead to an increase in physical activity at this intensity level, specifically.[248] The DPP lifestyle intervention was shown to be successful in the lifestyle participants[16] and was eventually given to all DPP participants prior to the start of the DPPOS.[241] Therefore, finding higher than expected levels of MVPA in the DPPOS cohort is plausible and may reflect the effects of a successful lifestyle intervention on MVPA.

Although, encouragement to reduce sedentary behavior, such as the amount of time spent watching television, was included briefly in session 4 of the intervention there were no explicit goals to reduce sedentary behavior or to increase light intensity physical activity (LPA). Therefore, it is reasonable to assume that the DPPOS participants would have similar levels of sedentary and light behavior as individuals in NHANES that are similar and age, gender, and diabetes status (impaired glucose tolerance and diabetes). These results suggest that, in general, the DPPOS participants spent as much, if not more, time in sedentary behavior and less time in LPA than individuals in NHANES with impaired glucose tolerance or diabetes. More specifically for individuals < 60 years of age the DPPOS participants spent more time sedentary and less time in LPA than similar age/gender individuals in NHANES and for individuals ≥ 60 years of age the values for time spent in sedentary behavior and LPA were more similar between the DPPOS participants and the NHANES participants with diabetes. This suggests that a more concerted effort should be placed on reducing sedentary behavior in lifestyle interventions.

The weighted NHANES subpopulation used in this comparison provides a large U.S. population representative sample of individuals with which to compare the DPPOS cohort. Both studies utilized comparable, objective measures of physical activity and sedentary behavior. Unfortunately, race/ethnicity could not be accounted for, despite the fact that this variable appeared to have an effect on estimates of physical activity and sedentary behavior. However, the more influential covariates of age and gender were accounted for in the analysis design.

Additionally, because the analysis of the NHANES study data requires incorporating the complex survey design elements (weights, strata, and clusters), only descriptive comparisons could be made between the NHANES study population and the DPPOS cohort. However, in this case the inability to present statistical comparisons for the results did not obscure the overall conclusions that the DPPOS participants spent more time, on average, in MVPA than expected, but not more time in light intensity physical activity or less time in sedentary behavior than expected, based on comparisons to a nationally representative sample.

Overall, these results provide valuable contributions to the existing body of literature regarding the relationship between the development of diabetes and time spent in sedentary behaviors and in different intensities of physical activity. First of all, this work provides evidence for the cross-sectional relationship between glucose tolerance and time spent in LPA and sedentary behavior, in addition to time spent in MVPA. However, because the results are not longitudinal, it is not clear whether low physical activity levels and high sedentary behavior lead to higher blood glucose levels or if individuals perform less physical activity and more sedentary behaviors as a result of higher blood glucose levels. This effort also provides evidence of a sustaining effect of the DPP lifestyle intervention program, on increasing time spent in MVPA among individuals at high risk for developing type 2 diabetes. However, these results also indicate that the DPPOS participants were at least as sedentary as the NHANES participants with diabetes. This would suggest that in future lifestyle interventions more effort needs to be placed on reducing sedentary behaviors in addition to the traditional focus on increasing MVPA.

8.0 DISSERTATION FINAL ASSESSMENT

8.1 OVERALL CONCLUSIONS

The high physical and economic burden of type 2 diabetes mellitus is an important public health concern.[4] A better understanding of important modifiable risk factors for impaired glucose metabolism and type 2 diabetes, such as physical inactivity, is still needed. Additionally, there are few estimates of physical activity and sedentary behavior in the current literature that are based on objectively measured data for populations with impaired glucose metabolism or type 2 diabetes. Furthermore, few studies have assessed whether methods used to measure physical activity and sedentary behavior, previously validated in the general population, are valid in populations with impaired glucose metabolism and type 2 diabetes mellitus.[181,182]

Prior to the larger research effort that involved this dissertation work, there were no published studies reporting accelerometer measured time spent in different intensities of physical activity or sedentary behavior for adults or children and adolescents with impaired glucose tolerance or type 2 diabetes. The results of this work (and the larger research project including Kriska et al. 2013)[233] add to the previous body of literature by indicating that in addition to differences between diabetes status groups in moderate-vigorous physical activity, individuals with diabetes appear to be more sedentary than similar age and gender individuals with normal glucose tolerance. This was true for the TODAY youth [233] and the DPPOS and NHANES adults populations ($\geq$ 40 years of age). Additionally, these results suggest that, for all examined subgroups of the Diabetes Prevention Program Outcome Study (DPPOS) participants, there were higher than expected levels of moderate-vigorous physical activity, indicating that the lifestyle intervention used in the DPP may have a lasting effect on increasing levels of moderate-vigorous physical activity. However, levels of light intensity physical activity and sedentary behavior were similar to individuals with impaired glucose tolerance or type 2 di abetes, in a nationally representative sample of similar aged adults which was to be expected.

Overall, the results of this effort support the idea that measurement methods capable of reporting accurate and reliable estimates of time spent in all intensities of physical activity and sedentary behavior are needed to further the understanding of how physical activity and inactivity relate to diabetes development. In relation to this, the results for the TODAY trial youth suggest that the 3 day physical activity recall (3DPAR) questionnaire may not be valid for measuring the quantity of time spent in physical activity or sedentary behavior in overweight/obese youth with type 2 diabetes. This is despite the fact that the 3DPAR has been previously validated as a measure of physical activity in the general youth population.[235,249]

The results of unpublished analytical procedures from the TODAY trial project indicated that small changes in the processing algorithms, related to the definition of non-wear, could impact the results of estimated time spent in physical activity and sedentary behavior. Therefore, prior to reporting physical activity and sedentary behavior levels for adults in the DPPOS cohort an examination of the impact of small changes to the definition on non-wear in the accelerometer processing algorithms for a population representative sample of adults from the National Health and Nutrition Examination Survey (NHANES) . The results of these analyses indicated that changing the parameters for movement allowances during monitor recorded non-wear time resulted in clinically significant differences in estimates of time spent sedentary, especially in older adults (aged ≥ 65 years). Therefore, suggesting that there is a need to better understand how accelerometer processing methods can impact on estimates of sedentary behavior, specifically. These results also suggest that there is a need for greater standardization across studies in the non-wear algorithms used in accelerometer processing for studies reporting sedentary behavior.

8.2 PUBLIC HEALTH SIGNIFICANCE

Without increased prevention and intervention efforts the rates of diabetes among adults in the United States is expected to rise to over 30% by 2050, primarily due to increases in type 2 diabetes.[8] In relation to this, a current goal for health people 2020 is to "reduce the disease and economic burden of diabetes mellitus and improve the quality of life for all persons who have, or are at risk for diabetes mellitus".[250] A physically inactive lifestyle and overweight/obesity are considered to be the most modifiable risk factors for type 2 diabetes and therefore, these risk factors are the target of most prevention and intervention efforts.[15]

Based on the existing body of literature, it is possible that all levels of physical activity (light, moderate, and vigorous intensity) may help to reduce incident type 2 diabetes.[214,223] There is now evidence that reducing the amount of time spent in sedentary behavior may provide an added benefit to the effects of moderate-vigorous physical activity on diabetes development.[40,41] These findings are particularly important due to the fact that populations are becoming increasingly sedentary as people are spending more time per day in activities that require low energy expenditure.[52-54] It is therefore likely that future intervention efforts will include specific guidelines aimed at increasing time spent in all intensities of physical activity and reducing time spent in sedentary behavior. As a result, there is a need for assessment of physical activity in populations with impaired glucose tolerance and type 2 diabetes that can capture all intensity levels of activity and sedentary behavior.

This current effort helps to advance the understanding of physical activity and sedentary behavior assessment methods in populations with impaired glucose tolerance and type 2 diabetes and provides estimates for the average amount of time individuals in these populations spend in different intensities of physical activity and sedentary behavior. Additionally, this effort provides an examination of the differences in the amount of time spent in physical activity and sedentary behavior between individuals with normal glucose metabolism and individuals with impaired glucose metabolism.

8.3 FUTURE DIRECTIONS

The results of the dissertation have increased the understanding of time spent in physical activity and sedentary behavior among individuals with impaired glucose tolerance and type 2 diabetes. Additionally, these results have confirmed the need to specifically validate physical activity measurement methods for use in collecting data on time spent in sedentary behavior and to ensure that methods previously validated in the general population are also validated for use in populations with impaired glucose tolerance and type 2 diabetes.

However, the results of this effort have generated new questions that warrant further investigation. First of all, these results suggest that additional effort should be put into identifying and/or generating valid subjective methods for measuring physical activity in populations with impaired glucose tolerance or type 2 diabetes. In relation to this, as part of the DPPOS accelerometer study, the agreement between the modifiable activity questionnaire (MAQ) and the accelerometer output will be examined to determine the efficacy of the MAQ for assessing both physical activity and domain specific sedentary behavior in a population of individuals with impaired glucose tolerance or type 2 diabetes.

Secondly, although the accelerometer has been determined to be the most valid and reliable method for measuring time spent in all intensities of physical activity and sedentary behavior, the results of this investigation suggest that a greater understanding is needed to determine how all aspects of accelerometer processing methods may affect estimates of time spent sedentary. Future efforts in this area of research should also lead to the development of algorithms for accelerometer processing that are valid in the general population, as well as, in individuals that spend more time in sedentary behavior (such as individuals with diabetes).

Also, future efforts to reduce the incidence of diabetes and its complications through lifestyle changes should increase the emphasis on reducing sedentary behaviors in traditional interventions that already focus on increasing MVPA. This will lead to more effective health outcomes for individuals who have developed or are at high risk for developing type 2 diabetes.

APPENDIX A

MEAN VALUES FOR PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR RELATED VARIABLES BY AGE, GENDER, AND DIABETES STATUS

Table A.1 Mean values for sedentary behavior, different intensities of physical activity, and wear time for male participants from the DPPOS, the NHANES 2003-06 fasting subsample (≥40 years of age), and the NHANES 2005-06 OGTT subsample (≥40 years of age) with ≥4 days of valid wear time.

		DPPOS	NHANES 2003-06					
			Diabetes		Impaired glucose tolerance		Normal glucose tolerance	
		ALL	Fasting Sample	OGTT Sample	Fasting Sample	OGTT Sample	Fasting Sample	OGTT Sample
39-59 years of age	Sedentary (min/day 0-99 ct)	551.56 (11.17)	491.28 (12.01)	519.48 (29.65)	498.15 (9.10)	485.79 (35.15)	464.87 (10.00)	485.84 (12.16)
	Light PA (min/day 100-1951 ct)	290.28 (9.61)	344.50 (13.35)	283.39 (26.11)	341.11 (8.50)	354.85 (14.54)	375.05 (7.01)	365.72 (8.03)
	Moderate-vigorous activity (min/day >=1952 ct)	30.83 (2.33)	23.99 (2.96)	21.85 (5.20)	28.54 (1.7)	26.85 (3.93)	39.43 (2.23)	38.94 (2.12)
	Total activity (Light + MVPA)	321.11 (10.56)	368.49 (15.26)	305.23 (27.31)	369.64 (9.19)	381.70 (13.71)	414.48 (8.30)	404.65 (9.02)
	Estimated Wear time (min/day)	872.68 (8.54)	859.77 (14.39)	824.71 (23.23)	867.79 (9.06)	867.49 (1.96)	879.35 (7.75)	824.71 (23.23)
60-69 years of age	Sedentary (min/day 0-99 ct)	559.68 (6.30)	552.53 (19.02)	453.33 (36.75)	532.14 (15.75)	548.44 (30.01)	539.41 (23.57)	473.59 (18.78)
	Light PA (min/day 100-1951 ct)	264.41 (5.65)	255.74 (14.86)	345.12 (32.79)	312.56 (9.29)	299.79 (22.34)	329.76 (13.68)	350.79 (16.87)
	Moderate-vigorous PA (min/day >=1952 ct)	21.27 (1.45)	11.51 (3.47)	49.51 (11.89)	20.22 (1.95)	15.83 (2.39)	19.40 (2.39)	18.46 (2.21)
	Total activity (Light + MVPA)	285.68 (6.12)	267.25 (17.46)	394.63 (39.78)	332.78 (9.87)	315.61 (23.25)	349.16 (13.66)	369.25 (17.27)
	Estimated Wear time (min/day)	845.36 (6.09)	819.78 (13.51)	847.96 (12.06)	864.92 (14.95)	864.06 (24.83)	888.57 (20.57)	842.84 (25.26)
70+ years of age	Sedentary (min/day 0-99 ct)	572.43 (6.50)	641.90 (33.97)	606.29 (31.20)	585.45 (12.22)	573.10 (17.65)	575.20 (12.54)	577.53 (19.56)
	Light PA (min/day 100-1951 ct)	227.20 (5.85)	246.56 (10.33)	269.73 (20.24)	252.30 (7.45)	252.29 (18.29)	260.48 (9.64)	260.22 (11.71)
	Moderate-vigorous PA (min/day >=1952 ct)	13.33 (1.43)	9.13 (2.73)	9.77 (2.34)	9.78 (1.32)	6.36 (2.05)	13.03 (2.87)	17.10 (6.29)
	Total activity (Light + MVPA)	240.53 (6.31)	255.69 (10.81)	279.50 (20.44)	262.08 (7.44)	258.65 (19.41)	273.51 (11.16)	277.33 (15.70)
	Estimated Wear time (min/day)	812.96 (5.97)	897.60 (31.92)	885.79 (40.69)	847.53 (12.06)	831.75 (11.60)	848.72 (8.77)	854.86 (17.37)

Table A.2 Mean values for sedentary behavior, different intensities of physical activity, and wear time for female participants from the DPPOS, the NHANES 2003-06 fasting subsample (≥40 years of age), and the NHANES 2005-06 OGTT subsample (≥40 years of age) with ≥4 days of valid wear time.

		DPPOS	NHANES 2003-06					
			Diabetes		Impaired glucose tolerance		Normal glucose tolerance	
		ALL	Fasting Sample	OGTT Sample	Fasting Sample	OGTT Sample	Fasting Sample	OGTT Sample
39-59 years of age	Sedentary (min/day 0-99 ct)	551.02 (3.82)	509.79 (23.58)	434.27 (25.39)	469.12 (11.2)	533.87 (28.44)	480.74 (9.12)	470.55 (12.71)
	Light PA (min/day 100-1951 ct)	292.23 (3.74)	325.51 (16.67)	377.23 (16.03)	355.97 (7.96)	307.56 (23.36)	359.90 (7.36)	365.80 (10.68)
	Moderate-vigorous PA (min/day >=1952 ct)	16.14 (0.75)	10.88 (2.25)	10.04 (1.82)	18.41 (1.91)	15.96 (2.26)	22.87 (1.56)	22.06 (2.32)
	Total PA (Light + MVPA)	308.37 (3.95)	336.39 (17.24)	387.27 (16.55)	374.38 (8.91)	323.53 (24.59)	382.78 (8.12)	387.85 (11.81)
	Estimated Wear time (min/day)	859.40 (3.71)	846.18 (14.54)	821.545 (20.29)	843.50 (8.79)	857.40 (18.85)	863.52 (6.40)	858.41 (7.86)
60-69 years of age	Sedentary (min/day 0-99 ct)	546.58 (4.05)	579.98 (33.78)	498.03 (23.20)	486.33 (12.63)	469.88 (18.00)	491.26 (11.17)	498.03 (23.20)
	Light PA (min/day 100-1951 ct)	277.72 (4.12)	280.14 (21.33)	329.73 (17.54)	333.23 (10.58)	390.17 (24.06)	350.82 (9.29)	300.71 (38.20)
	Moderate-vigorous activity (min/day >=1952 ct)	13.31 (1.01)	5.99 (1.46)	12.22 (2.09)	10.18 (1.59)	6.77 (2.30)	14.77 (1.52)	3.48 (1.27)
	Total activity (Light + MVPA)	291.03 (87.96)	286.13 (21.75)	341.95 (18.95)	343.41 (10.38)	396.94 (24.13)	365.59 (9.94)	304.18 (38.85)
	Estimated Wear time (min/day)	837.61 (4.39)	866.11 (33.08)	839.98 (19.89)	829.74 (9.69)	866.82 (21.45)	856.85 (10.79)	1036.95 (119.30)
70+ years of age	Sedentary (min/day 0-99 ct)	569.00 (5.51)	559.48 (9.01)	581.54 (18.00)	531.56 (13.53)	544.71 (18.83)	560.91 (14.53)	519.20 (23.41)
	Light PA (min/day 100-1951 ct)	244.97 (4.81)	233.24 (15.62)	287.25 (35.73)	285.88 (13.71)	263.04 (18.84)	275.82 (8.64)	294.50 (16.60)
	Moderate-vigorous PA (min/day >=1952 ct)	7.46 (0.83)	4.64 (0.56)	4.75 (1.32)	7.68 (1.97)	6.32 (2.36)	6.35 (1.19)	10.19 (3.26)
	Total activity (Light + MVPA)	252.43 (5.04)	237.88 (15.90)	292.00 (36.71)	293.56 (14.71)	269.36 (20.92)	282.17 (8.84)	304.70 (17.48)
	Estimated Wear time (min/day)	821.43 (4.97)	797.36 (16.74)	873.534 (34.13)	825.12 (9.68)	814.07 (18.44)	843.08 (12.98)	823.90 (17.19)

APPENDIX B

LIST OF ABBREVIATIONS

Table B.1 The following table lists various abbreviations and acronyms used throughout the dissertation. The page on which each one is first used is also given.

Abbreviation	Meaning	Page
3DPAR	Three Day Physical Activity Recall Questionnaire	8
A1C	Hemoglobin A1c	16
ACSM	American College of Sports Medicine	42
ADA	American Diabetes Association	16
BMI	Body mass index	10
BRFSS	Behavioral Risk Factor Surveillance System	23
CDC	Centers for Disease Control	9
CI	Confidence interval	2
CVD	Cardiovascular disease	2
DPP	Diabetes Prevention Program	3
DPPOS	Diabetes Prevention Program Outcomes Study	10
FPG	Fasting plasma glucose	16
GPS	Global Positioning System	28
LPA	Light intensity physical activity	50
LPL	Lipoprotein Lipase	38
MAQ	Modifiable Activity Questionnaire	63
MEC	Mobile examination center	54
METs	Metabolic equivalent units	20

Table B.1 Cont.

Abbreviation	Meaning	Page
MV/ MVPA	Moderate-vigorous intensity physical activity	50
NCHS	National Center for Health Statistics	9
NCI	National Cancer Institute	56
NHANES	National Health and Nutrition Examination Survey	8
NPV	Negative predictive value	85
OGTT	Oral glucose tolerance test	16
PA	physical activity	50
PPS	Probability proportional to measurement size	53
PPV	Positive predictive value	85
PSUs	Primary sampling units	53
SEM	Standard error of the mean	73
SQRT	Square root	75
TODAY	Treatment Options for Type 2 D iabetes in Adolescents and Youth study	7
TPA	Total physical intensity (light + moderate-vigorous)	50
WHO	World Health Organization	1
YBRFSS	Youth Behavioral Risk Factor Surveillance System	23

BIBLIOGRAPHY

1. American Diabetes A. Diagnosis and classification of diabetes mellitus. Diabetes Care 2012;35 Suppl 1:S64-71.
2. American Diabetes A. Standards of medical care in diabetes--2011. Diabetes Care 2011;34 Suppl 1:S11-61.
3. Diabetes Fact Sheet. 2011. (Accessed at http://www.who.int/mediacentre/factsheets/fs312/en/.)
4. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
5. King H, Rewers M. Diabetes in adults is now a Third World problem. World Health Organization Ad Hoc Diabetes Reporting Group. Ethnicity & disease 1993;3 Suppl:S67-74.
6. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. Diabet Med 1997;14 Suppl 5:S1-85.
7. van Dieren S, Beulens JW, van der Schouw YT, Grobbee DE, Neal B. The global burden of diabetes and its complications: an emerging pandemic. Eur J Cardiovasc Prev Rehabil 2010;17 Suppl 1:S3-8.
8. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Popul Health Metr 2010;8:29.
9. Imperatore G, Boyle JP, Thompson TJ, et al. Projections of type 1 and type 2 diabetes burden in the U.S. population aged <20 years through 2050: dynamic modeling of incidence, mortality, and population growth. Diabetes Care 2012;35:2515-20.
10. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. Bulletin of the World Health Organization 2004;82:844-51.
11. Emerging Risk Factors C, Seshasai SR, Kaptoge S, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med 2011;364:829-41.
12. Economic costs of diabetes in the U.S. In 2007. Diabetes Care 2008;31:596-615.
13. Economic consequences of diabetes mellitus in the U.S. in 1997. American Diabetes Association. Diabetes Care 1998;21:296-309.
14. Zhang P, Zhang X, Brown J, et al. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:293-301.
15. Paulweber B, Valensi P, Lindstrom J, et al. A European evidence-based guideline for the prevention of type 2 di abetes. Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme 2010;42 Suppl 1:S3-36.
16. 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 2002;346:393-403.

17. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 2006;49:289-97.
18. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.
19. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008;371:1783-9.
20. Sone H, Katagiri A, Ishibashi S, et al. Effects of lifestyle modifications on patients with type 2 diabetes: the Japan Diabetes Complications Study (JDCS) study design, baseline analysis and three year-interim report. Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme 2002;34:509-15.
21. Sone H, Tanaka S, Iimuro S, et al. Long-term lifestyle intervention lowers the incidence of stroke in Japanese patients with type 2 diabetes: a nationwide multicentre randomised controlled trial (the Japan Diabetes Complications Study). Diabetologia 2010;53:419-28.
22. Tuomilehto J, Schwarz P, Lindstrom J. Long-term benefits from lifestyle interventions for type 2 diabetes prevention: time to expand the efforts. Diabetes Care 2011;34 Suppl 2:S210-4.
23. Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ 2007;334:299.
24. Yoon U, Kwok LL, Magkidis A. Efficacy of lifestyle interventions in reducing diabetes incidence in patients with impaired glucose tolerance: A systematic review of randomized controlled trials. Metabolism 2012.
25. Toledo FG, Menshikova EV, Ritov VB, et al. Effects of physical activity and weight loss on skeletal muscle mitochondria and relationship with glucose control in type 2 diabetes. Diabetes 2007;56:2142-7.
26. 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 1997;20:537-44.
27. Shimada M, Ishibashi S, Gotoda T, et al. Overexpression of human lipoprotein lipase protects diabetic transgenic mice from diabetic hypertriglyceridemia and hypercholesterolemia. Arterioscler Thromb Vasc Biol 1995;15:1688-94.
28. Wojtaszewski JF, Hansen BF, Urso B, Richter EA. Wortmannin inhibits both insulin- and contraction-stimulated glucose uptake and transport in rat skeletal muscle. J Appl Physiol 1996;81:1501-9.
29. Yeh JI, Gulve EA, Rameh L, Birnbaum MJ. The effects of wortmannin on rat skeletal muscle. Dissociation of signaling pathways for insulin- and contraction-activated hexose transport. The Journal of biological chemistry 1995;270:2107-11.
30. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. Annual review of medicine 1998;49:235-61.
31. Lee AD, Hansen PA, Holloszy JO. Wortmannin inhibits insulin-stimulated but not contraction-stimulated glucose transport activity in skeletal muscle. FEBS letters 1995;361:51-4.

32. Bey L, Akunuri N, Zhao P, Hoffman EP, Hamilton DG, Hamilton MT. Patterns of global gene expression in rat skeletal muscle during unloading and low-intensity ambulatory activity. Physiol Genomics 2003;13:157-67.
33. Hamilton MT, Hamilton DG, Zderic TW. Exercise physiology versus inactivity physiology: an essential concept for understanding lipoprotein lipase regulation. Exercise and sport sciences reviews 2004;32:161-6.
34. Bey L, Hamilton MT. Suppression of skeletal muscle lipoprotein lipase activity during physical inactivity: a molecular reason to maintain daily low-intensity activity. J Physiol 2003;551:673-82.
35. Hamilton MT, Hamilton DG, Zderic TW. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. Diabetes 2007;56:2655-67.
36. Dunstan DW, Kingwell BA, Larsen R, et al. Breaking up pr olonged sitting reduces postprandial glucose and insulin responses. Diabetes Care 2012;35:976-83.
37. Wilmot EG, Edwardson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. Diabetologia 2012.
38. Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006;29:2102-7.
39. Qin L, Knol MJ, Corpeleijn E, Stolk RP. Does physical activity modify the risk of obesity for type 2 diabetes: a review of epidemiological data. Eur J Epidemiol 2010;25:5-12.
40. Owen N, Healy GN, Matthews CE, Dunstan DW. Too much sitting: the population health science of sedentary behavior. Exercise and sport sciences reviews 2010;38:105-13.
41. Owen N, Sparling PB, Healy GN, Dunstan DW, Matthews CE. Sedentary behavior: emerging evidence for a new health risk. Mayo Clinic proceedings Mayo Clinic 2010;85:1138-41.
42. Katzmarzyk PT. Physical activity, sedentary behavior, and health: paradigm paralysis or paradigm shift? Diabetes 2010;59:2717-25.
43. Grontved A, Hu FB. Television viewing and risk of type 2 di abetes, cardiovascular disease, and all-cause mortality: a meta-analysis. JAMA 2011;305:2448-55.
44. Healy GN, Dunstan DW, Salmon J, et al. Objectively measured light-intensity physical activity is independently associated with 2-h plasma glucose. Diabetes Care 2007;30:1384-9.
45. Dunstan DW, Salmon J, Healy GN, et al. Association of television viewing with fasting and 2-h postchallenge plasma glucose levels in adults without diagnosed diabetes. Diabetes Care 2007;30:516-22.
46. Healy GN, Wijndaele K, Dunstan DW, et al. Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). Diabetes Care 2008;31:369-71.
47. Healy GN, Dunstan DW, Salmon J, et al. Breaks in sedentary time: beneficial associations with metabolic risk. Diabetes Care 2008;31:661-6.
48. Healy GN, Matthews CE, Dunstan DW, Winkler EA, Owen N. Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. European heart journal 2011.
49. Matthews CE, Chen KY, Freedson PS, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. American journal of epidemiology 2008;167:875-81.
50. Peters TM, Moore SC, Xiang YB, et al. Accelerometer-measured physical activity in Chinese adults. Am J Prev Med 2010;38:583-91.

51. Pate RR, Mitchell JA, Byun W, Dowda M. Sedentary behaviour in youth. Br J Sports Med 2011;45:906-13.
52. Chau JY, Merom D, Grunseit A, Rissel C, Bauman AE, van der Ploeg HP. Temporal trends in non-occupational sedentary behaviours from Australian Time Use Surveys 1992, 1997 and 2006. Int J Behav Nutr Phys Act 2012;9:76.
53. Cui Z, Hardy LL, Dibley MJ, Bauman A. Temporal trends and recent correlates in sedentary behaviours in Chinese children. Int J Behav Nutr Phys Act 2011;8:93.
54. Bradley CB, McMurray RG, Harrell JS, Deng S. Changes in common activities of 3rd through 10th graders: the CHIC study. Med Sci Sports Exerc 2000;32:2071-8.
55. Kriska A, Caspersen CJ. Introduction to a collection of Physical Activity Questionnaires. Medicine and Science in Sports and Exercise 1997;29:5-9.
56. Kriska AM. Modifiable Activity Questionnaire. Med Sci Sports Exerc 1997;29:S73-S8.
57. Jacobs DR, Jr., Ainsworth BE, Hartman TJ, Leon AS. A simultaneous evaluation of 10 commonly used physical activity questionnaires. Med Sci Sports Exerc 1993;25:81-91.
58. Marshall AL, Miller YD, Burton NW, Brown WJ. Measuring total and domain-specific sitting: a study of reliability and validity. Med Sci Sports Exerc 2010;42:1094-102.
59. Matthews C. Calibration of accelerometer output for adults. Medicine and Science in Sports and Exercise 2005;37:s512-s22.
60. Pettee KK, Storti KL, Ainsworth BE, Kriska AM. Measurement of Physical Activity and Inactivity in Epidemiologic Studies. In: Lee I-M, ed. Epidemiologic Methods in Physical Activity Studies. New York,NY: Oxford University Press, Inc; 2009:15-33.
61. Oliver M, Badland HM, Schofield GM, Shepherd J. Identification of accelerometer nonwear time and sedentary behavior. Res Q Exerc Sport 2011;82:779-83.
62. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. Med Sci Sports Exerc 2011;43:357-64.
63. Kozey-Keadle S, Libertine A, Lyden K, Staudenmayer J, Freedson PS. Validation of wearable monitors for assessing sedentary behavior. Med Sci Sports Exerc 2011;43:1561-7.
64. Winkler EA, Gardiner PA, Clark BK, Matthews CE, Owen N, Healy GN. Identifying sedentary time using automated estimates of accelerometer wear time. Br J Sports Med 2011:436-42.
65. Winkler EA, Gardiner PA, Healy GN, et al. Distinguishing True Sedentary From Accelerometer Non-wearing Time: Accuracy Of Two Automated Wear-time Estimations: 1088: May 29 3:45 PM - 4:00 PM. Medicine & Science in Sports & Exercise 2009;41:171-2.
66. King WC, Li J, Leishear K, Mitchell JE, Belle SH. Determining activity monitor wear time: an influential decision rule. J Phys Act Health 2011;8:566-80.
67. Sirard JR, Forsyth A, Oakes JM, Schmitz KH. Accelerometer test-retest reliability by data processing algorithms: results from the Twin Cities Walking Study. J Phys Act Health 2011;8:668-74.
68. Hart TL, Swartz AM, Cashin SE, Strath SJ. How many days of monitoring predict physical activity and sedentary behaviour in older adults? Int J Behav Nutr Phys Act 2011;8:62-8.
69. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. J Sports Sci 2008;26:1557-65.
70. Zeitler P, Epstein L, Grey M, et al. Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with

rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes. Pediatr Diabetes 2007;8:74-87.
71. Szablewski L. Glucose Homeostasis and Insulin Resistance. In. Oak Park: Bentham Science Publishers; 2011.
72. Fromm HJ, Hargrove M. Essentials of biochemistry. In. Berlin ; New York: Springer; 2012.
73. Venes D, Taber CW. Taber's cyclopedic medical dictionary. Ed. 21, illustrated in full color / ed. Philadelphia: F. A. Davis Co.; 2009.
74. Gjedde A, Bauer W, Wong D. Metabolism of Glucose. In: Neurokinetics: Springer US; 2011:211-39.
75. Standards of medical care in diabetes--2011. Diabetes Care 2011;34 Suppl 1:S11-61.
76. Engelgau MM, Geiss LS, Saaddine JB, et al. The evolving diabetes burden in the United States. Ann Intern Med 2004;140:945-50.
77. Cowie CC, Rust KF, Ford ES, et al. Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. Diabetes Care 2009;32:287-94.
78. Hogan P, Dall T, Nikolov P. Economic costs of diabetes in the US in 2002. Diabetes Care 2003;26:917-32.
79. Lindstrom J, Louheranta A, Mannelin M, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care 2003;26:3230-6.
80. Eriksson KF, Lindgarde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. Diabetologia 1991;34:891-8.
81. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 2009;122:248-56 e5.
82. Vetter ML, Cardillo S, Rickels MR, Iqbal N. Narrative review: effect of bariatric surgery on type 2 diabetes mellitus. Ann Intern Med 2009;150:94-103.
83. Schauer PR, Burguera B, Ikramuddin S, et al. Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. Ann Surg 2003;238:467-84; discussion 84-5.
84. Barzilay JI, Spiekerman CF, Kuller LH, et al. Prevalence of clinical and isolated subclinical cardiovascular disease in older adults with glucose disorders: the Cardiovascular Health Study. Diabetes Care 2001;24:1233-9.
85. Tavani A, Bertuzzi M, Gallus S, Negri E, La Vecchia C. Diabetes mellitus as a contributor to the risk of acute myocardial infarction. Journal of clinical epidemiology 2002;55:1082-7.
86. Geiss LS, Herman W, Smith P. Mortality Among Perons with Non-Insulin Dependent Diabetes. In: Harris M, ed. Diabetes in America. 2nd ed. Bethesda, MD: National Institutes of Health; 1995:233-58.
87. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep 1985;100:126-31.
88. Caspersen CJ. Physical activity epidemiology: concepts, methods, and applications to exercise science. Exercise and sport sciences reviews 1989;17:423-73.
89. Taylor HL, Jacobs DR, Jr., Schucker B, Knudsen J, Leon AS, Debacker G. A questionnaire for the assessment of leisure time physical activities. J Chronic Dis 1978;31:741-55.

90. Dale D, Welk GJ, Matthews CE. Methods for Assessing Physical Activity and Challenges for Research. In: Welk GJ, ed. Physical Activity Assessment for Health-Related Research

Champaign, IL: Human Kinetics Publishers Inc.; 2002:19-33.
91. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32:S498-504.
92. Howley ET. Type of activity: resistance, aerobic and leisure versus occupational physical activity. Med Sci Sports Exerc 2001;33:S364-9; discussion S419-20.
93. Ridley K, Ainsworth BE, Olds TS. Development of a compendium of energy expenditures for youth. Int J Behav Nutr Phys Act 2008;5:45.
94. Dietz WH. The role of lifestyle in health: the epidemiology and consequences of inactivity. Proc Nutr Soc 1996;55:829-40.
95. van Poppel MN, Chinapaw MJ, Mokkink LB, van Mechelen W, Terwee CB. Physical activity questionnaires for adults: a systematic review of measurement properties. Sports Med 2010;40:565-600.
96. Haskell WL. Physical activity by self-report: a brief history and future issues. J Phys Act Health 2012;9 Suppl 1:S5-S10.
97. Chinapaw MJ, Mokkink LB, van Poppel MN, van Mechelen W, Terwee CB. Physical activity questionnaires for youth: a systematic review of measurement properties. Sports Med 2010;40:539-63.
98. Forsen L, Loland NW, Vuillemin A, et al. Self-administered physical activity questionnaires for the elderly: a systematic review of measurement properties. Sports Med 2010;40:601-23.
99. Blair SN, Haskell WL, Ho P, et al. Assessment of habitual physical activity by a seven-day recall in a community survey and controlled experiments. American journal of epidemiology 1985;122:794-804.
100. Washburn RA, Adams LL, Haile GT. Physical activity assessment for epidemiologic research: the utility of two simplified approaches. Prev Med 1987;16:636-46.
101. Clark BK, Healy GN, Winkler EA, et al. Relationship of Television Time with Accelerometer-Derived Sedentary Time: NHANES. Med Sci Sports Exerc 2010.
102. Macera CA, Ham SA, Jones DA, Kimsey CD, Ainsworth BE, Neff LJ. Limitations on the use of a single screening question to measure sedentary behavior. American journal of public health 2001;91:2010-2.
103. Kwon S, Hou N, Wang M. Comparison of physical activity levels between cancer survivors and non-cancer participants in the 2009 BRFSS. J Cancer Surviv 2012;6:54-62.
104. Ainsworth BE, Jacobs DR, Jr., Leon AS. Validity and reliability of self-reported physical activity status: the Lipid Research Clinics questionnaire. Med Sci Sports Exerc 1993;25:92-8.
105. Gardiner PA, Clark BK, Healy GN, Eakin EG, Winkler EA, Owen N. Measuring older adults' sedentary time: reliability, validity, and responsiveness. Med Sci Sports Exerc 2011;43:2127-33.
106. Clark BK, Sugiyama T, Healy GN, Salmon J, Dunstan DW, Owen N. Validity and reliability of measures of television viewing time and other non-occupational sedentary behaviour of adults: a review. Obesity Reviews 2009;10:7-16.
107. Montoye HJ. Estimation of habitual physical activity by questionnaire and interview. Am J Clin Nutr 1971;24:1113-8.

108. Kriska AM, Sandler RB, Cauley JA, LaPorte RE, Hom DL, Pambianco G. The assessment of historical physical activity and its relation to adult bone parameters. American journal of epidemiology 1988;127:1053-63.
109. Chasan-Taber L, Erickson JB, Nasca PC, Chasan-Taber S, Freedson PS. Validity and reproducibility of a physical activity questionnaire in women. Med Sci Sports Exerc 2002;34:987-92.
110. Healy GN, Dunstan DW, Salmon J, Shaw JE, Zimmet PZ, Owen N. Television time and continuous metabolic risk in physically active adults. Med Sci Sports Exerc 2008;40:639-45.
111. Sesso HD, Paffenbarger RS, Ha T, Lee IM. Physical activity and cardiovascular disease risk in middle-aged and older women. American journal of epidemiology 1999;150:408-16.
112. Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? JAMA 2001;285:1447-54.
113. Sallis JF, Grossman RM, Pinski RB, Patterson TL, Nader PR. The development of scales to measure social support for diet and exercise behaviors. Prev Med 1987;16:825-36.
114. Gauthier AP, Lariviere M, Young N. Psychometric properties of the IPAQ: a validation study in a sample of northern Franco-Ontarians. J Phys Act Health 2009;6 Suppl 1:S54-60.
115. King AC, Castro C, Wilcox S, Eyler AA, Sallis JF, Brownson RC. Personal and environmental factors associated with physical inactivity among different racial-ethnic groups of U.S. middle-aged and older-aged women. Health psychology : official journal of the Division of Health Psychology, American Psychological Association 2000;19:354-64.
116. Pate RR, Sallis JF, Ward DS, et al. Age-related changes in types and contexts of physical activity in middle school girls. Am J Prev Med 2010;39:433-9.
117. Kriska AM, Pereira MA, Hanson RL, et al. Association of physical activity and serum insulin concentrations in two populations at high risk for type 2 diabetes but differing by BMI. Diabetes Care 2001;24:1175-80.
118. In: Last JM, ed. A Dictionary of Edipemiology. 4th ed. New York, NY: Oxford University Press; 2001.
119. Terwee CB, Mokkink LB, van Poppel MN, Chinapaw MJ, van Mechelen W, de Vet HC. Qualitative attributes and measurement properties of physical activity questionnaires: a checklist. Sports Med 2010;40:525-37.
120. Sirard JR, Pate RR. Physical activity assessment in children and adolescents. Sports Med 2001;31:439-54.
121. Corder K, Ekelund U, Steele RM, Wareham NJ, Brage S. Assessment of physical activity in youth. J Appl Physiol 2008;105:977-87.
122. Bassett DR, Jr. Establishing Validity and Reliability of Physical Activity Assessment Instruments. In: Lee IM, ed. Epidedmiologic Methods in Physical Activity Studies. New York, NY: Oxford University Press; 2009:34-55.
123. Hart TL, Ainsworth BE, Tudor-Locke C. Objective and subjective measures of sedentary behavior and physical activity. Med Sci Sports Exerc 2011;43:449-56.
124. Baranowski T. Validity and reliability of self-report measures of physical activity. An information-processing perspective. Research Quarterly in Exercise and Sport 1988;59:314-27.
125. Durante R, Ainsworth BE. The recall of physical activity: using a cognitive model of the question-answering process. Med Sci Sports Exerc 1996;28:1282-91.
126. Lee IM. Epidemiologic methods in physical activity studies. Oxford ; New York: Oxford University Press; 2009.

127. Rodriguez DA, Brown AL, Troped PJ. Portable global positioning units to complement accelerometry-based physical activity monitors. Med Sci Sports Exerc 2005;37:S572-81.
128. Westerterp KR. Physical activity assessment with accelerometers. Int J Obes Relat Metab Disord 1999;23 Suppl 3:S45-9.
129. Chen KY, Bassett DR, Jr. The technology of accelerometry-based activity monitors: current and future. Med Sci Sports Exerc 2005;37:S490-500.
130. Welk G. Physical activity assessments for health-related research. Champaign, IL: Human Kinetics; 2002.
131. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc 1998;30:777-81.
132. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. Med Sci Sports Exerc 2005;37:S531-43.
133. Swartz AM, Strath SJ, Bassett DR, Jr., O'Brien WL, King GA, Ainsworth BE. Estimation of energy expenditure using CSA accelerometers at hip and wrist sites. Med Sci Sports Exerc 2000;32:S450-6.
134. Brage S, Wedderkopp N, Franks PW, Andersen LB, Froberg K. Reexamination of validity and reliability of the CSA monitor in walking and running. Med Sci Sports Exerc 2003;35:1447-54.
135. Leenders NY, Sherman WM, Nagaraja HN, Kien CL. Evaluation of methods to assess physical activity in free-living conditions. Med Sci Sports Exerc 2001;33:1233-40.
136. Nichols JF, Morgan CG, Chabot LE, Sallis JF, Calfas KJ. Assessment of physical activity with the Computer Science and Applications, Inc., accelerometer: laboratory versus field validation. Res Q Exerc Sport 2000;71:36-43.
137. Kim T, Kim Y, Yoon H, Shin T. A preliminary study on e stimation of energy expenditure at different locations of acceleration sensor during submaximal exercise. Conference proceedings : A nnual International Conference of the IEEE Engineering in Medicine and Biology Society IEEE Engineering in Medicine and Biology Society Conference 2009;2009:4902-5.
138. Choi L, Ward SC, Schnelle JF, Buchowski MS. Assessment of wear/nonwear time classification algorithms for triaxial accelerometer. Med Sci Sports Exerc 2012;44:2009-16.
139. Tudor-Locke C, Johnson WD, Katzmarzyk PT. U.S. population profile of time-stamped accelerometer outputs: impact of wear time. J Phys Act Health 2011;8:693-8.
140. Trost SG, Pate RR, Sallis JF, et al. Age and gender differences in objectively measured physical activity in youth. Med Sci Sports Exerc 2002;34:350-5.
141. 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 1998;84:362-71.
142. 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 2002;87:623-31.
143. Corder K, Brage S, Ramachandran A, Snehalatha C, Wareham N, Ekelund U. Comparison of two Actigraph models for assessing free-living physical activity in Indian adolescents. J Sports Sci 2007;25:1607-11.
144. De Vries SI, Van Hirtum HW, Bakker I, Hopman-Rock M, Hirasing RA, Van Mechelen W. Validity and reproducibility of motion sensors in youth: a systematic update. Med Sci Sports Exerc 2009;41:818-27.

145. Le Masurier GC, Tudor-Locke C. Comparison of pedometer and accelerometer accuracy under controlled conditions. Med Sci Sports Exerc 2003;35:867-71.
146. Leenders N, Sherman WM, Nagaraja HN. Comparisons of four methods of estimating physical activity in adult women. Med Sci Sports Exerc 2000;32:1320-6.
147. 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 2000;32:S471-80.
148. Campbell KL, Crocker PR, McKenzie DC. Field evaluation of energy expenditure in women using Tritrac accelerometers. Med Sci Sports Exerc 2002;34:1667-74.
149. Culhane KM, O'Connor M, Lyons D, Lyons GM. Accelerometers in rehabilitation medicine for older adults. Age and ageing 2005;34:556-60.
150. Garatachea N, Torres Luque G, Gonzalez Gallego J. Physical activity and energy expenditure measurements using accelerometers in older adults. Nutr Hosp 2010;25:224-30.
151. 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 2001;33:532-41.
152. Kochersberger G, McConnell E, Kuchibhatla MN, Pieper C. The reliability, validity, and stability of a measure of physical activity in the elderly. Archives of physical medicine and rehabilitation 1996;77:793-5.
153. Matthews CE, Ainsworth BE, Hanby C, et al. Development and testing of a short physical activity recall questionnaire. Med Sci Sports Exerc 2005;37:986-94.
154. Kilanowski C, Consalvi A, Epstein L. Validation of an electronic pedometer for measurement of physical activity in children. Pediatric Exercise Science 1999;11:63-8.
155. Macfarlane DJ, Chan D, Chan KL, Ho EY, Lee CC. Using three objective criteria to examine pedometer guidelines for free-living individuals. Eur J Appl Physiol 2008;104:435-44.
156. Tudor-Locke C, Ainsworth BE, Thompson RW, Matthews CE. Comparison of pedometer and accelerometer measures of free-living physical activity. Med Sci Sports Exerc 2002;34:2045-51.
157. Harris TJ, Owen CG, Victor CR, Adams R, Ekelund U, Cook DG. A comparison of questionnaire, accelerometer, and pedometer: measures in older people. Med Sci Sports Exerc 2009;41:1392-402.
158. Loprinzi PD, Cardinal JP. Measuring Children's Physical Activity and Sedentary Behaviors. Journal of Exercise Science and Fitness 2011;9:15-23.
159. Trost SG. State of the art reviews: Measurement of physical activity in children and adolescents. American Journal of Lifestyle Medicine 2007;1:299-314.
160. Welk GJ, Corbin CB, Dale D. Measurement issues in the assessment of physical activity in children. Res Q Exerc Sport 2000;71:S59-73.
161. McMurray RG, Ring KB, Treuth MS, et al. Comparison of two approaches to structured physical activity surveys for adolescents. Med Sci Sports Exerc 2004;36:2135-43.
162. McMurray RG, Ward DS, Elder JP, et al. Do overweight girls overreport physical activity? Am J Health Behav 2008;32:538-46.
163. Sallis JF. Self-report measures of children's physical activity. J Sch Health 1991;61:215-9.
164. Berman N, Bailey R, Barstow TJ, Cooper DM. Spectral and bout detection analysis of physical activity patterns in healthy, prepubertal boys and girls. American Journal of Human Biology 1998;10:289-97.

165. Klesges LM, Baranowski T, Beech B, et al. Social desirability bias in self-reported dietary, physical activity and weight concerns measures in 8- to 10-year-old African-American girls: results from the Girls Health Enrichment Multisite Studies (GEMS). Prev Med 2004;38 Suppl:S78-87.
166. 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 1995;27:1033-41.
167. Pate RR. Physical activity assessment in children and adolescents. Critical reviews in food science and nutrition 1993;33:321-6.
168. Goran MI, Kaskoun M, Johnson R, Martinez C, Kelly B, Hood V. Energy expenditure and body fat distribution in Mohawk children. Pediatrics 1995;95:89-95.
169. Bitar A, Fellmann N, Vernet J, Coudert J, Vermorel M. Variations and determinants of energy expenditure as measured by w hole-body indirect calorimetry during puberty and adolescence. Am J Clin Nutr 1999;69:1209-16.
170. Cooke CB, McDonagh MJ, Nevill AM, Davies CT. Effects of load on oxygen intake in trained boys and men during treadmill running. J Appl Physiol 1991;71:1237-44.
171. Daniels J, Oldridge N, Nagle F, White B. Differences and changes in VO2 among young runners 10 to 18 years of age. Medicine and science in sports 1978;10:200-3.
172. Harrell JS, McMurray RG, Baggett CD, Pennell ML, Pearce PF, Bangdiwala SI. Energy costs of physical activities in children and adolescents. Med Sci Sports Exerc 2005;37:329-36.
173. Mattocks C, Tilling K, Ness A, Riddoch C. Improvements in the measurement of physical activity in childhood obesity research: lessons from large studies of accelerometers. Clinical Medicine Pediatrics 2008;2:27-36.
174. Rowlands AV. Accelerometer assessment of physical activity in children: an update. Pediatr Exerc Sci 2007;19:252-66.
175. Baquet G, Stratton G, Van Praagh E, Berthoin S. Improving physical activity assessment in prepubertal children with high-frequency accelerometry monitoring: a methodological issue. Prev Med 2007;44:143-7.
176. Trost SG, Pate RR, Freedson PS, Sallis JF, Taylor WC. Using objective physical activity measures with youth: how many days of monitoring are needed? Med Sci Sports Exerc 2000;32:426-31.
177. Freedson P, Pober D, Janz KF. Calibration of accelerometer output for children. Med Sci Sports Exerc 2005;37:S523-30.
178. Hussey J, Bennett K, Dwyer JO, Langford S, Bell C, Gormley J. Validation of the RT3 in the measurement of physical activity in children. Journal of science and medicine in sport / Sports Medicine Australia 2009;12:130-3.
179. Pate RR, Almeida MJ, McIver KL, Pfeiffer KA, Dowda M. Validation and calibration of an accelerometer in preschool children. Obesity (Silver Spring) 2006;14:2000-6.
180. Pfeiffer KA, McIver KL, Dowda M, Almeida MJ, Pate RR. Validation and calibration of the Actical accelerometer in preschool children. Med Sci Sports Exerc 2006;38:152-7.
181. de Bruin ED, Hubli M, Hofer P, Wolf P, Murer K, Zijlstra W. Validity and reliability of accelerometer-based gait assessment in patients with diabetes on challenging surfaces. Journal of aging research 2012;2012:954378.
182. Miller GD, Jakicic JM, Rejeski WJ, et al. Effect of Varying Accelerometry Criteria on Physical Activity: The Look AHEAD Study. Obesity (Silver Spring) 2012:32-44.

183. Ward DS, Bar-Or O. Use of the Borg scale in exercise prescription for overweight youth. Can J Sport Sci 1990;15:120-5.
184. Norman A, Bellocco R, Bergstrom A, Wolk A. Validity and reproducibility of self-reported total physical activity--differences by relative weight. Int J Obes Relat Metab Disord 2001;25:682-8.
185. Schmidt MD, Freedson PS, Chasan-Taber L. Estimating physical activity using the CSA accelerometer and a physical activity log. Med Sci Sports Exerc 2003;35:1605-11.
186. Tudor-Locke C, Ainsworth BE, Whitt MC, Thompson RW, Addy CL, Jones DA. The relationship between pedometer-determined ambulatory activity and body composition variables. Int J Obes Relat Metab Disord 2001;25:1571-8.
187. Tudor-Locke C, Ham SA, Macera CA, et al. Descriptive epidemiology of pedometer-determined physical activity. Med Sci Sports Exerc 2004;36:1567-73.
188. Crouter SE, Schneider PL, Bassett DR, Jr. Spring-levered versus piezo-electric pedometer accuracy in overweight and obese adults. Med Sci Sports Exerc 2005;37:1673-9.
189. Feito Y, Bassett DR, Tyo B, Thompson DL. Effects of body mass index and tilt angle on output of two wearable activity monitors. Med Sci Sports Exerc 2011;43:861-6.
190. Hasson RE, Haller J, Pober DM, Staudenmayer J, Freedson PS. Validity of the Omron HJ-112 pedometer during treadmill walking. Med Sci Sports Exerc 2009;41:805-9.
191. Melanson EL, Knoll JR, Bell ML, et al. Commercially available pedometers: considerations for accurate step counting. Prev Med 2004;39:361-8.
192. Crouter SE, Churilla JR, Bassett DR, Jr. Estimating energy expenditure using accelerometers. Eur J Appl Physiol 2006;98:601-12.
193. Prentice AM, Goldberg GR, Murgatroyd PR, Cole TJ. Physical activity and obesity: problems in correcting expenditure for body size. Int J Obes Relat Metab Disord 1996;20:688-91.
194. Maffeis C, Zaffanello M, Pinelli L, Schutz Y. Total energy expenditure and patterns of activity in 8-10-year-old obese and nonobese children. Journal of pediatric gastroenterology and nutrition 1996;23:256-61.
195. Byrne NM, Hills AP, Hunter GR, Weinsier RL, Schutz Y. Metabolic equivalent: one size does not fit all. J Appl Physiol 2005;99:1112-9.
196. Cyarto EV, Myers AM, Tudor-Locke C. Pedometer accuracy in nursing home and community-dwelling older adults. Med Sci Sports Exerc 2004;36:205-9.
197. Storti KL, Pettee KK, Brach JS, Talkowski JB, Richardson CR, Kriska AM. Gait speed and step-count monitor accuracy in community-dwelling older adults. Med Sci Sports Exerc 2008;40:59-64.
198. Grant PM, Dall PM, Mitchell SL, Granat MH. Activity-monitor accuracy in measuring step number and cadence in community-dwelling older adults. Journal of aging and physical activity 2008;16:201-14.
199. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care 2010;33:e147-67.
200. Nwasuruba C, Khan M, Egede LE. Racial/ethnic differences in multiple self-care behaviors in adults with diabetes. Journal of general internal medicine 2007;22:115-20.
201. Jakicic JM, Gregg E, Knowler W, et al. Activity patterns of obese adults with type 2 diabetes in the look AHEAD study. Med Sci Sports Exerc 2010;42:1995-2005.

202. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW. Physical activity in U.S. adults with diabetes and at risk for developing diabetes, 2003. Diabetes Care 2007;30:203-9.
203. Pinhas-Hamiel O, Standiford D, Hamiel D, Dolan LM, Cohen R, Zeitler PS. The type 2 family: a setting for development and treatment of adolescent type 2 diabetes mellitus. Arch Pediatr Adolesc Med 1999;153:1063-7.
204. Goodyear LJ, Chang PY, Sherwood DJ, Dufresne SD, Moller DE. Effects of exercise and insulin on mitogen-activated protein kinase signaling pathways in rat skeletal muscle. Am J Physiol 1996;271:E403-8.
205. Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. Appl Physiol Nutr Metab 2010;35:725-40.
206. Ferreira LD, Pulawa LK, Jensen DR, Eckel RH. Overexpressing human lipoprotein lipase in mouse skeletal muscle is associated with insulin resistance. Diabetes 2001;50:1064-8.
207. Jensen DR, Schlaepfer IR, Morin CL, et al. Prevention of diet-induced obesity in transgenic mice overexpressing skeletal muscle lipoprotein lipase. Am J Physiol 1997;273:R683-9.
208. Gill JM, Cooper AR. Physical activity and prevention of type 2 diabetes mellitus. Sports Med 2008;38:807-24.
209. Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. Diabetes Care 2007;30:744-52.
210. Kriska AM, Saremi A, Hanson RL, et al. Physical activity, obesity, and the incidence of type 2 diabetes in a high-risk population. American journal of epidemiology 2003;158:669-75.
211. Hu FB, Sigal RJ, Rich-Edwards JW, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. JAMA 1999;282:1433-9.
212. Nygaard H, Tomten SE, Hostmark AT. Slow postmeal walking reduces postprandial glycemia in middle-aged women. Appl Physiol Nutr Metab 2009;34:1087-92.
213. Hostmark AT, Ekeland GS, Beckstrom AC, Meen HD. Postprandial light physical activity blunts the blood glucose increase. Prev Med 2006;42:369-71.
214. Tudor-Locke C, Schuna JM, Jr. Steps to preventing type 2 diabetes: exercise, walk more, or sit less? Frontiers in endocrinology 2012;3:1-7.
215. Demakakos P, Hamer M, Stamatakis E, Steptoe A. Low-intensity physical activity is associated with reduced risk of incident type 2 diabetes in older adults: evidence from the English Longitudinal Study of Ageing. Diabetologia 2010;53:1877-85.
216. Ford ES, Schulze MB, Kroger J, Pischon T, Bergmann MM, Boeing H. Television watching and incident diabetes: Findings from the European Prospective Investigation into Cancer and Nutrition-Potsdam Study. Journal of diabetes 2010;2:23-7.
217. Hu FB, Li TY, Colditz GA, Willett WC, Manson JE. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. JAMA 2003;289:1785-91.
218. Dunstan DW, Barr EL, Healy GN, et al. Television viewing time and mortality: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). Circulation 2010;121:384-91.
219. Wijndaele K, Healy GN, Dunstan DW, et al. Increased cardiometabolic risk is associated with increased TV viewing time. Med Sci Sports Exerc 2010;42:1511-8.
220. Zhang C, Solomon CG, Manson JE, Hu FB. A prospective study of pregravid physical activity and sedentary behaviors in relation to the risk for gestational diabetes mellitus. Arch Intern Med 2006;166:543-8.

221. Hu FB, Leitzmann MF, Stampfer MJ, Colditz GA, Willett WC, Rimm EB. Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. Arch Intern Med 2001;161:1542-8.
222. Cooper AR, Sebire S, Montgomery AA, et al. Sedentary time, breaks in sedentary time and metabolic variables in people with newly diagnosed type 2 diabetes. Diabetologia 2012;55:589-99.
223. Brown WJ, Bauman AE, Owen N. Stand up, sit down, keep moving: turning circles in physical activity research? Br J Sports Med 2009;43:86-8.
224. Tucker JM, Welk GJ, Beyler NK. Physical activity in U.S.: adults compliance with the Physical Activity Guidelines for Americans. Am J Prev Med 2011;40:454-61.
225. Brownson RC, Boehmer TK, Luke DA. Declining rates of physical activity in the United States: what are the contributors? Annu Rev Public Health 2005;26:421-43.
226. Jarvandi S, Davidson NO, Jeffe DB, Schootman M. Influence of lifestyle factors on inflammation in men and women with type 2 diabetes: results from the national health and nutrition examination survey, 1999-2004. Ann Behav Med 2012;44:399-407.
227. Lin EH, Katon W, Von Korff M, et al. Relationship of depression and diabetes self-care, medication adherence, and preventive care. Diabetes Care 2004;27:2154-60.
228. Nelson KM, Reiber G, Boyko EJ, Nhanes, III. Diet and exercise among adults with type 2 diabetes: findings from the third national health and nutrition examination survey (NHANES III). Diabetes Care 2002;25:1722-8.
229. Hays LM, Clark DO. Correlates of physical activity in a sample of older adults with type 2 diabetes. Diabetes Care 1999;22:706-12.
230. Resnick HE, Foster GL, Bardsley J, Ratner RE. Achievement of American Diabetes Association clinical practice recommendations among U.S. adults with diabetes, 1999-2002: the National Health and Nutrition Examination Survey. Diabetes Care 2006;29:531-7.
231. Greenspan SL, Resnick NM, Parker RA. Combination therapy with hormone replacement and alendronate for prevention of bone loss in elderly women: a randomized controlled trial. JAMA 2003;289:2525-33.
232. Camhi SM, Sisson SB, Johnson WD, Katzmarzyk PT, Tudor-Locke C. Accelerometer-determined moderate intensity lifestyle activity and cardiometabolic health. Prev Med 2011;52:358-60.
233. Kriska A, Delahanty L, Edelstein S, et al. Sedentary behavior and physical activity in youth with recent onset of type 2 diabetes. Pediatrics 2013;131:e850-6.
234. Copeland KC, Zeitler P, Geffner M, et al. Characteristics of Adolescents and Youth with Recent-Onset Type 2 Diabetes: The TODAY Cohort at Baseline. J Clin Endocrinol Metab 2010.
235. Pate R, Ross R, Dowda M, Trost S. Validation of a 3-Day Physical Activity Recall Instrument in Female Youth. Pediatric Exercise Science 2003;15:257-65.
236. Motl RW, Dishman RK, Dowda M, Pate RR. Factorial validity and invariance of a self-report measure of physical activity among adolescent girls. Res Q Exerc Sport 2004;75:259-71.
237. Stanley R, Boshoff K, Dollman J. The concurrent validity of the 3-day Physical Activity Recall questionnaire administered to female adolescents aged 12-14 years. Australian Occupational Therapy Journal 2007;54:294-302.
238. Lee KS, Trost SG. Validity and reliability of the 3-day physical activity recall in Singaporean adolescents. Res Q Exerc Sport 2005;76:101-6.

239. Trost SG, Ward DS, Moorehead SM, Watson PD, Riner W, Burke JR. Validity of the computer science and applications (CSA) activity monitor in children. Med Sci Sports Exerc 1998;30:629-33.
240. Roemmich JN, Clark PA, Walter K, Patrie J, Weltman A, Rogol AD. Pubertal alterations in growth and body c omposition. V. Energy expenditure, adiposity, and fat distribution. American journal of physiology 2000;279:E1426-36.
241. Knowler WC, Fowler SE, Hamman RF, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009;374:1677-86.
242. Kriska AM, Edelstein SL, Hamman RF, et al. Physical activity in individuals at risk for diabetes: Diabetes Prevention Program. Med Sci Sports Exerc 2006;38:826-32.
243. Robusto KM, Trost SG. Comparison of three generations of ActiGraph activity monitors in children and adolescents. J Sports Sci 2012;30:1429-35.
244. Sasaki JE, John D, Freedson PS. Validation and comparison of ActiGraph activity monitors. Journal of science and medicine in sport / Sports Medicine Australia 2011;14:411-6.
245. Saydah SH, Byrd-Holt D, Harris MI. Projected impact of implementing the results of the diabetes prevention program in the U.S. population. Diabetes Care 2002;25:1940-5.
246. Hage C, Lundman P, Ryden L, Mellbin L. Fasting glucose, HbA1c, or oral glucose tolerance testing for the detection of glucose abnormalities in patients with acute coronary syndromes. European journal of preventive cardiology 2012.
247. Kim KS, Kim SK, Lee YK, Park SW, Cho YW. Diagnostic value of glycated haemoglobin HbA(1c) for the early detection of diabetes in high-risk subjects. Diabet Med 2008;25:997-1000.
248. The Diabetes Prevention Program (DPP): description of lifestyle intervention. Diabetes Care 2002;25:2165-71.
249. Affuso O, Stevens J, Catellier D, et al. Validity of self-reported leisure-time sedentary behavior in adolescents. J Negat Results Biomed 2011;10:2.
250. Services USDoHaH. Healthy People 2020. In: Promotion OoDPaH, ed. Washington D.C.