PHYSICAL ACTIVITY, SEDENTARY BEHAVIOUR AND SLEEP:
ASSOCIATIONS WITH CARDIOMETABOLIC RISK IN
ABDOMINALLY OBESE MEN AND WOMEN

by

Karen Ashlee McGuire

A thesis submitted to the School of Kinesiology and Health Studies
In conformity with the requirements for
the degree of Doctor of Philosophy

Queen's University
Kingston, Ontario, Canada
(May, 2011)

Copyright ©Karen Ashlee McGuire, 2011
Abstract

Current guidelines suggest that physical activity must be performed at a moderate-to-vigorous intensity (MVPA) and accumulated in bouts of at least 10 consecutive minutes to elicit improvement in cardiorespiratory fitness (CRF). In the first study we sought to determine whether the duration and intensity of objectively measured incidental physical activity (IPA; activity performed below the designated threshold) was associated with CRF in abdominally obese, inactive men (n=43) and women (n=92). Secondary analyses examined the associations between light physical activity (LPA), sporadic moderate physical activity (MPA; accumulated in <10 minute bouts), and CRF. Both duration and intensity of IPA were positively associated with CRF among inactive, abdominally obese adults. Sporadic MPA, but not LPA, was an independent predictor of CRF.

Whereas some observations suggest that sedentary behaviour (SED) is negatively associated with health outcomes, other evidence fails to support this notion. The primary aim of the second study was to clarify the relationships between SED, LPA, and MVPA with 2-hour glucose and insulin resistance in inactive adults (43 men, 92 women) with abdominal obesity. Secondary analyses examined the association between SED, LPA, MVPA and other common cardiometabolic risk factors. Neither SED nor the physical activity variables were associated with 2-hour glucose or insulin resistance. SED was not associated with any cardiometabolic risk factor; with the exception of blood pressure, LPA was not associated with any cardiometabolic risk factor; and MVPA was independently associated with total cholesterol and triglycerides.
Whether IPA is associated with abdominal obesity is unknown. The purpose of study three was to determine the association between IPA and abdominal adipose tissue depots (visceral adipose tissue and subcutaneous adipose tissue) in inactive men (n=42) and women (n=84). Secondary analyses examined the associations between SED, sleep duration, and caloric intake with abdominal obesity. IPA was not associated with any measure of abdominal obesity, nor was LPA. After control for age and sex, MPA was negatively associated with visceral adipose tissue. SED and sleep duration were not associated with abdominal obesity. Caloric intake was not associated with abdominal obesity after control for age and sex.
Co-Authorship

Dr. Robert Ross is the sole co-author within this document. K. Ashlee McGuire was responsible for the conception of the studies (in collaboration with Dr. Ross), data collection, all statistical analyses of data, and writing of the manuscripts contained within the thesis. Dr. Ross provided critical revisions for intellectual content of the manuscripts.
Thesis Contributions

This thesis was a small component of a much larger, 6-month randomized controlled trial (SERENA Study) designed to determine the effects of exercise dose and intensity on cardiometabolic risk factors in abdominally obese men and women. Thus, data collection, management, cleaning, and analysis were a collaborative effort between myself, other graduate students, and staff members. My specific responsibilities were the acquisition, management, cleaning, and analysis of the accelerometry (physical activity, sedentary behaviour, and sleep duration) data and a substantial portion of the magnetic resonance imaging data. I worked closely with the data manager/programmer extraordinaire to create a custom program for the accelerometry data, and lastly, performed all statistical analyses.
Acknowledgements

Well, it is hard to believe that my PhD degree is over and my long-standing status as a student has ended. As is the case with many large projects, this degree was not a solo endeavor but was achieved with the help of many others. There are numerous individuals from both my personal and academic life who contributed substantially to the completion of my degree and to whom I am forever indebted. While I cannot adequately thank everyone, there are a few who deserve special mention and to whom I will try to do justice in the following note. So, in no particular order here goes …

The first thank you goes out to all of the wonderful participants of SERENA. Obviously, you are a critical component of this thesis and without you I would still be in the starting blocks. I really enjoyed meeting you all, listening to your stories on the treadmill, and in the past year bumping into you in the gym or running on the streets of Kingston. I am incredibly pleased that some of you have maintained your physical activity routine after completing the study and wish you all the best as you continue.

I also owe a big thank you to all of the staff in the Ross laboratory. There have been many of you in my short time here therefore I will only specifically mention a few who deserve a special thank you as I could not have collected and analyzed my data without you. Melinda – I don’t think there are words to describe how amazing you are and how helpful you have been to me. The success of SERENA thus far can be attributed in large measure to your work! Ehsan and Paula – I would be working on this degree for at least another 2 (probably more) years if I did not have your expert technical assistance! I am forever grateful for all of your hard work and extreme patience with me! Also, thank you to Lauren and John – the 2 of you have been assisting me with data...
collection since the beginning of SERENA and have been very accommodating, flexible, and helpful. Finally, Tammy, the collection of cardiometabolic risk factor data was possible due to your expertise so I am very grateful for your time and contributions.

Throughout the duration of my degree there have also been a number of graduate students in the laboratory to whom I owe a sincere thank you. Thank you to Peter and Travis who welcomed both myself and Andrew to the lab almost 4 years ago now and Peter for your very much appreciated advice throughout the home stretch. Danielle, despite your short stay I learned a lot from you and also acquired a great friend – thank you for both! To Kaitlyn and Morgan who joined the team mid-way through – I don’t even know where to start (or stop). Throughout the last few years I have really appreciated your friendship, support, encouragement, hilarious stories, and help. I cannot imagine the experience without you – thank you so much!! To the latest edition – Trevor – you fit in well with the 3 of us ladies and your support over my final few months was definitely appreciated! Lastly, James, thank you for the opportunity to supervise. Not only was it a great experience for me, but your humour and cheerful presence in the laboratory was very uplifting on those long work days.

Bob, I owe you a huge and very sincere thank you for providing me with the opportunity to complete a PhD under your supervision and for all of the time you invested in my growth as a young investigator. You have been a fantastic mentor and under your guidance I learned an incredible amount about the world of science. I am also leaving your supervision feeling more confident in myself and more prepared to face the unknown thanks to one particularly important life lesson you gave: never let the fear of failure stop you from pursuing your life goals. Thank you also for the social gatherings
and fun events you (Melinda or Pam) organized for the students and staff – very important for my development as an independent researcher;)

To my family here in Ontario (and spread from coast to coast) and to my other family out West – I appreciate all of the support, encouragement, and love you have provided throughout the duration of this degree. Mom and Dad, Jen and Scott, and Heidi and Steve – thank you for taking me in when I needed a weekend getaway and for absolutely everything. Tash and Dave, and Shay and Dan – I appreciate your supportive emails and phone calls from afar and wish you were all closer! Meyers - Gisele and Ray, and family - thank you for being so accommodating and supportive of me from the beginning, and for distracting me from my work at various time points over the past few years.

And finally, thank you Dylan. I couldn’t be any luckier - you have been incredibly supportive and very patient with me as I obtained yet another degree. Words cannot describe how appreciative I am of everything you have done for me throughout the duration of this degree and how much your love and support has helped me through. THANK YOU!!
# Table of Contents

Abstract ........................................................................................................................... ii  
Co-Authorship ................................................................................................................ iv  
Thesis Contributions ........................................................................................................ v  
Acknowledgements ........................................................................................................ vi  

**Chapter 1 Introduction** ................................................................................................... 1  

**Chapter 2 Literature Review** .......................................................................................... 5  
2.1 Physical Activity and Sedentary Behaviour: Prevalence and Problems ............ 5  
2.2 Overview of Daily Energy Expenditure ................................................................. 6  
   2.2.1 Total Daily Energy Expenditure ........................................................................ 6  
   2.2.2 The Movement Continuum .............................................................................. 7  
   2.2.3 Health Along the Movement Continuum ......................................................... 8  
2.3 Measurement of Physical Activity and Sedentary Behaviour .......................... 9  
   2.3.1 Self-Report Questionnaires to Measure Physical Activity and Sedentary  
       Behaviour ........................................................................................................... 13  
   2.3.2 Accelerometry to Measure Physical Activity and Sedentary Behaviour ....... 14  
2.4 Moderate-to-Vigorous Physical Activity and Health ..................................... 21  
   2.4.1 Physical Activity Guidelines .......................................................................... 21  
   2.4.2 Moderate-to-Vigorous Physical Activity Intensity ......................................... 22  
   2.4.3 Moderate-to-Vigorous Physical Activity Volume ........................................... 24  
   2.4.4 Moderate-to-Vigorous Physical Activity Duration ....................................... 26  
   2.4.5 Moderate-to-Vigorous Physical Activity Frequency ..................................... 28  
   2.4.6 Moderate-to-Vigorous Physical Activity and Health Outcomes: Mechanisms .29  
2.5 Light Physical Activity and Health ..................................................................... 31  
   2.5.1 Evidence from Self-Report Studies ............................................................... 31  
   2.5.2 Evidence from Accelerometry Studies ......................................................... 32  
   2.5.3 Light Physical Activity and Health: Potential Mechanisms ......................... 34  
2.6 Sedentary Behaviour and Health ...................................................................... 35  
   2.6.1 Evidence from Self-Report Studies ............................................................... 36  
   2.6.2 Evidence from Accelerometry Studies ......................................................... 36  
   2.6.3 Sedentary Behaviour Duration ..................................................................... 39
<table>
<thead>
<tr>
<th>Section Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6.4 Sedentary Behaviour, Physical Activity and Health Outcomes</td>
<td>39</td>
</tr>
<tr>
<td>2.6.5 Sedentary Behaviour and Health: Potential Mechanisms</td>
<td>40</td>
</tr>
<tr>
<td>2.7 Sleep and Health</td>
<td>43</td>
</tr>
<tr>
<td>2.7.1 The Autonomic Nervous System and Short Sleep Duration</td>
<td>43</td>
</tr>
<tr>
<td>2.7.1.1 Regulation of Satiety Hormones and Food Intake</td>
<td>46</td>
</tr>
<tr>
<td>2.7.2 Short Sleep Duration and Energy Expenditure</td>
<td>47</td>
</tr>
<tr>
<td>2.7.3 Sleep Duration, Physical Activity, Sedentary Behaviour, and Health</td>
<td>47</td>
</tr>
<tr>
<td>2.8 Caloric Intake</td>
<td>48</td>
</tr>
<tr>
<td>2.9 Summary</td>
<td>49</td>
</tr>
</tbody>
</table>

**Chapter 3** Incidental physical activity is positively associated with cardiorespiratory
fitness.................................................................51

**ABSTRACT**............................................................52

**INTRODUCTION**......................................................54

**METHODS**..............................................................56

Participants...............................................................56

Anthropometry...........................................................56

Cardiorespiratory Fitness..........................................57

Physical Activity.......................................................57

Statistical Analyses...................................................59

**RESULTS**...............................................................61

**DISCUSSION**..........................................................67

**Chapter 4** Sedentary behaviour is not associated with cardiometabolic risk in adults with
abdominal obesity .....................................................71

**ABSTRACT**............................................................72

**INTRODUCTION**......................................................74

**METHODS**..............................................................75

Participants...............................................................75

Anthropometric and Metabolic Tests.............................75

Physical Activity by Accelerometry................................76

Statistical and Power Analyses....................................78

**RESULTS**...............................................................80

**DISCUSSION**..........................................................86
List of Figures and Illustrations

Chapter 2
Figure 2-1 The movement continuum ................................................................. 8
Figure 2-2 Physical activity and sedentary behaviour profiles by accelerometry ....16
Figure 2-3 Moderate-to-vigorous physical activity and mortality .......................26
Figure 2-4 Sleep loss and health risk .................................................................45

Chapter 3
Figure 3-1 Associations of A) incidental physical activity duration and B) incidental
physical activity intensity with cardiorespiratory fitness ...................................64
Figure 3-2 Associations of A) light physical activity and B) moderate physical activity
with cardiorespiratory fitness ..........................................................................65
Figure 3-3 Tertiles of moderate physical activity and cardiorespiratory fitness with
 corresponding participant characteristics for each tertile ..........................66

Chapter 4
Figure 4-1 Association of A) 2-hour glucose (mmol/L) with B) sedentary behaviour
(min/d) and C) light physical activity (min/d) for each individual participant .......85

Chapter 5
Figure 5-1 Associations between incidental physical activity and A) visceral adipose
tissue, B) abdominal subcutaneous adipose tissue, C) total abdominal adipose tissue,
and D) waist circumference ...........................................................................105
Figure 5-2 Tertiles of moderate physical activity and visceral adipose tissue with
corresponding participant characteristics .....................................................106
List of Tables

Chapter 2
Table 2-1 Methods for assessing physical activity and sedentary behaviours ..........11
Table 2-2 Accelerometer calibration studies .................................................................19
Table 2-3 Mechanisms by which moderate-to-vigorous physical activity improves cardiometabolic risk factors ...........................................................................................30
Table 2-4 Independent associations between objectively measured light physical activity and health outcomes ........................................................................................................33
Table 2-5 Independent associations between objectively measured sedentary behaviour and health outcomes ........................................................................................................38

Chapter 3
Table 3-1 Participant characteristics .............................................................................62
Table 3-2 Regression analyses of physical activity and cardiorespiratory fitness .........63

Chapter 4
Table 4-1 Participant characteristics .............................................................................82
Table 4-2 Regression analyses of sedentary behaviour and physical activity (expressed as average minutes worn per day) with glucose metabolism ........................................83
Table 4-3 Regression analyses of sedentary behaviour and physical activity (expressed as percentage of wear time) with glucose metabolism ...................................................84

Chapter 5
Table 5-1 Participant characteristics ........................................................................... 102
Table 5-2 Regression analyses of physical activity and abdominal obesity .............103
Chapter 1

Introduction

The environmental exposures and lifestyle experienced by our hunter-gatherer ancestors demanded the daily accumulation of large volumes of physical activity for survival and required the synchronization of wake/sleep cycles with the rising and setting of the sun. Conversely, in modern society, energy-saving devices and advanced technology eliminate the need for physical activity, thereby providing an environment conducive to prolonged periods of sitting. Moreover, electrical lighting extends the number of hours available for daytime chores and commitments, leading to decreased time spent sleeping \(^1\). In concert with the technological and lifestyle changes that have occurred over the years is an increase in many chronic diseases and serious health conditions \(^2\). Although research has begun to shed light on the complex relationships between health and physical activity, sedentary behaviour (SED), and sleep, many unanswered questions remain.

The seminal work of Morris et al. \(^3\) describing reduced rates of mortality in bus conductors and postmen compared to bus drivers and telephone switchboard operators in the 1950’s marked the beginning of the physical activity and health research field. Since this study, many investigations have corroborated these findings and the numerous health benefits of physical activity are now well-established \(^4\)\(^-\)\(^7\). The results of these studies have culminated in the development of physical activity guidelines which recommend that adults accumulate at least 150 minutes of moderate physical activity, or
at least 75 minutes of vigorous physical activity, or some combination of moderate and vigorous intensity physical activity (MVPA) on a weekly basis. The guidelines further recommend that the moderate and/or vigorous physical activity be accumulated in bouts of at least 10 consecutive minutes in duration and be accrued in addition to routine activities of daily living. Thus, individuals who accumulate at least the minimum amount of physical activity as recommended by these guidelines are classified as active whereas those individuals who fail to meet these guidelines are classified as inactive. It is important to note however that there is a paucity of research specifically examining MVPA accumulated in bouts less than 10 minutes in duration. Thus, the association of non-bouted moderate and/or vigorous physical activity with health outcomes is largely unknown.

Research describing the benefits of participation in light physical activity (LPA) is also sparse. In fact, the suggestion to accumulate at least 60 minutes of LPA per day to obtain health benefits was recently removed from Canada’s Physical Activity Guidelines for Adults due to the absence of evidence to support the recommendation. Although recent investigations employing the use of accelerometry, which provides objective, time-stamped physical activity data for extended time periods, have begun to elucidate the relationship between LPA and various cardiometabolic risk factors, results are inconsistent. Therefore the association between LPA and health outcomes is not yet clearly delineated.

SED is an emerging area of health research that has gained substantial popularity in recent years due to the inverse association commonly observed between
SED and various health outcomes independent of physical activity. This suggests that SED affects cardiometabolic risk factors via a pathway that is distinct from physical activity. Indeed, studies have provided evidence of unique mechanisms triggered by prolonged SED. However, contradictory evidence exists. Thus, the association of SED with cardiometabolic risk factors requires further clarification.

Time spent sleeping is another form of SED however, in contrast to the SED that is accumulated throughout the waking period of a day, extended periods (i.e., 7 to 8 hours) spent sleeping are associated with positive health outcomes. Thus, the mechanisms by which daytime SED and nighttime SED affect health are distinct from each other. Although sleep duration has been associated with numerous health outcomes, whether it remains a significant predictor independent of physical activity and SED is unknown.

At present there are many questions regarding the relationships between MVPA, LPA, SED, and sleep with health risk that remain unresolved. Accordingly, the manuscripts in chapters 3 through 5 aim to address the following questions in a high-risk population of inactive, abdominally obese men and women:

1. Is incidental physical activity (i.e., activities of daily living that are of light intensity and/or accumulated in bouts less than 10 minutes in duration) associated with cardiorespiratory fitness? What are the independent contributions of light physical activity and sporadic moderate physical activity to cardiorespiratory fitness?
2. Is sedentary behaviour associated with cardiometabolic risk independently of moderate physical activity?

3. Is incidental physical activity (light physical activity and moderate physical activity) associated with abdominal obesity? Are sedentary behaviour, sleep duration, and caloric intake independent predictors of abdominal obesity?
Chapter 2

Literature Review

2.1 Physical Activity and Sedentary Behaviour: Prevalence and Problems

Currently only 15% of adult Canadians regularly participate in sufficient physical activity to substantially reduce the risk of numerous chronic diseases \(^4\)-\(^7\), \(^28\) and poor health outcomes \(^7\), \(^29\), \(^30\). Conversely, many Canadian adults habitually accumulate large volumes of SED throughout the day; approximately 69% of a typical day is spent in SED \(^28\), of which a substantial proportion is spent watching television \(^31\). Similar observations have been made in other countries around the globe, thus these trends are not unique to Canada \(^12\), \(^14\), \(^32\), \(^33\). Unfortunately, increased time spent in SED is associated with negative health outcomes such as increased risk of mortality and increased prevalence of cardiometabolic risk factors \(^12\), \(^13\), \(^17\), \(^34\)-\(^36\).

These statistics paint an unhealthy picture of Canadian adults, and adults worldwide. It is thought that these behavioural characteristics common to many adults are responsible, at least in part, for the dramatic increase observed in many chronic diseases such as obesity and type 2 diabetes \(^37\). Unfortunately, it is likely that the opportunities to accumulate physical activity sporadically throughout the day will decrease and the opportunities to enjoy energy-saving sedentary pursuits will increase as global advances in technology continue to occur \(^38\). Therefore it is likely that health issues related to physical inactivity and SED will increase in prevalence in the future \(^38\).
2.2 Overview of Daily Energy Expenditure

2.2.1 Total Daily Energy Expenditure

Physical activity and SED contribute to energy expenditure and only represent a small component of total daily energy expenditure (TDEE), which consists of three main components: 1) basal metabolic rate (BMR), 2) thermic effect of food, and 3) activity thermogenesis. BMR is the largest component of energy expenditure accounting for approximately 60% of TDEE in the average individual. It is the energy expended while laying at complete rest, in the morning, after sleep, and in the post-absorptive state; the energy required to maintain essential vital functioning. It is often used interchangeably with resting metabolic rate which is within 10% of BMR. Thermic effect of food is the increase in energy expenditure associated with the digestion, absorption, and storage of food and accounts for approximately 10 to 15% of TDEE. Activity thermogenesis is highly variable and can account for approximately 15% of TDEE in the average inactive individual or 50% of TDEE in highly active individuals (i.e., individuals who exceed consensus physical activity recommendations). It can be further subdivided into two components: 1) exercise-related activity thermogenesis and 2) non-exercise activity thermogenesis (NEAT). In most individuals, exercise-related activity thermogenesis is negligible or zero and even in those individuals who are highly active, NEAT is the predominant component of activity thermogenesis. NEAT is the energy expenditure of a variety of activities including but not limited to occupation, leisure, sitting, standing, walking, talking, and fidgeting. However, NEAT consists
primarily of low-to-moderate intensity ambulatory activities (≤ 50% maximal oxygen consumption) \(^{44}\).

### 2.2.2 The Movement Continuum

The numerous activities and behaviours incorporated under activity thermogenesis can be viewed along a movement continuum (Figure 2-1). At the far left end of the continuum are behaviours requiring ≤ 1.5 METs, where 1 MET corresponds to the resting metabolic rate or 3.5 ml oxygen uptake/kg body weight/minute \(^5\) and include activities such as sleeping, watching television, and commuting in a vehicle \(^{45}\). At the other extreme is vigorous intensity physical activity requiring ≥ 6 METs and includes activities such as running, playing tennis, or heavy manual labour \(^{45}\). LPA (> 1.5 and < 3 METs) includes activities such as standing, household chores, and food preparation \(^{45}\).
**2.2.3 Health Along the Movement Continuum**

The importance of examining activities of all intensities is illustrated by recent evidence indicating that each component of the movement continuum has unique and qualitatively different effects on numerous health outcomes and biological processes than all of the others. For example, using a rodent model Hamilton and colleagues demonstrated that the mechanisms that cause changes in lipoprotein lipase (LPL), an enzyme responsible for the uptake of triglycerides and cholesterol metabolism, differ substantially between exercise physiology and sedentary physiology.
After reducing ambulation for one day (i.e., imposing SED), the magnitude of LPL suppression was much greater than the increase detected after imposing high intensity exercise. Further, the effects of SED on LPL were greatest in the oxidative muscle fibres whereas with exercise, the effects were most pronounced in the glycolytic muscle fibres. This example only represents one small component of the biological processes that govern the relationship between SED, physical activity, and health. Also involved is personal motivation, health and mobility, genetics, other biological processes, and the environment in which we live. Thus, behaviour is complex and each component should be treated as a distinct construct to obtain a clear understanding of how health outcomes are affected. Although measurement of human movement has been difficult in the past, the advent of objective activity monitors, such as the accelerometer, has vastly improved our ability to capture activities across the full movement spectrum.

2.3 Measurement of Physical Activity and Sedentary Behaviour

The accelerometer is one of many measurement tools available to assess physical activity and/or SED. These tools vary substantially in terms of reliability (i.e., repeatability), validity (i.e., how well the behaviour is measured) and feasibility for use in large studies. Further, each has a unique set of strengths and weaknesses that determine their appropriateness to answer specific research questions and use in different environments. However, robust research requires the use of tools that are both valid and reliable to measure quantity and quality of physical activity and SED. While a detailed description of all the methodologies is beyond the scope of this review, Table
2-1 provides an overview of those used in the field. The most commonly employed methods utilized to assess physical activity and SED will be described in greater detail below. The reader is also encouraged to seek out other sources for further information on physical activity and SED measurement tools 51-53.
<table>
<thead>
<tr>
<th>Method</th>
<th>Feasibility</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-Report Questionnaire</td>
<td>high</td>
<td>Inexpensive, provide context to activity, low participant burden</td>
<td>Prone to bias (recall, social desirability, response), unable to capture sporadic, unplanned activity, often only measure one aspect of behaviour (i.e., leisure time)</td>
</tr>
<tr>
<td>Diary</td>
<td>moderate</td>
<td>Inexpensive, provide context to activity, detailed</td>
<td>Prone to bias (recall, social desirability, response), labour-intensive for participants</td>
</tr>
<tr>
<td>Pedometers</td>
<td>moderate</td>
<td>Objective, inexpensive, unobtrusive</td>
<td>Cannot store data for extended periods, under-estimates vigorous activity, only detect ambulatory movements, not water proof, cannot measure sedentary behaviour</td>
</tr>
<tr>
<td>Heart Rate Monitors</td>
<td>moderate</td>
<td>Objective, store data for extended time periods, noninvasive, inexpensive, capture frequency, intensity, and duration of some free-living activities, high resolution data collection</td>
<td>Sensitive to stress (emotional, environmental), provide no context to activity, difficulty assessing sedentary and low intensity behaviours</td>
</tr>
<tr>
<td>Accelerometers</td>
<td>moderate</td>
<td>Objective, capture frequency, intensity, and duration of all types of activity and provide a chronological recording, store data for extended time periods, high resolution data collection</td>
<td>Provide no context to activity, only detect ambulatory activity well, not water proof (some models), cannot detect the difference between sitting, lying, and standing still</td>
</tr>
<tr>
<td>Direct Observation</td>
<td>low</td>
<td>Captures frequency, intensity, and duration of all types of activity, provides context to activity, high resolution data</td>
<td>Costly, labour-intensive, requires extensive training, short collection period</td>
</tr>
<tr>
<td>Method</td>
<td>Measurement Objective</td>
<td>Measurement Accuracy</td>
<td>Measurement Context</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------</td>
<td>----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Doubly Labeled Water</td>
<td>low</td>
<td>Objective, gold standard measure of energy expenditure, accurate, extended measurement period</td>
<td>Costly, provides no context to activity, cannot assess physical activity or sedentary behaviour patterns</td>
</tr>
<tr>
<td>Indirect Calorimetry</td>
<td>low</td>
<td>Objective, criterion measure of activity intensity, high frequency sampling</td>
<td>Costly, burdensome to participants, short data collection periods, provides no context to activity, short data collection period</td>
</tr>
<tr>
<td>Calorimetry</td>
<td>low</td>
<td>Objective, criterion measure of activity intensity, high frequency sampling</td>
<td>Costly, cannot assess free-living activity, short data collection period</td>
</tr>
</tbody>
</table>
2.3.1 Self-Report Questionnaires to Measure Physical Activity and Sedentary Behaviour

Self-report questionnaires, of which there are a wide number available for use, have been employed most often to assess physical activity and SED. Although they are inexpensive and feasible for large-scale studies, they are limited in their ability to provide accurate or detailed information and are associated with numerous limitations that make interpretation of a complex behaviour like physical activity or SED difficult. Self-report measurement tools are best suited to the reporting of activities that are volitional or structured such as running or sports and/or that occupy long and distinct time periods, such as television viewing. As well, they typically only measure one aspect of physical activity, such as leisure time activity, or one component of SED, such as television viewing, which is used as a proxy for all other behaviours of a similar intensity, thereby only accounting for a portion of the total behaviour. The limitations of utilizing a proxy measure were recently demonstrated by Clark et al. who found that even though television viewing time was positively associated with objectively measured SED, the correlations were weak in magnitude (rank order correlations = 0.22, p < 0.001). Moreover, these correlations differed depending on sex, age, and employment status. Additionally, activities that are either sporadic or intermittent in nature, or are unstructured or low in intensity, are typically either not captured at all or not captured well by questionnaires. Finally, self-report tools are prone to various types of bias, such as recall and social desirability bias. For example, reliability of information gathered via questionnaire decreases with the length of the period surveyed and with increasing difficulty or length of the survey. In general, participants often
underestimate activities perceived as undesirable (e.g., sedentary time) and overestimate activities viewed as desirable (e.g., exercise)\textsuperscript{60}.

2.3.2 Accelerometry to Measure Physical Activity and Sedentary Behaviour

Objective activity measurement devices, such as accelerometers, overcome many of the limitations inherent to self-report tools, such as recall bias, and eliminate issues with cultural norms and perceptions of intensity or difficulty of physical activity while providing detailed information regarding physical activity and SED patterning (i.e., frequency, intensity, duration)\textsuperscript{50, 61}. Accelerometers are small, electronic devices which are typically worn on the hip and programmed to collect data in 1-minute intervals. The most important contribution of accelerometers is their ability to capture time-stamped sporadic, non-purposeful activities of all intensities\textsuperscript{59}. This is illustrated in Figure 2-2 which depicts a 24-hour accelerometer profile of two individuals, both similarly classified as inactive. However, careful inspection of the two profiles reveals very different physical activity and SED patterns. In profile A we can see that almost the entire waking portion of the day (i.e., 6:00 am to 10:30 pm) is spent in LPA (accelerometer counts per minute (cpm) 100 to 1951) and very little time is spent in SED (cpm < 100). Conversely, in profile B we can see that a substantial proportion of the day is spent in SED and a much smaller proportion is spent in LPA. Of note, individuals in both profiles A and B accumulated very little MVPA (cpm ≥ 1952) although the individual in profile A clearly has accrued more than the individual in profile B. This rich data provides the opportunity to determine which dimensions of physical activity and/or SED are most important for
specific health outcomes and what amount of physical activity/SED is required to achieve health benefit/detriment\textsuperscript{62}. 


The 24-hour physical activity and sedentary behaviour profile of individuals A and B measured by an Actigraph accelerometer. Physical activity intensity thresholds (Freedson et al. 1998) are indicated on the graphs: MVPA, moderate-to-vigorous physical activity, is that which falls above the green line (>1952 cpm, counts per minute); LPA, light physical activity, falls between the red and green line (100 to 1951 cpm); and SED, sedentary behaviour, falls below the red line (<100 cpm). Individual A wakes up ~6:00am and spends most of the day in LPA before retiring ~10:30pm. Individual B wakes up ~7:00am and spends most of the day in SED before retiring ~10:30pm.
Although accelerometers provide a wealth of data and their use has resulted in substantial advances in physical activity and SED research, they are not without limitations. The most noted limitations are their inability to provide context to the data collected, detect an increase in energy expenditure with upper body movements or movement up an incline, capture water-based activities or cycling, and distinguish between sitting, standing still, and lying down. In addition to the limitations inherent to the devices, there are also a number of issues imposed by methodologies employed during data acquisition, reduction, analysis, and interpretation.

There is currently no consistent method of data cleaning or reduction. In 2000, a supplement of the journal *Medicine and Science in Sports and Exercise* was dedicated to the topic of physical activity measurement issues and included manuscripts describing best practices to overcome this inconsistency in the literature. However, the issue remains. For example, Healy et al. used a criterion of at least 20 minutes of consecutive zero counts to identify non-wear periods in the Australian Diabetes, Obesity and Lifestyle Study whereas when examining data from the National Health and Nutrition Examination Survey, Healy et al. utilized a criterion of at least 60 minutes of consecutive zero counts, with allowance for up to 2 minutes of low counts (< 50 cpm). Methodological decisions such as these will influence the amount of time spent in SED and consequently, may alter the associations between the behaviour and a health outcome. It is also common in many studies to combine moderate and vigorous physical activity (both bouted and non-bouted) into one variable. There is evidence to suggest that both physical activity intensity and how physical activity is accumulated are
associated with health outcomes, thus this may be a cause of disparities between studies.

The raw data derived from the accelerometer (i.e., count) is proprietary and is specific to each manufacturer, making comparisons between models difficult. To overcome this issue, the count is commonly converted into physiologically relevant units such as intensity or energy expenditure using prediction equations. This is an essential step as it not only allows for comparison between studies but also allows for time spent in various intensities to be calculated; information relevant to the development or comparison to guidelines and public health messaging. With respect to the Actigraph accelerometer specifically however, numerous equations 64-73, shown in Table 2-2, that yield substantially different results currently exist for adults 74, complicating interpretation further. For example, a middle-aged female was monitored for seven consecutive days with the Actigraph accelerometer. Using the Freedson equation 64, she accumulated only 12 minutes per day of MVPA whereas using the Swartz equation 72 she accumulated 159 minutes per day of MVPA – a difference of approximately 2.5 hours of MVPA per day! From this one example it is clear that estimates of the population prevalence of physical activity and SED, and relationships with health outcomes may vary dramatically due to the prediction equation used. Moreover, results from a comprehensive review evaluating commonly used accelerometer prediction equations in three different accelerometer models indicated that none of the accelerometer equations produced an accurate estimate of energy expenditure across a wide range of activities and no equation was accurate at classifying activities across all intensities 75.
### Table 2-2 Accelerometer calibration studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Participants</th>
<th>Protocol</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedson et al. (1998)</td>
<td>25 males, 25 females</td>
<td>Laboratory-based walking and running</td>
<td>( \text{METs}=1.439008 + (0.000795 \times \text{cpm}) )</td>
</tr>
</tbody>
</table>
| Hendelman et al. (2000) | 10 male, 15 female            | Laboratory-based walking and free-living activities | Walking: \( \text{METs}=1.602+0.000638 \times \text{cpm} \)  
All activities: \( \text{METs}=2.922+0.000409 \times \text{cpm} \) |
| Nichols et al. (2000)   | 30 male, 30 female (lab) 15 male, 15 female (field) | Laboratory-based walking and running on treadmill and in the field. | \( \text{cpm}=1.226(\text{METs})-1.697 \) |
| Swartz et al. (2000)    | 31 men, 39 women              | Free-living activities                        | \( \text{METs}=2.606+0.0006863 \times \text{cpm} \) |
| Brage et al. (2003)     | 12 males                      | Laboratory-based walking and running on treadmill and in the field | \( \text{VO}_2/\text{kg}=0.00260 \times \text{cpm} - 0.07 \times \text{fitness} + 10.1 \) |
| Yngve et al. (2003)     | 32 males, 30 females          | Laboratory-based walking and running on treadmill and track | Treadmill: \( \text{METs}=0.0008249 \times \text{cpm}+1.136 \)  
Track: \( \text{METs}=0.0008198 \times \text{cpm}+0.751 \) |
| Leenders et al. (2003)  | 11 males, 17 females          | Laboratory-based walking and running          | \( \text{METs}=0.0006 \times \text{cpm}+2.240 \) |
| Crouter et al. (2006)   | 24 men, 24 women              | Free-living activities and walking and running on a track | If \( \text{cpm} \leq 50 \), \( \text{MET}=1.0 \)  
If \( \text{cpm}>50 \) and \( \text{CV} \) of counts per 10s are \( \leq 10 \), \( \text{METs}=2.379833 \times \exp(0.00013529 \times \text{cpm}) \) OR  
If \( \text{CV} \) of counts per 10s are 0 or \( > 10 \), \( \text{METs}=2.330519+(0.001646 \times \text{cpm})-[1.2017 \times 10^{-7}(\text{cpm})^2] + [3.3779 \times 10^{-12}(\text{cpm})^3] \) |
<p>| Lopes et al. (2009)     | 26 male and female            | Laboratory-based walking and running, and sedentary activities | ( \text{MET}=1.388400490262+0.001312683420044 \times \text{cpm} ) |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Activities</th>
<th>Equations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller et al. (2010)</td>
<td>14 males, 16 females (20-29 yrs)</td>
<td>Laboratory-based walking and running</td>
<td>20-29 yrs: METs=0.0008151 x cpm + 1.495</td>
</tr>
<tr>
<td></td>
<td>7 males, 23 females (40-49 yrs)</td>
<td></td>
<td>40-49 yrs: METs=0.0007453 x cpm + 1.399</td>
</tr>
<tr>
<td></td>
<td>13 males, 17 females (60-69 yrs)</td>
<td></td>
<td>60-69 yrs: METs=0.0006560 x cpm + 1.973</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20-69 yrs: METs=0.0007695 x cpm + 1.532</td>
</tr>
</tbody>
</table>

Calibration studies creating prediction equations in adults using the Actigraph accelerometer worn on the hip. METs: metabolic equivalents, cpm: accelerometer counts per minute, VO₂: oxygen consumption, kg: kilogram, CV: co-efficient of variation.
The threshold commonly used to indicate SED (cpm < 100) with the Actigraph accelerometer in adult populations\textsuperscript{13,14} was not empirically derived and was initially utilized in youth\textsuperscript{76}. It was only recently that the validity of this threshold was assessed. Kozey-Keadle et al.\textsuperscript{77} reported that SED was significantly underestimated and that a cut-point of < 150 cpm might be more appropriate for use in free-living situations. More concerning however, was the observation that the Actigraph accelerometer had low precision (i.e., had large random error) when detecting SED.

Thus, when designing an investigation or interpreting data pertaining to physical activity and/or SED, there are many factors to consider and care is required to ensure that the data is collected, analyzed, and interpreted in a manner that will optimize its utility. This in turn will provide scientists, health professionals, and organizations alike with a clearer understanding of the complexities of physical activity and SED. Consequently, decision makers and leading health authorities will be in a better position to create guidelines and recommendations.

2.4 Moderate-to-Vigorous Physical Activity and Health

2.4.1 Physical Activity Guidelines

Consensus physical activity guidelines, such as the \textit{Canadian Physical Activity Guidelines for Adults}\textsuperscript{10} or the \textit{Physical Activity Guidelines for Americans}\textsuperscript{78}, suggest that adults accumulate at least 150 minutes of moderate physical activity, or at least 75 minutes of vigorous physical activity, or some combination of moderate and vigorous
physical activity on a weekly basis \(^8,^9,^79\). Aerobic activities have generally been the focus of physical activity guidelines due to their positive association with a very broad range of health benefits \(^80\), however it is recommended that adults also participate in activities that task the musculoskeletal system and maintain or improve flexibility for maximum health benefit. Additionally, consensus physical activity guidelines suggest that physical activity be accumulated in bouts of at least 10 minutes in duration and be in addition to incidental physical activity (IPA; activities of daily living which are typically of light intensity and/or sporadic in nature) \(^8,^9\). By inference, these guidelines suggest that to acquire substantial physical activity-related health benefit, a specific threshold of activity must be reached and that physical activity accumulated below the designated threshold does not impart marked benefit in terms of health outcomes. However, it should be recognized that research on the value of activities outside these specific parameters has been limited and future studies are required to explore these relationships. Despite this limitation, physical activity guidelines are based on decades of strong evidence linking increased physical activity with reduced risk for numerous health outcomes.

### 2.4.2 Moderate-to-Vigorous Physical Activity Intensity

Scientific evidence describing the benefits of physical activity on health began in the early 1950’s with the seminal work conducted by Morris and colleagues \(^3\) among employees of the London Transport Executive and Post Office. They found that bus conductors and postmen (i.e., employees who spent most of the workday walking and climbing stairs) had lower rates of mortality from heart disease than bus drivers and
telephone switchboard operators (i.e., employees who spent most of the workday sitting) 3.

In the 60 years since this study, numerous investigations have corroborated the findings of Morris et al. and the protective effect of physical activity on numerous health outcomes has been well-established 5, 6, 9. Studies such as the Harvard Alumni Study 81, a prospective analysis of physical activity and mortality in men supported the notion that health benefits resulted from habitual structured, vigorous intensity physical activity with the observation that men engaging in structured moderately vigorous or vigorous activity (i.e., sports) lived for approximately 1.5 years longer than less active men. Subsequent studies also compiled convincing evidence to suggest that many of the health-related benefits of physical activity could occur through moderate intensity physical activities, such as walking. For example, a landmark study by Lee et al. 82 indicated that women who walked at least 1 hour per week or whose walking pace was at least moderate intensity (i.e., 4.8 km/hr or 3.0 mph) experienced approximately half the risk of coronary heart disease as women who did not walk regularly. Although it was found that recreational time spent walking was more important than walking pace, it is noteworthy that even walking at a light intensity (i.e., 3.2 km/hr or 2.0 mph) was associated with an approximate 40% reduction in risk of coronary heart disease compared with not walking regularly 82.

To date, a plethora of studies have been conducted demonstrating that regularly performed physical activity throughout the moderate to vigorous intensity range is beneficial for the prevention of many chronic diseases, such as type 2 diabetes,
cardiovascular disease, osteoporosis, some cancers, and obesity, and the management of cardiometabolic risk factors, such as abdominal obesity, insulin resistance, dyslipidemia, and high blood pressure.

Whether vigorous or moderate physical activity provides greater health benefits is debatable. Although results from a recent review concluded that vigorous physical activity provides greater benefit compared to moderate physical activity with respect to diastolic blood pressure, glucose metabolism, and cardiorespiratory fitness (CRF), there were no differences in benefit with respect to systolic blood pressure, lipid profile, and fat loss between the two physical activity intensities. Thus, there is some evidence to suggest that vigorous physical activity imparts greater health protection however, when total volume of activity is the same, the data are less convincing. The critical point is that both vigorous and moderate physical activity convey strong health benefits when performed regularly. Consequently the combination, MVPA, is commonly recommended as a therapeutic strategy for the management of cardiometabolic risk and chronic disease prevention by various health organizations.

### 2.4.3 Moderate-to-Vigorous Physical Activity Volume

The volume of physical activity has been consistently and directly related to the size of the reduction in risk for numerous health outcomes. For example, as illustrated in Figure 2-3, there is an inverse, dose-response relationship between the relative risk of mortality and hours of physical activity in adults. With respect to volume of physical activity there are a few key points which are denoted on the figure:
There appears to be no lower threshold for benefits. Any increase in physical activity above baseline, irrespective of the size of increase, is associated with risk reduction. 2) The greatest rate of risk reduction occurs at the lowest end of the physical activity spectrum. Thus, even in those individuals not meeting consensus physical activity guidelines, health benefits can be experienced. 3) For each increase in physical activity there is a corresponding increase in health benefit with no obvious upper threshold. As a caveat, with each increase in physical activity the reduction in risk is smaller. 4) There is no single amount of physical activity that confers that greatest amount of health benefit however there is a significant reduction in risk with the accumulation of 2 to 4 hours per week. Although the exact shape of this dose-response curve differs for various conditions, a similar inverse, dose-response relationship is commonly observed.
Figure 2-3 Moderate-to-vigorous physical activity and mortality

Risk of all-cause mortality by hours per week of moderate-to-vigorous physical activity in adults. Key aspects of this dose-response curve include: 1) There is no lower threshold for benefits. Something is better than nothing. 2) The greatest rate of risk reduction occurs at the lowest end of the physical activity spectrum. Relatively small increases in physical activity will result in substantial health benefits. 3) For each increase in physical activity there is a corresponding increase in health benefit with no obvious upper threshold. However, with each increase in physical activity, the resulting benefit is smaller. 4) There is no single amount of physical activity that confers the greatest amount of health benefit however there is strong evidence that a significant reduction in risk occurs with the accumulation of 2 to 4 hours per week. Adapted from the Physical Activity Guidelines Advisory Committee, 2008 and Powell et al., 2010.

2.4.4 Moderate-to-Vigorous Physical Activity Duration

To date, most of the physical activity research has been conducted examining the influence of bouted or structured MVPA on health outcomes. Bout length is most commonly 30 or 60 minutes in length although there is a paucity of research using a bout length as low as 10 minutes.\textsuperscript{7,80} Within these parameters typically used in the
literature, duration of physical activity bouts does not appear to influence health benefits differently. Results vary slightly depending on the health outcome under examination however in general, similar health benefits are derived through both accumulated and continuous physical activity that is of the same total amount and intensity. For example, in a group of obese women, Jakicic and colleagues prescribed either: 1) 20 to 40 minutes of continuous physical activity per day or 2) 20 to 40 minutes of physical activity per day accumulated in multiple bouts of 10 minutes. Similar changes in CRF and weight were observed between the two groups.

Very limited research is available describing the effects of physical activity accumulated in < 10 minute durations. Dunn et al. conducted a randomized controlled trial examining the effects of traditional physical activity (i.e., continuous MVPA performed for 30 minutes 5 days per week) compared to lifestyle physical activity (i.e., accumulated 30 minutes of MVPA on most days of the week in a manner uniquely adapted for each individual's lifestyle) on CRF and cardiovascular disease risk factors. Although the group performing traditional physical activity had a greater improvement in cardiovascular disease risk factors, both groups experienced an increase in CRF, decrease in body fat percentage, and improvement in cardiovascular disease risk factors. A major limitation of this study however, is that it is unclear how the lifestyle group accumulated physical activity and what the average bout length was. It is possible that much of it was still accrued in bouts of at least 10 minutes, thus the findings are difficult to interpret.
More recently, a cross-sectional investigation using accelerometry data from the National Health and Nutrition Examination Survey in the United States compared the associations of bouted (accumulated in bouts ≥ 10 minutes) MVPA to non-bouted MVPA (accumulated in bouts < 10 minutes) on anthropometric indicators of obesity in adults. Results indicated that the association between bouted MVPA and obesity (both waist circumference and body mass index; BMI) was 3 to 4 times stronger than the association between non-bouted MVPA and obesity. It is noteworthy however, that higher non-bouted MVPA was negatively associated with obesity, suggesting that all MVPA may be beneficial. In contrast, another cross-sectional study found that bouted MVPA (accumulated in bouts ≥ 5 minutes) was not a significant predictor of clustered metabolic risk or any individual metabolic risk factor. Other cross-sectional studies have summed total MVPA (bouted and non-bouted) as one variable. Using this method, inconsistent associations between MVPA and various cardiometabolic risk factors have been noted. Thus, further investigation is required to more clearly define the influence of bouts or non-bouts of MVPA on health outcomes.

### 2.4.5 Moderate-to-Vigorous Physical Activity Frequency

Very little research has been conducted to examine the effects of frequency of physical activity on health outcomes when the total amount of activity is held constant. Observations do suggest that if total volume is the same, the benefits of three to five sessions per week are similar. Frequency of physical activity < 3 days/week has rarely been investigated. Lee et al. noted that, regardless of frequency, men who met physical activity recommendations and performed an equivalent volume and intensity of
activity had similar health profiles. However, compared to inactive men, those who accumulated this activity in only one or two sessions over the weekend (i.e., weekend warriors) were not at a decreased risk of mortality whereas those who accumulated this activity in three or more sessions over the week were at a reduced risk. This suggests that increased frequency of activity may be important for long-term health however more studies are required.

2.4.6 Moderate-to-Vigorous Physical Activity and Health Outcomes: Mechanisms

MVPA has been purported to decrease health risk directly via acute and chronic changes to the metabolic and vascular system, and indirectly by its influence on energy balance (i.e., body weight). An exhaustive review of the many direct mechanisms by which MVPA decreases health risk is beyond the scope of this manuscript however, Table 2-3 provides a brief summary of the effects of MVPA on select cardiometabolic risk factors. The reader is encouraged to seek further information from other excellent sources\textsuperscript{80, 99-102}. 

29
Table 2-3 Mechanisms by which moderate-to-vigorous physical activity improves cardiometabolic risk factors

<table>
<thead>
<tr>
<th>Cardiometabolic Risk Factor</th>
<th>Mechanism(s) responsible for improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose Metabolism</td>
<td>↑GLUT-4 translocation (↑glucose uptake)</td>
</tr>
<tr>
<td></td>
<td>↑GLUT-4 protein content</td>
</tr>
<tr>
<td></td>
<td>↑mitochondrial content</td>
</tr>
<tr>
<td></td>
<td>↑capillarization</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>↑endothelial function</td>
</tr>
<tr>
<td></td>
<td>↓peripheral resistance</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>↑lipoprotein lipase</td>
</tr>
<tr>
<td></td>
<td>↑oxidation of free fatty acids</td>
</tr>
<tr>
<td>Low Cardiorespiratory Fitness</td>
<td>↑mitochondrial content</td>
</tr>
<tr>
<td></td>
<td>↑oxidative and non-oxidative enzymes</td>
</tr>
<tr>
<td></td>
<td>↑capillary density of muscle</td>
</tr>
<tr>
<td></td>
<td>↑stroke volume</td>
</tr>
<tr>
<td></td>
<td>↑oxidation of free fatty acids (relative to carbohydrate)</td>
</tr>
<tr>
<td></td>
<td>↑resistance to fatigue</td>
</tr>
<tr>
<td>Obesity</td>
<td>↑energy expenditure</td>
</tr>
<tr>
<td></td>
<td>↓adipocyte size</td>
</tr>
</tbody>
</table>

GLUT-4, muscle glucose transporter

Indirectly, MVPA exerts its influence on health outcomes through its effects on obesity. It is well-known that obesity is a risk factor for many common cardiometabolic risk factors and chronic diseases, and that health risk is most pronounced in those individuals who present with abdominal adiposity. It has been noted that with decreasing amounts of MVPA, individuals present with increasing levels of obesity. Further, obese individuals who undergo a physical activity intervention experience
significant reductions in total obesity, abdominal obesity, and cardiometabolic risk factors \cite{83,84}. Generally, the greatest reductions in health risk are seen in those individuals who lose the greatest amount of weight \cite{83,84}. However, it is noteworthy that even in those individuals who do not lose a significant amount of weight, reductions in abdominal obesity and improvements in health outcomes are observed \cite{83,84,107}. Thus, accumulating habitual MVPA is associated with the maintenance of a healthy weight, prevention of weight gain, weight reduction, and consequently, more favourable health outcomes \cite{5}.

2.5 Light Physical Activity and Health

In comparison to the plethora of research conducted on MVPA and health outcomes, very little attention has been given to the influence of LPA on health. Due to the availability of improved methods of capturing LPA \cite{61} and improved efforts to understand the role of total energy expenditure on obesity \cite{49}, interest in LPA has been increasing in recent years. However, unlike MVPA, associations between LPA and health outcomes are inconsistent.

2.5.1 Evidence from Self-Report Studies

In women, Lee and colleagues \cite{82} demonstrated that walking accumulated at a very low intensity (i.e., < 2.0 mph or 3.2 km/hr) was associated with a substantial reduction in risk of coronary heart disease. Similarly, Hu et al. \cite{108} reported that the number of hours spent standing and walking around the home were associated with a
23% reduction in the relative risk of obesity and a 17% reduction in the relative risk of type 2 diabetes in middle-aged women. Recent observations revealed that LPA performed at least once per week was associated with a reduction in the risk of type 2 diabetes compared to those who were inactive only in adults ≥ 70 year of age \textsuperscript{109}, suggesting that LPA may become more important for health benefit with increasing age. In men, LPA (defined as leisure activities expending 2 to 4 kcal/minute) was associated with CRF in univariate analyses, however after control for other variables including heavy activities, LPA was no longer a significant predictor of CRF \textsuperscript{110}.

2.5.2 Evidence from Accelerometry Studies

In studies using objective measurement devices, an inverse association between LPA and cardiometabolic risk factors has been found in adults \textsuperscript{12, 13, 111} (see Table 2-4 for details). Importantly, these results were independent of MVPA. However, evidence to the contrary has also been published. Balkau et al. \textsuperscript{15} reported that LPA and insulin sensitivity were not associated after control for MVPA. Likewise, findings from Ekelund and colleagues \textsuperscript{14, 22} indicated that LPA was not a significant predictor of cardiometabolic risk factors in adults. Thus, at present the associations of LPA with cardiometabolic risk factors are unclear.
Table 2-4 Independent associations between objectively measured light physical activity and health outcomes

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
<th>Glucose Metabolism</th>
<th>Waist Circumference</th>
<th>Triglycerides</th>
<th>High Density Lipoproteins</th>
<th>Blood Pressure</th>
<th>Clustered Metabolic Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ekelund et al.</td>
<td>103 men, 155 women</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Healy et al.</td>
<td>60 men, 107 women</td>
<td>√</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Balkau et al.</td>
<td>346 men, 455 women</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Healy et al.</td>
<td>67 men, 102 women</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
</tr>
<tr>
<td>Ekelund et al.</td>
<td>81 men, 111 women</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Camhi et al.</td>
<td>709 men, 768 women</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>X</td>
<td>√</td>
</tr>
</tbody>
</table>

Checkmark (√) indicates a significant association between light physical activity and a health outcome after statistical control for sedentary behaviour and other physical activity variables. NA, not assessed; X, no association.
2.5.3 Light Physical Activity and Health: Potential Mechanisms

Various mechanisms have been proposed to explain how LPA may exert health benefit. In individuals with spinal cord injury, six months of very low intensity treadmill walking (i.e., < 0.6 km/hr) was associated with a 126% increase in muscle glucose transporter (GLUT-4) content and improved glucose tolerance\textsuperscript{112}. In another similar study, Chillibeck et al.\textsuperscript{113} observed a 72% increase in GLUT-4 content and improved insulin sensitivity following 8 weeks of low intensity (i.e., 6 W) electrical stimulation in paralyzed human skeletal muscle. This evidence indicates a role for LPA in glucose metabolism.

Bey and Hamilton\textsuperscript{20} found in rodents that low intensity treadmill walking and standing after a period of SED increased the activity of LPL approximately 8-fold in the exercising lower limbs. Moreover, up to 95% of the LPL activity normally present in the capillaries of muscles was dependent on this low intensity activity. This data suggests that LPL reduction can be prevented or LPL levels maintained by non-fatiguing contractions\textsuperscript{20}.

LPA might also play a role in weight maintenance and obesity prevention. Although very low intensity activities, such as standing or walking at 1 mph, may seem trivial they can double total energy expenditure compared to resting levels\textsuperscript{114}. Thus, over the course of a 24-hour period they may contribute substantially to total energy expenditure. Levine and colleagues\textsuperscript{115} observed that lean inactive individuals participated in approximately 2.5 hours more low intensity ambulatory and standing
activity than obese inactive individuals. This equates to an approximate 350 kcal/day. Further evidence comes from overfeeding studies where lean inactive individuals consumed an excess of 1000 kcal/day. Despite tight regulation of caloric intake and energy expenditure, a 10-fold variation in fat gain and 8-fold variation in NEAT were found. Not surprisingly, those individuals who increased NEAT the most in response to overfeeding gained the least amount of fat whereas those who had minimal changes in NEAT gained the most fat.\(^{116}\)

### 2.6 Sedentary Behaviour and Health

Bernadino Ramazzini, an occupational physician, advised in the 17\(^{\text{th}}\) century that sedentary workers should perform physical exercise to counteract the harmful effects of prolonged sitting.\(^{117}\) For centuries since, leading health authorities, health professionals, and scholars have been proclaiming the deleterious effects of SED on various health outcomes.\(^{118}\) However, only in recent years has SED actually been measured directly (as opposed to being assumed based on the presence or absence of MVPA) using a variety of self-report questionnaires and objective measurement tools.\(^{118}\) Thus, there is considerable inconsistency in the literature with respect to the parameters used to define SED. This has lead to confusion and has made comparisons between investigations difficult.\(^{118}\) Regardless, research describing the associations or effects of SED on numerous health outcomes has gained substantial popularity. Although there is a wealth of data describing the negative impact of SED, often examined in terms of time
spent watching television, on health \textsuperscript{38, 49, 56}, this is not consistent across all studies \textsuperscript{14, 15, 22}.

2.6.1 Evidence from Self-Report Studies

Self-reported SED, most commonly assessed by television viewing time \textsuperscript{54}, has been consistently associated with an increased risk of cardiovascular disease and all-cause (but not cancer) mortality \textsuperscript{35, 36, 119}, type 2 diabetes, and obesity \textsuperscript{108, 120}. For example, in adult men and women followed for 12 years in the Canadian Fitness Survey there was a dose response relationship between sitting time and cardiovascular disease and all-cause mortality. Those who spent most of their time sitting had a 54\% increased risk of all-cause mortality compared to those who spent almost none of their time sitting \textsuperscript{35}. Likewise, Hu et al. \textsuperscript{108} observed that women who watched television for more than 40 hours per week had a 70\% and 94\% increased risk of type 2 diabetes and obesity, respectively. Sitting and television viewing time has also been associated with cardiometabolic risk factors, with stronger associations found in women compared to men \textsuperscript{121}.

2.6.2 Evidence from Accelerometry Studies

Ekelund and colleagues \textsuperscript{22} and Healy and associates \textsuperscript{12, 13} were the first to assess the relationship between objectively measured (by accelerometry) SED and cardiometabolic risk factors. Whereas Ekelund et al. \textsuperscript{22} reported that SED was marginally associated with fasting insulin but no other cardiometabolic risk factors, Healy et al. \textsuperscript{12, 13} observed a significant association of SED with many cardiometabolic risk factors. (Table 36)
Furthermore, observations by Healy et al.\textsuperscript{12,13} remained after statistical control for MVPA. Subsequent to these initial studies, some have reported observations equivalent to Healy et al.\textsuperscript{34}, whereas others report findings in agreement with Ekelund and colleagues\textsuperscript{14,15}. Thus, there is inconsistency within the literature and at present, the associations of SED with cardiometabolic risk factors requires clarification.
**Table 2-5** Independent associations between objectively measured sedentary behaviour and health outcomes

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
<th>Glucose Metabolism</th>
<th>Waist Circumference</th>
<th>Triglycerides</th>
<th>High Density Lipoproteins</th>
<th>Blood Pressure</th>
<th>Clustered Metabolic Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ekelund et al. 2007</td>
<td>103 men, 155 women</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Healy et al. 2007</td>
<td>60 men, 107 women</td>
<td>√</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Balkau et al. 2008</td>
<td>346 men, 455 women</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Healy et al. 2008</td>
<td>67 men, 102 women</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
</tr>
<tr>
<td>Ekelund et al. 2009</td>
<td>81 men, 111 women</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Healy et al. 2011</td>
<td>2378 men, 2379 women</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>X</td>
<td>√</td>
</tr>
</tbody>
</table>

Checkmark (√) indicates a significant association between sedentary behaviour and a health outcome after statistical control for physical activity. NA, not assessed; X, no association.
2.6.3 Sedentary Behaviour Duration

Preliminary evidence suggests that the pattern in which SED is accumulated may also be associated with cardiometabolic risk factors. The total number of interruptions in SED was associated with a significantly lower waist circumference, BMI, triglycerides, and 2-hour glucose in middle-aged men and women. Individuals in the highest quartile of SED breaks (i.e., those who had the greatest number of breaks in SED) had an average waist circumference value 5.95 cm lower than individuals in the lowest quartile of SED breaks. These results were subsequently confirmed in a larger, multi-ethnic investigation. It is important to recognize however, that SED breaks were of light intensity (i.e., LPA) and LPA was not entered into any of the regression models examining the association between SED breaks and cardiometabolic risk factors due to multicollinearity. Therefore, it is difficult to discern whether it is actually the number of SED breaks or the number of LPA bouts that is improving cardiometabolic risk.

2.6.4 Sedentary Behaviour, Physical Activity and Health Outcomes

There is conflicting evidence describing: a) the joint associations of SED and physical activity on health outcomes, and b) whether or not SED remains a significant predictor of health outcomes independent of physical activity. Sugiyama et al. found that compared to individuals who had low SED and were active, individuals who either had a) low SED and were inactive or b) high SED and were active were both at a 55% increased risk of obesity, suggesting that high SED and low physical activity impart a similar magnitude of health risk. Sisson and colleagues reported that ≥ 4 hours per
day of leisure time SED was associated with a 94% increased odds of having the metabolic syndrome in men irrespective of whether or not the physical activity guidelines were being met whereas in women, high leisure time SED was associated with a 54% increased odds of metabolic syndrome only in those not meeting the physical activity recommendations. Similarly, another study found that in inactive men there was a significant trend across categories of time spent riding in a car and cardiovascular disease mortality but not in active men.  

In most studies, inclusion of physical activity in the multivariate regression models did not alter the results between SED and health outcomes whereas in others the associations were attenuated or became non-significant. Although differences in the measurement of both SED and physical activity, along with differences in health outcomes studied make comparisons between studies difficult, early evidence suggests that SED and physical activity influence health risk via unique pathways. However, further studies are required to clarify the combined influence of SED and physical activity on various outcomes and determine the independent contribution of SED to health risk.

2.6.5 Sedentary Behaviour and Health: Potential Mechanisms

There is evidence that the negative effects of SED on metabolic health are mediated, at least in part, by changes in LPL activity. LPL facilitates the uptake of free fatty acids into the muscle and adipose tissue. Hence, low levels of LPL are associated with increased levels of triglycerides and decreased levels of high-density lipoprotein.
(HDL) cholesterol \(^{38}\). To examine the impact of SED on LPL activity, Bey and Hamilton \(^{20}\) employed the hind-limb unloading technique; rodents were suspended by their tail to prevent ambulation on their hind limbs for extended time periods. After 12 hours of hind-limb unloading LPL activity was decreased to 63% of control animals (i.e., animals allowed to roam freely). Consequently, there was a significant decrease in triglyceride-derived fatty acid uptake and a reduction in HDL concentration. These changes occurred due to changes in transcription factors and not LPL mRNA \(^{20}\).

In healthy men and women, an 18% decrease in LPL activity along with a decrease in HDL and an increase in both triglyceride levels and fasting insulin levels was documented following 20 days of bed rest without change in body weight \(^{125}\). Likewise, Hamburg et al. \(^{126}\) observed a significant increase in total cholesterol, plasma triglycerides, glucose, and insulin resistance after 5 days of complete bed rest (i.e., 23.5 hours per day) in healthy adults. In persons with spinal cord injury, who have reduced neural input to the lower limbs and are immobilized (i.e., sedentary), there is also a reduced capacity for glucose transport and hence, decreased glucose tolerance \(^{127-129}\). Combined, these findings support a role of SED in increased cardiometabolic risk. However, it is important to note that these situations are extreme and do not represent typical behaviour patterns displayed by free-living humans \(^{118}\).

To overcome this limitation a recent study investigated the effects of a 2-week reduction of daily steps on metabolic parameters in healthy young males, thereby providing a glimpse into the effects of increased SED in a free-living environment \(^{130,131}\). Participants, none of whom performed > 2 hours per week of planned exercise or walked
< 3500 steps per day at baseline, were instructed to reduce their daily steps to 1500 per
day for 2 weeks by taking elevators instead of stairs, riding in vehicles instead of
walking, et cetera. At the end of the study period, there was an increase in plasma
insulin and triglycerides, and intra-abdominal fat mass along with a reduction of glucose
uptake, CRF, and lean mass of the legs\textsuperscript{130, 131}. Equivalent findings were reported by
Stephen et al.\textsuperscript{21} who observed a 39% reduction in insulin action after only one day of
sitting versus a minimal sitting condition. The changes noted in these studies provide
evidence that reduced daily activity (or increased SED), not unlike what is commonly
observed in today’s society, is linked to detrimental metabolic changes.

In addition to the molecular or physiological pathways that SED may use to
impact health, various behavioural mechanisms have also been proposed. The first is
that SED displaces time available to participate in MVPA\textsuperscript{132}. Although this seems like a
logical explanation, the association between SED and MVPA is typically quite low (i.e., r
= -0.11\textsuperscript{58} to -0.27\textsuperscript{13}) and therefore does not provide strong support for this hypothesis.
The suggestion that SED displaces time available for LPA\textsuperscript{12} is more plausible as strong
associations (i.e., r = -0.96\textsuperscript{13}) have been observed between these two behaviours.
Lastly, it has been hypothesized that during SED, there are increased opportunities for
snacking which may lead to positive energy balance and weight gain\textsuperscript{133}. 

42
2.7 Sleep and Health

Substantial evidence has accumulated in recent years indicating that sleep duration, extended nighttime SED, is inversely associated with health outcomes such as obesity \(^{23-27}\); a major risk factor for numerous chronic health conditions in both adult men and women \(^{23, 25, 134}\). In general, individuals who sleep between 7 and 8 hours per night are less likely to be obese than those who sleep 7 or fewer hours per night \(^{23}\). For example, in a study of over 1.1 million individuals, women and men sleeping less than 7 hours per night had a 1.39 kg/m\(^2\) and a 0.57 kg/m\(^2\) greater BMI, respectively, than individuals sleeping for 7 hours per night \(^{135}\). A recent study employing radiographic imaging (computed tomography) found that over five years, abdominal subcutaneous adipose tissue increased by approximately 41 cm\(^2\) and visceral adipose tissue by 13 cm\(^2\) in individuals under the age of 40 years who slept ≤ 5 hours per night compared to individuals of the same age who slept 6 to 7 hours per night \(^{136}\). Various mechanisms have been postulated to explain how short sleep duration may contribute to obesity and lead to ill health.

2.7.1 The Autonomic Nervous System and Short Sleep Duration

Our circadian and metabolic regulatory systems developed to be functional for the environmental exposures and lifestyle experienced by our hunter-gatherer ancestors \(^1\). Through repeated exposure to metabolic cues such as light, sleep, activity, and nutrient intake, our central biological clock evolved to synchronize activity, food consumption, and rest to the circadian and circannual cycles using hormones and the
autonomic nervous system. For our ancestors, these environmental cues were the changing seasons, and rising and setting of the sun. Thus, in the summer when the days were long and food plentiful, short sleep duration would lead to increased caloric intake and fat deposition. In contrast, presently the days are always long due to electrical lighting - resulting in a chronic state of short sleep duration, and we have access to an endless supply of palatable foods. This results in a year-round accumulation of body weight\textsuperscript{26}. Consequently, our normal autonomic balance has been disrupted. Studies inducing sleep deprivation have demonstrated an increase in sympathetic nervous system activity\textsuperscript{137,138} which is hypothesized to cause obesity or exacerbate metabolic complications associated with obesity\textsuperscript{26} (Figure 2-4).
Figure 2-4 Sleep loss and health risk

- **SLEEP LOSS**
  - ↑Fatigue
    - ↓Physical Activity
    - ↑Sedentary Behaviour
  - ↓Energy Expenditure
- ↑Sympathetic Nervous System Activity
  - ↑Growth Hormone
  - ↑Cortisol
  - ↓Leptin
  - ↑Ghrelin
- ↑Blood Pressure
- Impaired Glucose Metabolism
- ↑Appetite
- ↑Opportunity to Eat
  - ↑Caloric Intake
  - Weight Gain (Obesity)
2.7.1.1 Regulation of Satiety Hormones and Food Intake

Leptin, an anorexigenic hormone and long-term indicator of energy balance, and ghrelin, an endogenous orexigenic regulator of food intake, are both hormones affected by sleep duration via an increase in sympathetic nervous system activity\(^{139}\). In a seminal study performed in young university-aged men, it was noted that after six days of 4 hours of sleep per night, ghrelin levels increased by 28% and leptin levels decreased by 18%\(^{140}\). Normally, leptin levels are elevated with sleep\(^{141}\) and this elevation persists whether participants receive continuous enteral nutrition or not, and whether sleep occurs in the daytime or nighttime suggesting that sleep *per se* affects leptin regulation\(^{142}\). Changes in these appetite-regulating hormones were associated with an appetite increase of 23%\(^{140}\).

It is possible that the changes in both leptin and ghrelin may be a normal response to the body requiring increased energy intake to compensate for the longer hours spent awake\(^{143}\). Longer hours spent awake also represent an increased opportunity to consume food and beverages\(^{26}\), especially if the wake-time is spent in sedentary activities such as television viewing where snacking is quite common\(^{144}\) or knowledge-based learning which increases caloric consumption\(^{145}\). Alterations in food preferences have also been observed with sleep curtailment; an increase of 33 to 45% in appetite for energy-rich foods with a high carbohydrate content have been found\(^{140}\). Changes in both appetite and food preference may then contribute to weight gain and obesity.
2.7.2 Short Sleep Duration and Energy Expenditure

Inadequate sleep has also been associated with increased daytime sleepiness, fatigue, stress, and a pessimistic outlook, all of which could contribute to a decrease in an individual’s overall wellbeing. Additionally, excessive daytime fatigue and sleepiness could lead to decreased daily energy expenditure although this is not a consistent finding within the epidemiological literature. Whereas some reported that short sleep duration was significantly associated with higher levels of vigorous physical activity, others found that short sleep duration was associated with a reduction in physical activity levels. Interestingly, it has been shown that short duration sleepers watch less television but work longer hours than normal (or healthy) duration sleepers, thus it is difficult to discern whether SED is increased in those who sleep less.

2.7.3 Sleep Duration, Physical Activity, Sedentary Behaviour, and Health

Although the separate associations between sleep duration and health risk, and physical activity and health risk are well-established, the relationship of sleep duration with health outcomes independent of physical activity is less clear. A limited number of studies using self-report measurement tools have explored this relationship however results are inconsistent with some noting that sleep duration is an independent predictor of obesity whereas others do not. In the Nurses’ Health Study physical activity did not influence the relationship between sleep duration and obesity. Similarly, in men and women participating in the Quebec Family Study, short sleep
duration predicted weight gain over six years independently of vigorous physical activity \(^{149}\). On the other hand, St-Onge and colleagues \(^{158}\) found that sleep duration was not associated with BMI after statistical control for physical activity level. Thus, further investigation using objective measurement tools is required to shed light on the independent contributions of sleep duration and physical activity to all health outcomes.

There is currently a paucity of data describing the associations between sleep duration, SED, and health outcomes in adults. Vioque et al. \(^{155}\) found in a representative sample in Spain that television viewing did not attenuate the association between sleep duration and obesity in adults. Although it has been suggested that increased television viewing time may displace time spent sleeping \(^{153}\), a 3-week randomized controlled trial in adults that reduced television viewing time by 50% found that sleep duration remained the same \(^{157}\). Given the impact of both SED and sleep on various health factors, this area requires substantial research and will be a ripe area for future research.

### 2.8 Caloric Intake

As was mentioned in previous sections, it has been postulated that one of the detrimental consequences of both increased SED and decreased sleep duration may be an increase in caloric intake \(^{26, 144, 145}\). The cost associated with the increased consumption of calories is a positive energy balance and ultimately, weight gain. Thus, it would make intuitive sense that individuals with the highest caloric intake would present with the highest levels of obesity. However, within the literature there is conflicting
evidence describing the association between caloric intake and obesity with some reporting a significant positive association \textsuperscript{158} and others reporting no association \textsuperscript{158-160}. For example, Trichopoulou et al. \textsuperscript{158} reported that in a large sample of men, energy intake was a significant predictor of waist-to-hip ratio. Conversely, Halkjaer et al. \textsuperscript{159} found that total energy intake was not associated with 5-year changes in waist circumference in a large Danish cohort of men and women. Methodological limitations of self-reported food intake are likely to account for at least some of the differences between studies. It is well-known that self-report questionnaires are associated with substantial bias and the under-reporting of energy intake, with the degree of under-reporting increasing with increasing obesity \textsuperscript{161, 162}. Therefore it is difficult to discern true relationships between caloric intake and health outcomes. Nonetheless, when examining obesity, energy intake is an important component of the energy balance equation to examine.

\textbf{2.9 Summary}

Presently, approximately 85\% of Canadian adults fail to accumulate sufficient physical activity to experience substantial health benefits. Additionally, adults spend a disproportionate amount of time engaging in SED and regularly report obtaining insufficient amounts of sleep. Unfortunately, opportunities to conserve energy will continue to increase with advancing technology and employment and entertainment options will continue to displace time traditionally reserved for sleeping. Given the negative influence these behaviours exert on numerous health outcomes, this situation
represents a major public health challenge. Thus, it is important to understand more clearly the impact of physical activity, SED, and sleep on health risk.

Although the use of objective physical activity and SED measurement tools has led to substantial improvements in our ability to capture these complex behaviours and assess their relationships with numerous health outcomes, considerable inconsistency exists in the literature and questions critical to our understanding of the associations of physical activity, SED, and sleep with cardiometabolic risk remain: In individuals who do not accumulate bouted moderate-to-vigorous physical activity, is low intensity, sporadic, incidental physical activity associated with cardiorespiratory fitness? Independent of habitual physical activity, is sedentary behaviour associated with cardiometabolic risk in men and women with abdominal obesity? Is incidental physical activity associated with abdominal adipose tissue depots? The following three studies in chapters 3 to 5 will examine these questions. Findings from these studies may have important implications for public health messaging and strategies aimed at reducing health risk associated with physical inactivity.
Chapter 3

Incidental physical activity is positively associated with cardiorespiratory fitness
ABSTRACT

**Purpose:** The primary aim was to determine whether incidental physical activity (IPA), expressed either as duration or intensity, was associated with cardiorespiratory fitness (CRF).

**Methods:** Participants were inactive, abdominally obese men (n = 43; waist circumference ≥ 102 cm) and women (n = 92; waist circumference ≥ 88 cm) recruited from Kingston, Canada. IPA (accelerometer counts per minute (cpm) > 100) was determined by accelerometry over 7 days and categorized into duration (min/d) and intensity (cpm). In secondary analyses, IPA was further categorized as light physical activity (LPA; cpm 100 to 1951), and sporadic moderate physical activity (MPA; cpm ≥ 1952 accumulated in bouts less than 10 consecutive minutes). CRF was assessed using a maximal treadmill exercise test.

**Results:** Participants accumulated 308.2 ± 98.8 (mean ± SD) minutes of IPA per day of which 19.2 ± 13.5 minutes were spent in sporadic MPA. Mean CRF was 26.8 ± 4.7 ml/kg body weight/min. IPA duration was positively associated with CRF in the univariate model ($r^2 = 0.03$, $p < 0.05$) and after control for sex and body mass index (BMI; $r^2 = 0.53$, $p < 0.01$). Likewise, IPA intensity was positively associated with CRF in univariate ($r^2 = 0.18$, $p < 0.001$) and multivariate analyses ($r^2 = 0.56$, $p < 0.01$). After further control for each other, IPA duration was not associated with CRF ($p = 0.05$) whereas IPA intensity remained a significant predictor ($r^2 = 0.57$, $p < 0.001$). In secondary analyses, LPA was not associated with CRF ($p > 0.05$). Sporadic MPA was associated with CRF ($r^2 = 0.20$, $p < 0.001$) and remained a positive correlate after control for sex, BMI, and the other physical activity variables ($r^2 = 0.60$, $p < 0.001$).
Conclusion: In this study both duration and intensity of IPA were positively associated with CRF among inactive, abdominally obese adults. Sporadic MPA, but not LPA, was an independent predictor of CRF.
INTRODUCTION

Unequivocal evidence demonstrates that moderate or high levels of cardiorespiratory fitness (CRF) are associated with a reduced risk of cardiovascular disease and all-cause mortality independent of other risk factors. One of the primary determinants of CRF is habitual physical activity. Current guidelines suggest that physical activity must be performed at a minimum level of 40 to 50% of heart rate reserve or 64 to 70% of maximal heart rate (i.e., moderate-to-vigorous physical activity) and accumulated in bouts of at least 10 minutes in duration to elicit improvement in CRF. This infers that, with respect to CRF, the benefits of physical activity do not occur along a continuum and that physical activity performed below the designated threshold would not influence CRF. This notion is supported by self-report questionnaires demonstrating that light physical activity (LPA; physical activity performed at 20 to 39% of heart rate reserve or 50 to 63% of maximal heart rate) is not independently associated with CRF. However, by design self-report measurement tools are prone to various forms of bias, such as recall and social desirability bias, and typically do not capture incidental physical activity (IPA; i.e., physical activity accrued through activities of daily living that is low in intensity and/or lasts less than 10 consecutive minutes). Thus, the association between objectively measured, IPA and CRF remains to be determined. Demonstration that IPA alone is sufficient to improve CRF would reinforce the notion that all physical activity is beneficial regardless of the intensity and pattern in which it is accumulated and thus, would have important clinical and public health implications.
Accelerometry provides an objective measure of daily physical activity patterning and overcomes many of the limitations inherent to self-report questionnaires. Thus we sought to determine whether the duration and intensity of objectively measured IPA was associated with CRF. Secondary analyses examined the associations between LPA, moderate physical activity (MPA) and CRF. We explored these associations in a sample of abdominally obese men and women who by consensus guidelines were defined as inactive and failed to accumulate physical activity in a pattern thought to improve CRF. This sample of abdominally obese, inactive adults represents over 60% of the North American population who are at substantially increased health risk.
METHODS

Participants

Participants for this study were men and women aged 35 to 65 years who were inactive, did not smoke, had an elevated waist circumference (defined as at least 102 cm in men and at least 88 cm in women), and a body mass index (BMI) between 25.0 to 39.9 kg/m². Participants were recruited for participation in an exercise intervention (MCT190617). The exclusion criteria included any physical impairment that would make physical activity difficult or unsafe according to the participant’s physician (history of myocardial infarction, stroke, coronary bypass surgery or angioplasty in the last 6 months, peripheral artery disease, unstable angina or ischemia); if they had diabetes or were taking glucose-lowering medication; if they consumed > 21 alcoholic drinks per week. The study was approved by the Queen’s University Health Sciences Research Ethics Board. All participants received medical clearance from their personal physician and gave written informed consent before participation in the study.

Anthropometry

Body mass and height were measured to the nearest 0.1 cm and 0.1 kg, respectively, with participants dressed in standard T-shirts and shorts. These measures were used to calculate BMI (kg/m²). Waist circumference was obtained in a standing position using the mean of two measures acquired at the superior edge of the iliac crest measured to the nearest 0.1 cm.
**Cardiorespiratory Fitness**

CRF measured as oxygen consumption per unit of time (peak $\dot{V}O_2$) was determined using a maximal treadmill test combined with standard open-circuit spirometry techniques (SensorMedics Corp, Yorba Linda, California). The relative value of maximal oxygen consumption (ml/kg body weight/min) was used in all analyses. CRF values were classified based on sex and age specific standards. ¹⁶⁹

**Physical Activity**

Physical activity was measured with the Actigraph GT3X accelerometer (Actigraph, Pensacola, Florida). Although this is a triaxial accelerometer, only the vertical axis was used for analysis. Accelerometers were programmed to collect data in 1-minute epochs over a 7-day period and were worn on an elastic belt positioned over the right hip at all times except during water-based activities. Additionally, participants completed a log sheet indicating when they went to bed at night, woke up in the morning, and removed the accelerometer.

To be included in the analysis, participants were required to wear the accelerometer for at least four complete days (including one weekend day) within the monitoring period. A complete day was defined as at least 10 hours of wear time during the day. Wear time was calculated after extended periods of consecutive zero counts ≥ 60 minutes and sleep time (determined using both the participant logs and visual examination of the data) were excluded. Twenty participants either did not meet the
compliance criteria for accelerometer wear time or were missing data. Therefore a total of 135 participants (43 men and 92 women) were used in the analyses.

The accelerometer cutpoints in this study used to translate the ‘count’ value into an estimate of physical activity intensity were those developed by Freedson and colleagues. \(^{64}\) IPA was defined as counts per minute (cpm) \(\geq 100\), LPA as 100 to 1951 cpm, MPA as 1952 to 5724 cpm, and vigorous physical activity as \(\geq 5725\). Ninety-two percent of the participants in this study did not accumulate any vigorous physical activity. Of those who did, < 5 minutes was accrued per participant over the entire wear period. Therefore all physical activity \(\geq 1952\) cpm was defined as MPA. Activity accumulated during each complete day of monitoring was quantified as: 1) average duration, in minutes per day (min/d), of each IPA, LPA, and MPA 2) average intensity, in cpm, of IPA, LPA, and MPA 3) average minutes of sporadic MPA per day (accumulated in < 10 consecutive minutes), and 4) average minutes of MPA per day accumulated in bouts (\(\geq 10\) consecutive minutes in duration). This duration is consistent with recommendations suggesting that MPA should be accumulated in bouts of 10 minutes or more for health/fitness benefit. \(^{5, 9, 166}\) Since periods of rest are common during activity (e.g., waiting for a light to change colour at a crosswalk during a run), participants were required to spend at least 80% of the bouts above the threshold value for the bout to be counted. For example, in a 10-minute bout of MPA only 8 of those minutes would need to fall at or above 1952 cpm. Thirty-seven participants did not accrue any bouted MPA. In the remaining participants, < 1 bout of MPA per day was accumulated therefore all MPA was classified as sporadic.
**Statistical Analyses**

Descriptive characteristics are summarized as mean values ± standard deviations (SD). All physical activity variables except IPA intensity were logarithmically transformed due to skewed distributions. Sex differences in descriptive characteristics and physical activity variables were determined using Independent Student’s T-tests. Sex differences in the relationship between physical activity and CRF were tested by adding the interaction terms to the regression models. No differences were detected therefore analyses were collapsed across sex. To assess the primary objective, the association between the duration and intensity of IPA and CRF, the following linear regression models were used: 1) unadjusted, 2) control for time accelerometer worn and sex, 3) control for time accelerometer worn, sex, and BMI, and 4) control for time accelerometer worn, sex, BMI, and each other. To assess the secondary objective, the association between LPA, MPA and CRF, the same models outlined above were used with the following exception: in model 4, covariates entered were time accelerometer worn, sex, BMI, and each other. Results from the regression analyses are summarized as unstandardized beta values (95% Confidence Intervals).

Participants were then divided into tertiles according to sporadic MPA accumulation and CRF scores were converted to metabolic equivalent units (METs; 1 MET is the energy cost of resting quietly and is defined as an oxygen uptake of 3.5 ml/kg body weight/min ) General linear models were used to identify differences between groups after controlling for sex, BMI, and MPA intensity. Tertile 1, the group with the lowest accumulation of daily MPA, was used as the referent group.
Significance was set at $p < 0.05$ for main effects and at $p < 0.1$ for interaction. These $p$ values along with $R^2$ values were utilized to determine statistical significance as opposed to examining patterns within the data and effect sizes. All statistical analyses were performed using IBM® SPSS® 19.0 software (IBM Corporation, Somers, NY).
RESULTS

Participant characteristics are shown in Table 3-1. Women had lower levels of CRF and participated in fewer minutes of MPA than men (p < 0.01). Approximately 5 hours of IPA, which consisted primarily of LPA (i.e., 94%), were accumulated daily in men and women combined. None of the participants accumulated sufficient physical activity to meet the consensus physical activity guidelines of at least 150 minutes per week of moderate-to-vigorous physical activity accumulated in bouts of at least 10 consecutive minutes. Participants achieved CRF values in the low to good range (i.e., 26 to 35 ml/kg/min for men and 20 to 31 ml/kg/min for women).

As illustrated in Figure 3-1, IPA duration was significantly associated with CRF \((r^2 = 0.03, p < 0.05; \text{Table 3-2})\) and remained a positive correlate after statistical control for sex and BMI \((p < 0.01)\). Similarly, IPA intensity was positively associated with CRF \((r^2 = 0.18, p < 0.05)\) and remained a significant predictor after statistical control for sex and BMI \((p < 0.01)\). After control for each other, there was a trend for significance between IPA duration and CRF \((p = 0.05)\) whereas IPA intensity remained significantly associated \((p < 0.001)\).

As illustrated in Figure 3-2, LPA was not a significant predictor of CRF \((p > 0.05)\). Results remained the same after statistical control for sex, BMI, and MPA \((p > 0.1; \text{Table 3-2})\). MPA was associated with CRF in the univariate analysis \((r^2 = 0.23, p < 0.001)\) and remained a significant predictor after control for sex, BMI, and LPA \((r^2 = 0.60, p < 0.001)\).
Participants were then divided into tertiles based on accumulated sporadic MPA, and CRF was converted to MET values (Figure 3-3). In addition to accumulating very low levels of MPA, men and women in the referent group (tertile 1) had low CRF values. After control for sex, BMI, and MPA intensity, participants in both tertiles 2 (mean = 16.9 min/d of MPA) and 3 (mean = 33.6 min/d of MPA) had a higher MET value than those in tertile 1 (mean = 6.2 min/d of MPA) (p < 0.01). Participants in tertile 3 also had a significantly higher MET value than participants in tertile 2 (p < 0.05).

**Table 3-1** Participant characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 43)</th>
<th>Women (n = 92)</th>
<th>Total (n = 135)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.3 ± 8.3</td>
<td>52.5 ± 7.3</td>
<td>53.1 ± 7.6</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>32.9 ± 3.4</td>
<td>32.9 ± 5.0</td>
<td>32.9 ± 4.6</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>115.9 ± 8.5</td>
<td>107.3 ± 11.3**</td>
<td>110.0 ± 11.2</td>
</tr>
<tr>
<td>Cardiorespiratory Fitness (ml/kg body weight/min)</td>
<td>31.0 ± 3.9</td>
<td>24.9 ± 3.8**</td>
<td>26.8 ± 4.7</td>
</tr>
<tr>
<td><strong>Physical Activity (Accelerometry)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime Wear (min/d)</td>
<td>970.9 ± 127.9</td>
<td>940.2 ± 88.1</td>
<td>950.0 ± 103.0</td>
</tr>
<tr>
<td>IPA Duration (min/d)</td>
<td>306.5 ± 129.6</td>
<td>309.0 ± 81.4</td>
<td>308.2 ± 98.8</td>
</tr>
<tr>
<td>IPA Intensity (cpm)</td>
<td>736.5 ± 143.7</td>
<td>660.8 ± 128.9</td>
<td>684.9 ± 137.9</td>
</tr>
<tr>
<td>LPA Duration (min/d)</td>
<td>282.6 ± 117.5</td>
<td>292.0 ± 77.4</td>
<td>289.0 ± 91.7</td>
</tr>
<tr>
<td>LPA Intensity (cpm)</td>
<td>556.4 ± 78.9</td>
<td>531.7 ± 73.9</td>
<td>539.6 ± 76.1</td>
</tr>
<tr>
<td>MPA Duration (min/d)</td>
<td>23.9 ± 17.4</td>
<td>17.0 ± 10.6*</td>
<td>19.2 ± 13.5</td>
</tr>
<tr>
<td>MPA Intensity (cpm)</td>
<td>2886.7 ± 353.5</td>
<td>2765.5 ± 374.1</td>
<td>2804.1 ± 370.6</td>
</tr>
</tbody>
</table>

Data are means ± SD. Significant difference between sexes: *(p < 0.01), **(p < 0.001)

BMI: body mass index; IPA: incidental physical activity; LPA: light physical activity; MPA: moderate physical activity; cpm: counts per minute; min/d: minutes per day.
Table 3-2 Regression analyses of physical activity and cardiorespiratory fitness

<table>
<thead>
<tr>
<th>Model</th>
<th>Variable</th>
<th>B</th>
<th>95% CI</th>
<th>P</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>IPA Duration (min/d)</td>
<td>0.31</td>
<td>0.02 to 0.60</td>
<td>0.04</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>IPA Intensity (cpm)</td>
<td>0.01</td>
<td>0.01 to 0.02</td>
<td>0.001</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>LPA Duration (min/d)</td>
<td>0.28</td>
<td>-0.01 to 0.58</td>
<td>0.06</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>MPA Duration (min/d)</td>
<td>1.45</td>
<td>0.99 to 1.90</td>
<td>0.001</td>
<td>0.23</td>
</tr>
<tr>
<td>Model 2</td>
<td>IPA Duration (min/d)</td>
<td>0.35</td>
<td>0.12 to 0.57</td>
<td>0.003</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>IPA Intensity (cpm)</td>
<td>0.01</td>
<td>0.01 to 0.01</td>
<td>0.001</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>LPA Duration (min/d)</td>
<td>0.36</td>
<td>0.14 to 0.59</td>
<td>0.002</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>MPA Duration (min/d)</td>
<td>1.09</td>
<td>0.71 to 1.47</td>
<td>0.001</td>
<td>0.49</td>
</tr>
<tr>
<td>Model 3</td>
<td>IPA Duration (min/d)</td>
<td>0.30</td>
<td>0.10 to 0.50</td>
<td>0.004</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>IPA Intensity (cpm)</td>
<td>0.01</td>
<td>0.01 to 0.01</td>
<td>0.001</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>LPA Duration (min/d)</td>
<td>0.28</td>
<td>0.08 to 0.49</td>
<td>0.008</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>MPA Duration (min/d)</td>
<td>0.99</td>
<td>0.65 to 1.33</td>
<td>0.001</td>
<td>0.60</td>
</tr>
<tr>
<td>Model 4</td>
<td>IPA Duration (min/d)</td>
<td>0.20</td>
<td>-0.00 to 0.40</td>
<td>0.05</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>IPA Intensity (cpm)</td>
<td>0.01</td>
<td>0.00 to 0.01</td>
<td>0.001</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>LPA Duration (min/d)</td>
<td>0.06</td>
<td>-0.15 to 0.27</td>
<td>0.55</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>MPA Duration (min/d)</td>
<td>1.36</td>
<td>0.61 to 2.10</td>
<td>0.001</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Model 1: unadjusted
Model 2: adjusted for sex
Model 3: adjusted for sex and body mass index
Model 4: adjusted for sex, body mass index, and other physical activity variable
IPA: incidental physical activity; LPA: light physical activity; MPA: moderate physical activity; cpm: counts per minute; min/d: minutes per day; CI: confidence intervals.
Figure 3-1 Associations of A) incidental physical activity duration and B) incidental physical activity intensity with cardiorespiratory fitness

A

Cardiorespiratory Fitness (ml/kg body weight/min)

Incidental Physical Activity Duration (min/d)

$r = 0.20, p < 0.01$

B

Incidental Physical Activity Intensity (cpm)

$r = 0.41, p < 0.01$
Figure 3-2 Associations of A) light physical activity and B) moderate physical activity with cardiorespiratory fitness

A

Cardiorespiratory Fitness (ml/kg body weight/min)

Light Physical Activity (min/d)

r = 0.18, p > 0.05

B

Cardiorespiratory Fitness (ml/kg body weight/min)

Moderate Physical Activity (min/d)

r = 0.46, p < 0.01
Figure 3-3 Tertiles of moderate physical activity and cardiorespiratory fitness with corresponding participant characteristics for each tertile

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>45</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>M/F</td>
<td>14/31</td>
<td>15/30</td>
<td>14/31</td>
</tr>
<tr>
<td>MPA Duration (min/d)</td>
<td>6.7 ± 2.9</td>
<td>17.3 ± 4.0</td>
<td>33.6 ± 12.3</td>
</tr>
<tr>
<td>MPA Intensity (cpm)</td>
<td>2612.0 ± 313.2</td>
<td>2816.4 ± 337.7</td>
<td>2983.9 ± 367.9</td>
</tr>
<tr>
<td>CRF (METs)</td>
<td>7.1 ± 1.4</td>
<td>7.7 ± 1.2</td>
<td>8.2 ± 1.3</td>
</tr>
<tr>
<td>CRF (ml/kg/min)</td>
<td>25.2 ± 4.5</td>
<td>27.0 ± 4.2</td>
<td>29.0 ± 3.9</td>
</tr>
</tbody>
</table>

a: significantly different than tertile 1 (p = 0.004)
b: significantly different than tertile 1 (p < 0.001)
c: significantly different than tertile 2 (p = 0.04)

Data are mean ± SD. METs, metabolic equivalents; MPA, moderate physical activity; CRF, cardiorespiratory fitness; min/d, minutes per day; cpm, counts per minute.
DISCUSSION

The primary finding of this study was that both the duration and intensity of IPA were significantly associated with CRF in this sample of inactive, abdominally obese men and women independent of sex and BMI. Given the established association of CRF with morbidity and mortality, these observations have important clinical and public health implications and provide empirical evidence that the positive effects of physical activity on CRF occur along a continuum.

To our knowledge this is the first study to assess the association between objectively measured IPA and CRF. Our findings counter the notion that to improve CRF, physical activity must be accumulated at a minimum threshold of 40 to 50% of heart rate reserve or 64 to 70% of maximal heart rate and accumulated in bouts of at least 10 consecutive minutes. To the contrary, our results indicate that non-purposeful activity accrued sporadically throughout the day is associated with higher CRF. Although we also found that IPA intensity was a stronger predictor of CRF than IPA duration, the average IPA intensity was low. The average accelerometer count values we observed (i.e., 100 to 1951) are associated with walking at a slow, leisurely pace (i.e., < 5.0 km/h). Moreover, even the physical activity accumulated sporadically as MPA was equivalent to walking at a comfortable pace (i.e., 5.8 km/h). These results are encouraging and provide options that may be more feasible and enjoyable for inactive individuals attempting to engage in physical activity for health benefit.

It is important to note that even though IPA was significantly associated with CRF, this observation was driven in large part by the sporadically obtained MPA and not
LPA. Stated differently, despite the accumulation of approximately 5 hours of LPA, the differences in CRF were due to the participation in 20 minutes of MPA. This is consistent with previous literature demonstrating that physical activity intensity is positively associated with CRF

Previous studies have reported a relationship between bouted MPA and CRF however this is the first study to specifically examine the association between sporadic MPA and CRF. This was made possible with the use of accelerometers, objective measurement tools that provide minute-by-minute recording of physical activity thereby overcoming the limitations inherent to self-report questionnaires and allowing for a detailed examination of physical activity patterns. It is noteworthy that even though sporadic MPA was a significant predictor of CRF, most participants in this study achieved peak CRF values in the lower end of the CRF spectrum. Thus, although sporadic MPA is associated with higher CRF in inactive individuals, it is doubtless true that a much greater difference would be observed in individuals accumulating bouted MPA and/or vigorous physical activity. For example, men and women aged 50 to 59 years who regularly perform bouted or structured moderate-to-vigorous physical activity may have CRF values > 11 METs and > 9 METs, respectively, which is approximately 2 METs higher than the average MET values observed in this study.

A 1 MET increase in CRF is associated with a 13% and 15% reduction in all-cause mortality and cardiovascular disease, respectively. This suggests that the 0.5 MET difference in CRF between individuals in the middle tertile compared to the lowest may be associated with a decreased risk of 6.5% for all-cause mortality and 7.5% for
cardiovascular disease. This is a substantial reduction in risk for only a 10 minute increase in sporadic MPA per day. Further, the 1.0 MET (~3.5 ml/kg/min) difference in CRF between individuals in the highest tertile of MPA compared to the lowest may be associated with a risk reduction of 13% in all-cause mortality and 15% in cardiovascular disease. Stated differently, in our study a 30 minute increase in the accumulation of sporadic MPA was associated with a 1.0 MET increase in CRF and potentially, a significant risk reduction in morbidity and mortality.

It is important to note that despite the daily accumulation of approximately 5 hours of IPA, all of the participants in the current study were abdominally obese and therefore thought to be at increased health risk as compared to individuals without abdominal obesity. Nevertheless, previous research has demonstrated that in individuals presenting with obesity, those who have higher CRF are at a substantially decreased risk of morbidity and mortality compared to those with low CRF. In men with elevated abdominal obesity and moderate to high levels of CRF (~9 to 10 METs), the risk of all-cause mortality was no different than lean men with high CRF. By comparison, the men in our study who were in the highest tertile of MPA had a similar average CRF (~9 METs).

The current study was cross-sectional and conducted in a sample relatively homogenous in terms of abdominal obesity and physical activity levels. However, given that a large percentage of the North American population is both abdominally obese and does not meet consensus physical activity recommendations, our results are relevant to a large proportion of the general population.
In summary, the duration and intensity of incidental physical activity is positively associated with CRF suggesting that all forms of physical activity carry health benefit and that the need to target thresholds of physical activity to improve CRF may not be required. Health care providers are encouraged to promote all forms of physical activity to improve CRF, an established risk factor of morbidity and mortality. Further studies are required to determine whether the associations found in the present investigation hold true in a more heterogeneous sample (i.e., in individuals of different ethnicity or phenotype) and whether IPA is associated with corresponding improvement in cardiometabolic risk factors.
Chapter 4

Sedentary behaviour is not associated with cardiometabolic risk in adults with abdominal obesity
ABSTRACT

Objective: The primary aim of this study was to determine whether time spent sedentary (SED) was associated with 2-hour glucose and insulin resistance in adults with abdominal obesity. We also examined the association between light physical activity (LPA) and sporadic (accumulated in bouts < 10 minutes in duration) moderate-to-vigorous physical activity (MVPA) with glucose metabolism.

Methods: Participants were 135 inactive, abdominally obese adults recruited from Kingston, Canada. SED and physical activity were determined by accelerometry over 7 days and summarized as SED (accelerometer counts per minute (cpm) < 100), LPA (cpm 100 to 1951), and MVPA (cpm ≥ 1952). A 75 g oral glucose tolerance test was used to ascertain 2-hour glucose; the homeostasis model of assessment was used to determine insulin resistance (HOMA-IR); lipid, lipoproteins and blood pressure were determined using standard protocols. Secondary analyses considered the association of SED and physical activity with other cardiometabolic risk factors.

Results: Participants spent 627.2 ± 82.9 min/d in SED, 289.0 ± 91.7 min/d in LPA and 19.2 ± 13.5 min/d in MVPA. Neither SED nor the physical activity variables were associated with 2-hour glucose or HOMA-IR (p > 0.05). In secondary analyses, SED was not associated with any cardiometabolic risk factor (p > 0.1); with the exception of blood pressure (p < 0.05), LPA was not associated with any cardiometabolic risk factor (p > 0.1); and MVPA was independently associated with total cholesterol and triglycerides (p < 0.05).
**Conclusions:** Objectively measured SED was not associated with 2-hour glucose or HOMA-IR. Our findings also suggest that the accumulation of LPA and sporadic MVPA are not associated with glucose metabolism in adults with abdominal obesity.
INTRODUCTION

Sedentary behaviours (SED), which include activities such as television viewing or computer screen time, have gained widespread interest due to observations suggesting they have a negative impact on a variety of health outcomes \(^{16, 121, 178}\). Evidence from Healy et al. \(^{12, 13}\) indicates that, independent of moderate-to-vigorous physical activity (MVPA), time spent in SED is positively associated with 2-hour glucose, waist circumference, and clustered metabolic risk in middle-aged adults. In contrast, Ekelund and colleagues \(^{14}\) did not find a significant relationship between SED and insulin resistance in adults. Subsequently, others \(^{15, 22}\) observe a univariate association of SED with select cardiometabolic risk factors however this association is not independent of MVPA or total activity. Although small differences in participant characteristics and accelerometry data reduction techniques exist between studies, there is no consistent pattern that would explain the disparate findings.

Whether time spent SED explains cardiometabolic risk beyond MVPA has important public health implications and thus we sought to clarify the relationships between SED, LPA, and MVPA with 2-hour glucose and insulin resistance in a population of inactive adults with abdominal obesity. Secondary analyses examined the association between SED, LPA, MVPA and other common cardiometabolic risk factors (triglycerides, total cholesterol, high-density lipoproteins, and blood pressure).
METHODS

Participants

Participants for this study were men and women aged 35 to 65 years who were inactive, did not smoke, had an elevated waist circumference (defined as at least 102 cm in men and at least 88 cm in women), and a body mass index (BMI) between 25.0 to 39.9 kg/m². Potential participants were excluded if they reported any physical impairment which would make physical activity difficult, or unsafe including history of myocardial infarction, stroke, coronary bypass surgery or angioplasty in the last 6 months; peripheral artery disease, unstable angina or ischemia; if they had diagnosed diabetes or were taking glucose-lowering medication; if they consumed > 21 alcoholic drinks per week. The study was approved by the Queen’s University Health Sciences Research Ethics Board. All participants gave written informed consent before participation in the study.

Anthropometric and Metabolic Tests

Body mass and height were measured to the nearest 0.1 cm and 0.1 kg, respectively, with participants dressed in standard T-shirts and shorts. These measures were used to calculate BMI (kg/m²). Waist circumference was obtained in a standing position using the mean of two measures acquired at the superior edge of the iliac crest measured to the nearest 0.1 cm.

Glucose tolerance was measured by means of a 2-hour glucose tolerance test the morning after an overnight fast. Blood samples were collected from the antecubital
vein at the following time-points: 0, 30, 60, 90, and 120 minutes after ingestion of 75 g of Glucodex. Plasma glucose was determined using enzymatic methods on the Synchron LX® Systems (Beckman Coulter, Inc., Brea, CA, USA). Insulin was determined with a chemiluminescent immunoassay using the Beckman Coulter UniCel Dxi 800 Access® Immunoassay System (Beckman Coulter, Inc., Brea, CA, USA). The homeostasis model assessment for insulin resistance (HOMA-IR) was used as a measure of insulin resistance and was calculated as fasting plasma glucose (mmol/L) x fasting serum insulin (μU/mL) / 22.5. HOMA-IR was available for 99 participants. Blood samples to determine fasting triglycerides (TG), total cholesterol, and high-density lipoprotein cholesterol (HDL) were also obtained in the morning after a 12- to 14-hour overnight fast. Serum total cholesterol, TG, and HDL levels were determined using standard enzymatic methods on the Synchron LX® Systems (Beckman Coulter, Inc., Brea, CA, USA). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using the BP Tru Blood Pressure Monitor (BPTru Medical Devices, Coquitlam, BC, Canada) in the morning after an overnight fast.

**Physical Activity by Accelerometry**

Physical activity was measured with the Actigraph GT3X accelerometer (Actigraph, Pensacola, Florida, USA). Although this is a triaxial accelerometer, only the vertical axis was used for analysis. Accelerometers were programmed to collect data in 1-minute epochs over 7 consecutive days and were worn on an elastic belt positioned over the right hip at all times except during water-based activities. Additionally,
participants completed a log sheet indicating when they went to bed at night, woke up in the morning, and removed the accelerometer.

To be included in the analysis, participants were required to wear the accelerometer for at least four complete days (including one weekend day) within the monitoring period. A complete day was defined as at least 10 hours of wear time during the day. Wear time was calculated after extended periods of consecutive zero counts ≥ 60 minutes and sleep time (determined using both the participant logs and visual examination of the data) were excluded. Twelve participants did not meet the compliance criteria and were removed from the analysis. The accelerometer cutpoints in this study used to translate the ‘count’ value into an estimate of physical activity intensity were those developed by Freedson and colleagues. LPA was defined as 100 to 1951 counts per minute (cpm) and MVPA as cpm ≥ 1952. SED was defined as < 100 cpm, an arbitrary cutpoint commonly used. Activity accumulated during each complete day of monitoring was quantified in both absolute and relative terms: 1) average duration, in minutes per day, of each SED, LPA, MVPA, and total physical activity (LPA + MPVA; TPA), 2) percentage of time per day spent in each SED, LPA, MVPA, and TPA, 3) average minutes of MVPA per day accumulated in sporadic bouts (1 to 9 minutes), and 4) average minutes of MVPA per day accumulated in extended bouts (≥ 10 minutes). The latter bout duration is consistent with the consensus recommendation that physical activity be accumulated in intervals lasting 10 minutes or more for health benefit. Since periods of rest are common during activity (e.g., waiting for a light to change colour at a crosswalk during a walk), participants were required to spend at least 80% of the bout above the threshold value. For example, in a 10-minute bout of MVPA only 8 of
those minutes would need to fall above 1952 cpm. The bouted MVPA was used to determine whether participants were meeting physical activity guidelines.

**Statistical and Power Analyses**

Descriptive characteristics are summarized as mean values ± standard deviations (SD). TG, HDL, HOMA-IR and all physical activity variables were logarithmically transformed due to skewed distributions. Associations between variables were examined using Pearson correlation coefficients. Differences between sex were determined using Independent Student’s T-tests. Sex differences in the relationship between physical activity and cardiometabolic risk factors were tested by adding the interaction terms to the regression models. With the exception of SBP and DBP, no differences were detected. Therefore analyses were collapsed across sex for all variables except blood pressure. To assess the association between SED, LPA, MVPA and cardiometabolic risk factors, linear regression models were used. Regression models using both the absolute and relative SED and physical activity variables were conducted. Only the covariates that significantly influenced the regression models were retained. Thus, when 2-hour glucose or HOMA-IR was the outcome variable the following models were used: 1) adjusted for time accelerometer worn and 2) adjusted for time accelerometer worn and waist circumference. To assess the association between SED, LPA, MVPA and other common cardiometabolic risk factors (total cholesterol, TG, HDL, SBP and DBP), the following models were used: 1) adjusted for time accelerometer worn, 2) adjusted for time accelerometer worn, sex, age, waist circumference, and 3) adjusted for time accelerometer worn, sex, age, waist
circumference, and the other physical activity variables. In all regression models, multicollinearity was assessed using the variance inflation factor and tolerance statistic. Significance was set at $p < 0.05$ for main effects and at $p < 0.1$ for interaction. These $p$ values along with $R^2$ values were utilized to determine statistical significance as opposed to examining patterns within the data and effect sizes. All statistical analyses were performed using IBM® SPSS® 19.0 software (IBM Corporation, Somers, NY).

Power calculations were based on our primary outcomes (2-hour glucose and HOMA-IR). In our convenience sample of 135 with 2-hour glucose values, we estimate that we have 95% power to detect a correlation of 0.3 with an alpha of $p < 0.05$. In our sample of 99 participants with HOMA-IR data we have 85% power to detect a correlation of 0.3 at an alpha of $p < 0.05$. 
RESULTS

The participant characteristics are shown in Table 4-1. Men had a higher waist circumference, TG, and DBP (p < 0.01) whereas women had higher HDL (p < 0.001). Men participated in more MVPA than women (p < 0.01).

Accelerometers were worn for a median of 7 days and for 16 hours per day on average. Participants spent 66% of their waking hours in SED, 30% in LPA, and only 2% in MVPA. Although all participants were confirmed as inactive according to the consensus recommendation that adults accumulate 30 minutes of daily MVPA in bouts of ≥ 10 minutes, approximately 5 hours of LPA and 20 minutes of sporadic MVPA were accumulated daily (Table 4-1).

When expressed as a percentage of wear time, SED was negatively correlated with LPA (r = -0.85, p < 0.01) and MVPA (r = -0.39, p < 0.05) whereas LPA and MVPA were positively correlated (r = 0.35, p < 0.01). SED, LPA, and MVPA were not associated with waist circumference (p > 0.1). Waist circumference was positively correlated with 2-hour glucose (r = 0.18, p < 0.05) and HOMA-IR (r = 0.52, p < 0.01).

Neither SED nor the physical activity variables were associated with 2-hour glucose or HOMA-IR after control for time accelerometer worn and waist circumference (p > 0.05). Results were the same regardless of whether SED and the physical activity variables were expressed in absolute or relative terms (Table 4-2 and Table 4-3). Results were not different for TPA (data not shown). To further illustrate the relationship between SED, physical activity and 2-hour glucose, individual data were plotted in ascending order for 2-hour glucose along with the corresponding data, in the same
order, for both SED and LPA. As illustrated in Figure 4-1, with increasing 2-hour glucose, there is no clear corresponding increase in SED or decrease in LPA.

In secondary analyses, SED was not associated with any of the cardiometabolic risk factors (p > 0.1). LPA was not significantly associated with total cholesterol, TG, or HDL (p > 0.1) but was a significant independent predictor of both SBP and DBP (p < 0.01) in men, explaining 16% and 22% of the variance, respectively and DBP in women (p < 0.05). MVPA was significantly associated with total cholesterol and TG after control for time accelerometer worn, age, sex, waist circumference, and other physical variables (p < 0.05) however the variance explained by MVPA was less than 10%. Results with TPA as the independent variable were the same as those for LPA (data not shown). Similarly to the primary analyses, results were the same when SED and the physical activity variables were expressed as either absolute or relative values with the following exception: when LPA and TPA were expressed as a percentage of wear time the association with SBP and DBP was not significant in either sex (p > 0.1).
<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 43)</th>
<th>Women (n = 92)</th>
<th>Total (n = 135)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.3 ± 8.3</td>
<td>52.5 ± 7.3</td>
<td>53.1 ± 7.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>32.9 ± 3.4</td>
<td>32.9 ± 5.0</td>
<td>32.9 ± 4.6</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>115.9 ± 8.4</td>
<td>107.3 ± 11.3*</td>
<td>110.0 ± 11.2</td>
</tr>
<tr>
<td>2-hour Glucose (mmol/L)</td>
<td>7.0 ± 2.0</td>
<td>6.9 ± 1.7</td>
<td>6.9 ± 1.8</td>
</tr>
<tr>
<td>HOMA-IR^</td>
<td>2.7 ± 1.6</td>
<td>2.2 ± 1.7</td>
<td>2.3 ± 1.7</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>5.0 ± 0.9</td>
<td>5.3 ± 1.1</td>
<td>5.2 ± 1.0</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.8 ± 1.0</td>
<td>1.4 ± 0.7**</td>
<td>1.5 ± 0.8</td>
</tr>
<tr>
<td>High-Density Lipoproteins (mmol/L)</td>
<td>1.0 ± 0.3</td>
<td>1.3 ± 0.3*</td>
<td>1.2 ± 0.4</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>123 ± 12</td>
<td>121 ± 15</td>
<td>122 ± 14</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>81 ± 7</td>
<td>78 ± 9**</td>
<td>79 ± 8</td>
</tr>
</tbody>
</table>

**Physical Activity (Accelerometry)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 43)</th>
<th>Women (n = 92)</th>
<th>Total (n = 135)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wear Time (min/d)</td>
<td>970.9 ± 127.9</td>
<td>940.2 ± 88.1</td>
<td>950.0 ± 103.0</td>
</tr>
<tr>
<td>Average Daily Intensity (cpm)</td>
<td>536.1 ± 199.7</td>
<td>535.8 ± 143.6</td>
<td>535.9 ± 162.8</td>
</tr>
<tr>
<td>Sedentary Behaviour (min/d)</td>
<td>647.8 ± 72.0</td>
<td>617.8 ± 86.2</td>
<td>627.2 ± 82.9</td>
</tr>
<tr>
<td>Average Sedentary Intensity (cpm)</td>
<td>10.7 ± 3.0</td>
<td>11.3 ± 2.7</td>
<td>11.0 ± 2.8</td>
</tr>
<tr>
<td>Time in Sedentary Behaviour (%)</td>
<td>67.6 ± 8.7</td>
<td>65.8 ± 7.8</td>
<td>66.4 ± 8.1</td>
</tr>
<tr>
<td>Light Physical Activity (min/d)</td>
<td>282.6 ± 117.5</td>
<td>292.0 ± 77.4</td>
<td>289.0 ± 91.7</td>
</tr>
<tr>
<td>Average Light Activity Intensity (cpm)</td>
<td>556.4 ± 78.9</td>
<td>531.7 ± 73.9</td>
<td>539.6 ± 76.1</td>
</tr>
<tr>
<td>Time in Light Activity (%)</td>
<td>28.6 ± 7.8</td>
<td>31.0 ± 7.2</td>
<td>30.2 ± 7.5</td>
</tr>
<tr>
<td>Moderate-to-Vigorous Physical Activity (min/d)</td>
<td>23.9 ± 17.4</td>
<td>17.0 ± 10.6**</td>
<td>19.2 ± 13.5</td>
</tr>
<tr>
<td>Average Moderate-to-Vigorous Activity Intensity (cpm)</td>
<td>2886.7 ± 353.5</td>
<td>2765.5 ± 374.1</td>
<td>2804.1 ± 370.7</td>
</tr>
<tr>
<td>Time in Moderate-to-Vigorous Activity (%)</td>
<td>2.4 ± 1.5</td>
<td>1.8 ± 1.1</td>
<td>2.0 ± 1.3</td>
</tr>
<tr>
<td>Total Physical Activity (min/d)</td>
<td>306.5 ± 129.6</td>
<td>309.0 ± 81.4</td>
<td>308.2 ± 98.8</td>
</tr>
</tbody>
</table>

Data are means ± SD. Significant difference between sex: *p < 0.001, **p < 0.01  
^p = 99 for HOMA-IR. BMI, body mass index; HOMA-IR, homeostasis model assessment for insulin resistance; min/d, minutes per day; cpm, accelerometer counts per minute.
**Table 4-2** Regression analyses of sedentary behaviour and physical activity (expressed as average minutes worn per day) with glucose metabolism

<table>
<thead>
<tr>
<th></th>
<th>2-Hour Glucose (N = 135)</th>
<th></th>
<th>HOMA-IR (N = 99)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI)</td>
<td>P</td>
<td>R²</td>
<td>B (95% CI)</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED (min/d)</td>
<td>0.00 (-0.00 to 0.01)</td>
<td>0.31</td>
<td>0.00</td>
<td>0.00 (-0.00 to 0.00)</td>
</tr>
<tr>
<td>LPA (min/d)</td>
<td>-0.14 (-0.28 to 0.00)</td>
<td>0.06</td>
<td>0.03</td>
<td>-0.01 (-0.04 to 0.03)</td>
</tr>
<tr>
<td>MVPA (min/d)</td>
<td>-0.13 (-0.35 to 0.09)</td>
<td>0.23</td>
<td>0.01</td>
<td>-0.00 (-0.05 to 0.05)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED (min/d)</td>
<td>0.00 (-0.00 to 0.01)</td>
<td>0.39</td>
<td>0.02</td>
<td>0.00 (-0.00 to 0.00)</td>
</tr>
<tr>
<td>LPA (min/d)</td>
<td>-0.12 (-0.26 to 0.02)</td>
<td>0.10</td>
<td>0.04</td>
<td>-0.01 (-0.05 to 0.02)</td>
</tr>
<tr>
<td>MVPA (min/d)</td>
<td>-0.14 (-0.35 to 0.08)</td>
<td>0.22</td>
<td>0.03</td>
<td>-0.01 (-0.05 to 0.04)</td>
</tr>
</tbody>
</table>

Model 1: adjusted for time accelerometer worn
Model 2: adjusted for time accelerometer worn and waist circumference
HOMA-IR, homeostasis model assessment for insulin resistance; CI, confidence intervals; SED, sedentary behaviour; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity.
Table 4-3 Regression analyses of sedentary behaviour and physical activity (expressed as percentage of wear time) with glucose metabolism

<table>
<thead>
<tr>
<th></th>
<th>2-Hour Glucose (N = 135)</th>
<th></th>
<th></th>
<th>HOMA-IR (N = 99)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI) P R²</td>
<td>B (95% CI)</td>
<td>P R²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED (%)</td>
<td>0.01 (-0.03 to 0.05)</td>
<td>0.54</td>
<td>0.01</td>
<td>0.00 (-0.00 to 0.01)</td>
<td>0.52</td>
<td>0.00</td>
</tr>
<tr>
<td>LPA (%)</td>
<td>-0.02 (-0.06 to 0.02)</td>
<td>0.38</td>
<td>0.00</td>
<td>0.00 (-0.01 to 0.01)</td>
<td>0.94</td>
<td>0.00</td>
</tr>
<tr>
<td>MVPA (%)</td>
<td>-0.35 (-0.99 to 0.29)</td>
<td>0.28</td>
<td>0.00</td>
<td>-0.00 (-0.11 to 0.11)</td>
<td>0.96</td>
<td>0.00</td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED (%)</td>
<td>0.01 (-0.03 to 0.05)</td>
<td>0.63</td>
<td>0.02</td>
<td>0.00 (-0.00 to 0.01)</td>
<td>0.39</td>
<td>0.30</td>
</tr>
<tr>
<td>LPA (%)</td>
<td>-0.02 (-0.06 to 0.02)</td>
<td>0.43</td>
<td>0.02</td>
<td>-0.00 (-0.01 to 0.01)</td>
<td>0.65</td>
<td>0.29</td>
</tr>
<tr>
<td>MVPA (%)</td>
<td>-0.34 (-0.97 to 0.29)</td>
<td>0.29</td>
<td>0.03</td>
<td>-0.01 (-0.11 to 0.08)</td>
<td>0.78</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Model 1: adjusted for time accelerometer worn
Model 2: adjusted for time accelerometer worn and waist circumference
HOMA-IR, homeostasis model assessment for insulin resistance; CI, confidence intervals; SED, sedentary behaviour; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity.
Figure 4-1 Association of A) 2-hour glucose (mmol/L) with B) sedentary behaviour (min/d) and C) light physical activity (min/d) for each individual participant.
DISCUSSION

The primary finding of this study was that time spent in SED was not associated with glucose metabolism in inactive men and women with abdominal obesity. These results, combined with a prior investigation 14 question the unique contribution of SED to cardiometabolic risk in adults. We also observed that the average accumulation of approximately 5 hours of LPA plus an additional 20 minutes of sporadic MVPA on a daily basis was not associated with 2-hour glucose or HOMA-IR in this cross-sectional analysis. This observation supports the consensus recommendation that for health benefit physical activity should be accumulated in bouts of at least 10 minutes.

Our primary finding is consistent with observations by Ekelund et al. 14 who report that SED is not a significant predictor of HOMA-IR in overweight men and women with a family history of type 2 diabetes. However, our results counter those of Healy and colleagues 12 which suggest that, independent of both LPA and MVPA, SED is negatively associated with 2-hour glucose in men and women recruited from the general Australian population (AusDiab Study). Somewhat consistent with Healy et al.12, data from the RISC Study 15 and ProActive Trial 22, indicate a significant relationship between SED and HOMA-IR in univariate analyses however after statistical control for total activity or MVPA these associations are no longer significant. Thus at present the relationship of SED with glucose metabolism in adults is unclear.

The participants in our study had a more deleterious cardiometabolic risk factor profile and were more obese than participants in the prior studies however this is not likely to affect the relationship between SED, physical activity, and cardiometabolic risk
factors. Further, there is no distinct difference in participant characteristics or statistical analyses between the investigations that may explain the differences in findings. For example, the participants in our study are similar in age to those in the AusDiab study \textsuperscript{12, 13} whereas the cardiometabolic risk factor profile is very similar between participants in the ProActive Trial \textsuperscript{14} and AusDiab study \textsuperscript{12, 13}. Alternatively, the discrepancies may be explained in part by measurement limitations and inconsistent physical activity profiling.

Although the use of accelerometry to objectively measure SED and physical activity represents a major advance in physical activity research, these devices are not without limitations. For example, accelerometers are unable to detect variations in SED due to fidgeting or provide context to the behaviour and cannot capture certain activities such as cycling. Therefore differences between populations in SED pursuits and activities not captured by the accelerometer may influence relationships of SED and physical activity with health outcomes. Additionally, there are currently no published studies comparing the output of earlier Actigraph models to the GT3X utilized in the present investigation. It is possible that there is a difference between models in the ability to detect activity at the lower end of the movement spectrum \textsuperscript{179}. Consequently, the amount of time spent in SED and LPA may be influenced.

In the literature there is also considerable inconsistency in the presentation of physical activity patterning despite the use of common cutpoints to classify physical activity intensity. For example, it is unclear whether the participants in the AusDiab Study accumulated MVPA sporadically or in bouts. Given the consensus recommendation that MVPA be accumulated in bouts of at least 10 minutes to confer
benefit across a wide range of health outcomes \(^5,9\), the associations between MVPA and cardiometabolic risk factors could differ depending on how the participants accrued daily MVPA and could explain why others find that MVPA is a significant predictor of both 2-hour glucose \(^{12}\) and HOMA-IR \(^{14}\). Thus, it would be helpful to the field of SED and physical activity research to standardize how variables are reported as this would enable direct comparisons between studies and help to eliminate confusion.

In this study secondary analyses revealed that SED was not associated with other common cardiometabolic risk factors in abdominally obese, inactive adults. Although Ekelund and colleagues \(^{22}\) report similar findings, these results do not support recent evidence derived from animal models where, after only one day of hind-limb suspension (to remove ambulation), a significant decrease in lipoprotein lipase activity, TG uptake, and HDL concentrations is noted \(^{20}\). We also observed that with few exceptions, LPA and MVPA were not associated with other common cardiometabolic risk factors. Whereas our results are similar to some \(^{13, 15}\), they counter others \(^{13, 22}\). Substantial differences in populations studied, methodology and statistical analyses that may influence the results were not noted. Thus, it is difficult to reconcile the inconsistent results.

The findings from our study were derived from a relatively homogenous sample of middle-aged, inactive adults with abdominal obesity. However, in North America approximately 34% of adults are obese \(^{168}\) and approximately 55% do not meet consensus recommendations for physical activity \(^{33}\). Thus, our results are generalizable to a large percentage of the adult population.
In summary, whether time spent sedentary independently predicts cardiometabolic risk in adults remains to be resolved. Given the public health implications, it is important that this question be answered and thus, it would be helpful if future investigations using accelerometry employed standardized methodology in order to facilitate direct comparison between studies.
Chapter 5

Incidental physical activity patterns and abdominal obesity in inactive men and women
ABSTRACT

Objective: The aim was to determine the association between objectively measured incidental physical activity (IPA; i.e., activities of daily living) and abdominal obesity in a sample of inactive men and women. Secondary analyses examined the associations between sedentary behaviour, sleep duration, and caloric intake with abdominal obesity.

Methods: Participants were inactive, abdominally obese men (n = 42; waist circumference ≥ 102 cm) and women (n = 84; waist circumference ≥ 88 cm) recruited from Kingston, Canada. Physical activity, sedentary behaviour (SED), and sleep duration were determined by accelerometry over 7 days. Daytime data were summarized as incidental physical activity (accelerometer counts per min (cpm) > 100), light physical activity (LPA; cpm 100 to 1951), sporadic moderate physical activity (MPA; cpm ≥ 1952, accumulated in < 10 consecutive minutes) and SED (cpm < 100). Caloric intake was determined using a self-reported 7-day food diary. Magnetic resonance imaging was used to acquire measures of abdominal obesity (visceral adipose tissue (VAT) and subcutaneous adipose tissue (ASAT)).

Results: Participants spent on average, 310.2 ± 102.6 min/d in IPA, 627.8 ± 86.9 min/d in SED, and 434.9 ± 62.0 min/d sleeping. Average caloric intake was 1911.3 ± 474.9 kcal/day. IPA was not associated with any measure of abdominal obesity (p > 0.1) nor was LPA. Sporadic MPA was negatively associated with VAT (p < 0.01) after control for age and sex. SED and sleep duration were not associated with abdominal obesity (p > 0.1). Caloric intake was positively associated with VAT (p < 0.001) in univariate analyses however control for age and sex abolished the relationship (p > 0.1).
Conclusion: In this study IPA was not associated with abdominal obesity among inactive men and women whereas sporadic MPA was a significant predictor of VAT.
INTRODUCTION

Abdominal obesity is associated with an increased risk of numerous chronic health conditions including type 2 diabetes and cardiovascular disease\textsuperscript{180}. One of the modifiable determinants of abdominal obesity is physical activity\textsuperscript{181}. Indeed, it has been reported that individuals with a high waist circumference (WC), an anthropometric indicator of abdominal obesity, accumulate less physical activity than individuals with a low WC. Moreover, the pattern of physical activity accumulation may also influence WC. Strath et al.\textsuperscript{97} report that in men and women, moderate-to-vigorous physical activity accumulated in bouts of at least 10 consecutive minutes is a stronger predictor of WC than physical activity of the same intensity accumulated in bouts lasting less than 10 consecutive minutes. Conversely, Ekelund et al.\textsuperscript{22} found no association between bouted moderate-to-vigorous physical activity and WC. However, neither study considered the association between patterns of incidental physical activity (IPA), physical activity of all intensities accrued through activities of daily living, and abdominal obesity. Further, the independent associations with abdominal subcutaneous adipose tissue (ASAT) and visceral adipose tissue (VAT) were not determined. This is important to assess as the increased health risk associated with abdominal obesity may be driven in large part by specific adipose tissue depots, namely VAT\textsuperscript{182}. Demonstration that IPA and abdominal obesity are related would reinforce the notion that physical activity-related health benefits occur along a continuum.

It has also been demonstrated that sedentary behaviour (SED) is positively associated with WC\textsuperscript{13}, yet it is currently unknown whether or not SED is associated with
ASAT and VAT. Identifying SED as an independent predictor of ASAT or VAT would lend support to the belief that prolonged periods spent SED are detrimental to health.

Using accelerometers, physical activity measurement devices capable of capturing sporadic and low intensity activity across the movement spectrum, we sought to determine the association between IPA and abdominal obesity (VAT and ASAT) in an inactive sample of men and women. Secondary analyses considered the association of SED, sleep duration, and caloric intake with abdominal obesity.
METHODS

Participants

Participants for this study were men and women aged 35 to 69 years who were inactive, did not smoke, had an elevated waist circumference (defined as $\geq 102$ cm in men and $\geq 88$ cm in women), and a body mass index (BMI) between 25.0 to 39.9 kg/m$^2$. Potential participants were recruited as part of a large exercise trial (MCT190617) and were therefore excluded if they reported any physical impairment that would make physical activity difficult, or unsafe including history of myocardial infarction, stroke, coronary bypass surgery or angioplasty in the last 6 months; peripheral artery disease, unstable angina or ischemia; if they had diagnosed diabetes or were taking glucose-lowering medication; if they consumed > 21 alcoholic drinks per week. The study was approved by the Queen’s University Health Sciences Research Ethics Board. All participants gave written informed consent before participation in the study.

Abdominal Obesity

Waist circumference was obtained in a standing position using the mean of two measures acquired at the superior edge of the iliac crest measured to the nearest 0.1 cm.

Abdominal adipose tissue depots were acquired using magnetic resonance imaging; a General Electric 1.5 Tesla magnet using a procedure described in detail elsewhere $^{183}$. The magnetic resonance imaging data was analyzed with a specially designed image analysis software (Tomovision Inc., Montreal, Canada) using an
established protocol. Abdominal adipose tissue was derived using five images extending from 5 cm below to 15 cm above L4-L5. To determine VAT and ASAT, an automated filter, morpho, separated adipose tissue from lean tissue based on threshold values. Next, the subcutaneous and visceral depots of adipose tissue were separated by outlining the perimeter of the tissues with a mouse-controlled pointer and filling the area with a specific colour. Areas of the respective tissues were calculated automatically by the software by multiplying the number of pixels by the coloured area. Adipose tissue volumes (L) were then calculated based on the truncated cone formula and converted to mass units (kg) using the assumed constant density (0.92 kg/L). Total abdominal adipose tissue (TAAT) was defined as the sum of VAT plus ASAT.

**Caloric Intake**

Caloric intake was determined using a self-reported 7-day food dairy. Prior to completing the food diary participants were given instructions by the study nutritionist on how to complete it correctly. Average daily caloric intake was calculated and used in analyses.

**Physical Activity by Accelerometry**

Physical activity was measured with the Actigraph GT3X accelerometer (Actigraph, Pensacola, Florida, USA). Although this is a triaxial accelerometer only the vertical axis was used for analysis. Accelerometers were programmed to collect data in 1-minute epochs over 7 consecutive days and were worn on an elastic belt positioned over the right hip at all times except during water-based activities. Additionally,
participants completed a log sheet indicating when they went to bed at night, woke up in the morning, and removed the accelerometer.

To be included in the analysis for daytime IPA, light physical activity (LPA), moderate physical activity (MPA), and SED participants were required to wear the accelerometer for at least four days (including one weekend day). A day was defined as at least 10 hours of wear time and was calculated after extended periods of consecutive zero counts ≥ 60 minutes were removed. To be included in the analysis for sleep duration, participants were required to wear the accelerometer for at least 19.2 hours during a 24-hour period (i.e., 80% of a full 24-hour day) for at least four days (including one weekend day). Daytime wear and sleep duration were determined using both the participant logs and visual examination of the data. Total wear time was calculated after extended periods of consecutive zero counts ≥ 60 minutes were removed from the daytime wear. Sleep duration was calculated after periods of activity (defined as bouts ≥ 5 minutes in length and > 100 accelerometer counts per minute (cpm)) were excluded from the nighttime wear. Total minutes of sleep accumulated per night were summed over the entire wear period and divided by the total number of days the accelerometer was worn to derive average sleep duration.

The accelerometer cutpoints in this study used to translate the raw data into an estimate of physical activity intensity were those developed by Freedson and colleagues. IPA was defined as > 100 cpm and then further sub-divided into LPA (100 to 1951 cpm), MPA (1952 to 5724 cpm), and vigorous physical activity (≥ 5725 cpm). Since over 90% of the participants in this study did not accumulate any vigorous physical activity
and of those who did, < 5 minutes per participant was accrued over the entire wear period, all physical activity ≥ 1952 cpm was defined as MPA. Initially, MPA was subdivided into sporadic MPA per day (accumulated in < 10 consecutive minutes) and MPA per day accumulated in bouts (≥ 10 consecutive minutes in duration). However, 37 participants did not accrue any bouted MPA and in those who did, < 1 bout of MPA per day was accumulated. Therefore all MPA was classified as sporadic. SED was defined as < 100 cpm, an arbitrary cutpoint commonly used. 13, 76 For each of the variables acquired by accelerometry (IPA, LPA, MPA, and SED), total minutes spent in each intensity were summed over the entire wear period and then divided by the total number of days worn to derive average minutes per day spent in each intensity. Average cpm was also determined for each accelerometer variable by summing all cpm within each intensity category and dividing by total minutes accumulated in each intensity category. For the analysis, activity accumulated during each complete day of monitoring was quantified as a percentage of time per day spent in each IPA, LPA, MPA, SED, and sleep duration to account for different lengths of wear time. A total of 126 participants were included in the analyses for daytime accelerometry variables and a total of 111 participants were included in the analyses for sleep duration.

**Statistical and Power Analyses**

All statistical analyses were performed using IBM® SPSS® 19.0 software (IBM Corporation, Somers, NY). Descriptive characteristics are summarized as mean values ± standard deviations (SD). All measures of abdominal obesity, except WC, and all physical activity variables were normalized using either log or square-root
transformations. Differences between sex were determined using Independent Student’s T-tests. Sex differences in the relationship between accelerometry variables or caloric intake and abdominal obesity were tested by adding the interaction terms to the regression models. No differences were detected therefore all analyses were collapsed across sex. To assess whether IPA, LPA, MPA, SED, or sleep duration was associated with abdominal obesity the following models were used for each VAT, ASAT, TAAT, and WC: 1) adjusted for time accelerometer worn, 2) adjusted for time accelerometer worn, age, and sex, 3) adjusted for time accelerometer worn, age, sex, and caloric intake. To assess the association between caloric intake and abdominal obesity the following models were used for each VAT, ASAT, TAAT, and WC: 1) unadjusted, 2) adjusted for age and sex, 3) adjusted for age, sex, and MPA. Results for the regression analyses were reported as unstandardized beta (95% confidence intervals).

Participants were then divided into tertiles according to sporadic MPA accumulation to compare VAT. A regression model was used to identify differences between groups after controlling for age and sex. Tertile 1, the group with the lowest accumulation of daily MPA, was used as the referent group.

Significance was set at p < 0.05 for main effects and at p < 0.1 for interaction. These p values along with R^2 values were utilized to determine statistical significance as opposed to examining patterns within the data and effect sizes. Power calculations were based on measures of abdominal obesity (VAT, ASAT, and TAAT). In our sample of 126 participants with daytime activity measures, we estimate that we have 80% power to detect a correlation of 0.25 with an alpha of p < 0.05.
RESULTS

Participant characteristics are shown in Table 5-1. On average, participants wore the accelerometer for 15.8 ± 1.8 daytime hours and approximately 7.3 ± 1.0 hours were spent sleeping. Of the time spent awake, approximately 67% was accumulated as SED, 30% as LPA, and 2% as MPA. None of the participants met the physical activity guidelines of 150 minutes per week of MPA accumulated in bouts of at least 10 consecutive minutes. Women had a lower WC and VAT than men but higher ASAT (p < 0.001). Women also participated in fewer minutes of MPA per day (p < 0.05) and had a lower daily caloric intake (p < 0.001).

As can be seen in Figure 5-1, IPA was not associated with any measure of abdominal obesity (p > 0.1). This was true in both univariate analyses and after control for age and sex (Table 5-2). Likewise, LPA was not associated with abdominal obesity (p > 0.1; Table 5-2). Sporadic MPA was not associated with abdominal obesity in univariate analyses (p > 0.1; Table 5-2) however after control for age and sex, MPA was negatively associated with VAT (p = 0.04), accounting for 3% of the variance in the model. The addition of physical activity intensity did not appreciably change the associations between physical activity duration and abdominal obesity. Associations with abdominal adipose tissue at the L4-L5 slice were the same as those with abdominal adipose tissue volume (data not shown).

Participants were then divided into tertiles based on accumulated sporadic MPA to further examine the association with VAT (Figure 5-2). After control for age and sex,
participants in tertile 3 (mean = 35.1 min/d of MPA or 3.5% of the day) had lower VAT than those in tertile 1 (mean = 6.7 min/d of MPA or 0.7% of the day) \((p < 0.05)\).

Neither SED nor sleep duration was significantly associated with any measure of abdominal obesity in univariate or multivariate analyses \((p > 0.1)\). Caloric intake was positively associated with VAT \((p < 0.001)\) and WC \((p = 0.002)\) but not ASAT or TAAT \((p > 0.05)\). However, after further control for age and sex, caloric intake was not significantly associated with any measure of abdominal obesity \((p > 0.1)\).
## Table 5-1 Participant characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 42)</th>
<th>Women (n = 84)</th>
<th>Total (n = 126)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>54.2 ± 8.6</td>
<td>52.8 ± 7.3</td>
<td>53.3 ± 7.7</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>32.9 ± 3.5</td>
<td>33.1 ± 5.0</td>
<td>33.0 ± 4.5</td>
</tr>
<tr>
<td><strong>Abdominal Obesity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>116.0 ± 8.6</td>
<td>107.8 ± 10.9*</td>
<td>110.5 ± 10.9</td>
</tr>
<tr>
<td>Visceral Adipose Tissue (kg)</td>
<td>5.2 ± 1.6</td>
<td>3.1 ± 1.1*</td>
<td>3.8 ± 1.6</td>
</tr>
<tr>
<td>L4-L5 Visceral Adipose Tissue</td>
<td>230.0 ± 65.5</td>
<td>161.4 ± 61.5*</td>
<td>184.3 ± 70.5</td>
</tr>
<tr>
<td>(cm²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Adipose Tissue (kg)</td>
<td>5.2 ± 1.6</td>
<td>7.1 ± 2.2*</td>
<td>6.5 ± 2.2</td>
</tr>
<tr>
<td>L4-L5 Subcutaneous Adipose Tissue (cm²)</td>
<td>317.9 ± 92.8</td>
<td>405.3 ± 127.2*</td>
<td>376.2 ± 123.7</td>
</tr>
<tr>
<td>Total Adipose Tissue (kg)</td>
<td>10.4 ± 2.5</td>
<td>10.2 ± 2.9</td>
<td>10.3 ± 2.8</td>
</tr>
<tr>
<td>L4-L5 Total Adipose Tissue (cm²)</td>
<td>553.7 ± 127.5</td>
<td>570.4 ± 160.4</td>
<td>564.9 ± 150.0</td>
</tr>
<tr>
<td>Caloric Intake (kcal/day)</td>
<td>2247.4 ± 502.0</td>
<td>1739.2 ± 355.4*</td>
<td>1911.3 ± 474.9</td>
</tr>
<tr>
<td><strong>Activity (Accelerometry)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime Wear (min/d)</td>
<td>970.2 ± 132.0</td>
<td>937.3 ± 87.3</td>
<td>948.2 ± 105.0</td>
</tr>
<tr>
<td>Incidental Physical Activity (min/d)</td>
<td>312.4 ± 135.9</td>
<td>309.1 ± 82.0</td>
<td>310.2 ± 102.6</td>
</tr>
<tr>
<td>Time in Incidental Physical Activity (%)</td>
<td>31.6 ± 9.3</td>
<td>32.9 ± 7.5</td>
<td>32.4 ± 8.1</td>
</tr>
<tr>
<td>Light Physical Activity (min/d)</td>
<td>287.0 ± 121.7</td>
<td>292.2 ± 78.3</td>
<td>290.5 ± 94.5</td>
</tr>
<tr>
<td>Time in Light Physical Activity (%)</td>
<td>29.0 ± 8.3</td>
<td>31.1 ± 7.2</td>
<td>30.4 ± 7.6</td>
</tr>
<tr>
<td>Moderate Physical Activity (min/d)</td>
<td>25.5 ± 19.6</td>
<td>16.9 ± 10.5**</td>
<td>19.7 ± 14.7</td>
</tr>
<tr>
<td>Time in Moderate Physical Activity (%)</td>
<td>2.6 ± 1.7</td>
<td>1.8 ± 1.1</td>
<td>2.0 ± 1.4</td>
</tr>
<tr>
<td>Sedentary Behaviour (min/d)</td>
<td>651.1 ± 84.9</td>
<td>616.1 ± 85.9</td>
<td>627.8 ± 86.9</td>
</tr>
<tr>
<td>Time in Sedentary Behaviour (%)</td>
<td>67.8 ± 9.7</td>
<td>65.8 ± 7.7</td>
<td>66.5 ± 8.4</td>
</tr>
<tr>
<td><strong>Sleep (Accelerometry)†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Wear Time (min/d)</td>
<td>1407.9 ± 124.5</td>
<td>1391.2 ± 84.5</td>
<td>1396.8 ± 99.4</td>
</tr>
<tr>
<td>Sleep Duration (min/n)</td>
<td>424.1 ± 81.8</td>
<td>439.5 ± 61.6</td>
<td>434.9 ± 62.0</td>
</tr>
<tr>
<td>Time Sleeping (%)</td>
<td>30.2 ± 5.4</td>
<td>31.6 ± 4.1</td>
<td>31.1 ± 4.6</td>
</tr>
</tbody>
</table>

Data are means ± SD. Significant difference between sex: *(p < 0.001), **(p < 0.05) †for sleep characteristics n = 37 (men), n = 74 (women), n = 111 (total)
Table 5-2 Regression analyses of physical activity and abdominal obesity

<table>
<thead>
<tr>
<th></th>
<th>Incidental Physical Activity</th>
<th>Light Physical Activity</th>
<th>Moderate Physical Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI)</td>
<td>P</td>
<td>R²</td>
</tr>
<tr>
<td>VAT (kg)</td>
<td>-0.43 (-1.00 to 0.14)</td>
<td>.14</td>
<td>.02</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>-0.34 (-0.79 to 0.12)</td>
<td>.15</td>
<td>.01</td>
</tr>
<tr>
<td>Model 3</td>
<td>-0.32 (-0.79 to 0.14)</td>
<td>.17</td>
<td>.01</td>
</tr>
<tr>
<td>ASAT (kg)</td>
<td>-0.13 (-0.73 to 0.47)</td>
<td>.67</td>
<td>.00</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>-0.24 (-0.78 to 0.30)</td>
<td>.37</td>
<td>.01</td>
</tr>
<tr>
<td>Model 3</td>
<td>-0.22 (-0.76 to 0.32)</td>
<td>.43</td>
<td>.00</td>
</tr>
<tr>
<td>TAAT (kg)</td>
<td>-0.37 (-1.00 to 0.24)</td>
<td>.23</td>
<td>.01</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>-0.39 (-1.00 to -0.22)</td>
<td>.20</td>
<td>.01</td>
</tr>
<tr>
<td>Model 3</td>
<td>-0.36 (-0.98 to 0.25)</td>
<td>.24</td>
<td>.01</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>-5.50 (-20.79 to 9.78)</td>
<td>.48</td>
<td>.00</td>
</tr>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>-5.17 (-19.60 to 9.25)</td>
<td>.48</td>
<td>.00</td>
</tr>
<tr>
<td>Model 3</td>
<td>-4.90 (-19.38 to 9.59)</td>
<td>.51</td>
<td>.00</td>
</tr>
</tbody>
</table>

Model 1: adjusted for time accelerometer worn
Model 2: adjusted for time accelerometer worn, age, and sex
Model 3: adjusted for time accelerometer worn, age, sex, and calories
VAT, visceral adipose tissue; ASAT, abdominal subcutaneous adipose tissue; TAAT, total abdominal adipose tissue; WC, waist circumference; CI, confidence intervals.
Figure 5-1 Associations between incidental physical activity and A) visceral adipose tissue, B) abdominal subcutaneous adipose tissue, C) total abdominal adipose tissue, and D) waist circumference.
Figure 5-2 Tertiles of moderate physical activity and visceral adipose tissue with corresponding participant characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>42</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>M/F</td>
<td>14/28</td>
<td>14/28</td>
<td>14/28</td>
</tr>
<tr>
<td>MPA (min/d)</td>
<td>6.7 ± 2.9</td>
<td>17.4 ± 4.4</td>
<td>35.1 ± 14.5</td>
</tr>
<tr>
<td>MPA (%)</td>
<td>0.7 ± 0.3</td>
<td>2.0 ± 0.5</td>
<td>3.5 ± 1.2</td>
</tr>
<tr>
<td>VAT (kg)</td>
<td>4.1 ± 1.5</td>
<td>4.0 ± 1.9</td>
<td>3.4 ± 1.4</td>
</tr>
<tr>
<td>VAT (cm²)</td>
<td>196.0 ± 66.7</td>
<td>193.3 ± 79.2</td>
<td>163.5 ± 61.3</td>
</tr>
</tbody>
</table>

*Significantly different than tertile 1, p < 0.05.

MPA, moderate physical activity; VAT, visceral adipose tissue.
DISCUSSION

The primary finding of this study was that objectively measured IPA was not significantly associated with abdominal obesity among inactive men and women. Assuming that our 1-week objective measure of physical activity reflects the routine lifestyles of our participants over time, habitual participation in approximately 5 hours of activities of daily living is not sufficient to attenuate the accumulation of abdominal adipose tissue. In other words, IPA is unable to offset even subtle increases in energy intake. Given that most adults fail to meet consensus physical activity guidelines, our results are relevant to a large percentage of the population and thus have important public health implications.

To our knowledge this is the first study to assess the association between objectively measured IPA and the abdominal adipose tissue depots VAT and ASAT. Our results suggest that the association between IPA and abdominal obesity does not occur along a continuum. Conversely, our finding that sporadic MPA but not LPA is associated with VAT implies that this relationship is threshold based and that physical activity may need to be of at least moderate intensity to provide benefit. It is noteworthy however, that the average intensity of the MPA accumulated by participants in this study was equivalent to walking at a comfortable pace (i.e., 5.8 km/h) and importantly, was accrued sporadically - in bouts lasting less than 10 minutes in duration. Therefore participation in physical activity of this nature would not impose time constraints or be perceived as exceptionally daunting or difficult to inactive individuals attempting to engage in physical activity to decrease health risk.
That sporadic MPA was negatively associated with VAT extends the results of a previous study indicating that accumulating moderate-to-vigorous physical activity in bouts lasting less than 10 consecutive minutes was independently associated with a lower WC in adults. In our study, sporadic MPA was not a significant predictor of WC however it was negatively associated with VAT. This novel observation highlights the limitations of WC to detect variation in VAT between individuals with similar WC and demonstrates the value of obtaining measures of body composition with radiographic imaging.

We did not find SED to be a significant predictor of abdominal obesity. This is consistent with some but not all previous research examining the association between objectively measured SED and WC. There is no clear difference in participant characteristics that might explain the discrepant findings. However, differences may be explained in part by measurement limitations of the accelerometer. Accelerometers are unable to detect variations in SED due to fidgeting and cannot differentiate between sitting, lying down, and standing still. Additionally, it has been demonstrated that there are differences between Actigraph models in their ability to detect acceleration at the low end of the movement spectrum. Thus, it is possible that the association between SED and abdominal obesity differs between studies due to limitations inherent to the accelerometer and/or the use of different Actigraph models.

We did not find sleep duration to be a significant predictor of abdominal obesity in our sample. Although some previous research has reported a significant inverse association between sleep duration and WC, others have not corroborated this
finding. It is plausible that sleep duration may not be a major contributing factor to variability in abdominal adipose tissue depots among individuals who are all abdominally obese. Indeed, it is noteworthy that in our sample, the average sleep duration was over 7 hours – a duration that is generally not thought to be associated with poor health outcomes.

Although we report that caloric intake is associated with WC and VAT in univariate analysis, this association did not remain independent of age and sex. Within the literature there is conflicting evidence describing the association between caloric intake and WC. Methodological limitations of self-reported food intake, such as the under-reporting of energy intake, are likely to account for at least some of the differences between studies.

The current study was cross-sectional and conducted in a sample relatively homogenous in terms of abdominal obesity and physical activity levels. However, given that a large percentage of the North American population is both abdominally obese and does not meet consensus physical activity recommendations, our results are relevant to a large proportion of the general population.

In summary, in this sample of inactive men and women, incidental physical activity was not associated with abdominal adipose tissue. However, sporadically accrued moderate physical activity was a significant marker of visceral adipose tissue.
Chapter 6
General Discussion

6.1 How have we contributed?

While there is substantial literature describing the health benefits of accumulating physical activity in a manner consistent with consensus physical activity recommendations (i.e., participating in 150 min/wk of physical activity that is at least moderate intensity and accumulated in bouts of at least 10 consecutive minutes in duration), relatively little is known about the activities that occur throughout the day that are of an intensity and duration not considered in the physical activity recommendations. However, advances in physical activity/inactivity measurement tools have allowed us the opportunity to more precisely capture activity throughout the 24-hour period and we are beginning to understand how activities across the movement continuum impact health. In this thesis we contribute to the discussion involving the relationships of daily physical activity and SED accumulated in a manner inconsistent with the consensus guidelines and health outcomes in an inactive, abdominally obese sample of men and women.

One of the most remarkable findings in this thesis was the marked heterogeneity of physical activity and SED patterns in this sample of participants labeled as ‘sedentary’ or ‘inactive’. Although none of the participants included in the analyses met the consensus physical activity guidelines, participation in sporadic MPA ranged from 2 to
80 min/d (mean = 19.2 ± 13.5) and LPA ranged from 136 to 864 min/d (mean = 289.0 ± 91.7). Even in those participants at the lowest end of the physical activity spectrum, approximately 2.5 hours of IPA (the sum of LPA and MPA) was accumulated in an average day. This is indeed a remarkable amount of daily physical activity. Moreover, it is likely that we have underestimated physical activity accumulation in our sample because the cutpoints used in the studies presented were derived from a young, lean population. Participants also accumulated a large amount of SED (mean = 627.2 ± 82.9 min/d) and again, the total amount accrued over the average day varied substantially between participants (range = 412 min/d). However, I have no doubt that most individuals, irrespective of phenotype and including those who incorporate 30 or more minutes of bouted MVPA into their day, would also accumulate a similar amount of SED. Thus, the ‘sedentary’ and ‘inactive’ labels often applied to the sample examined in this thesis are somewhat misleading.

It is quite common in research to dichotomize individuals as either active (i.e., meeting the consensus guidelines) or inactive (i.e., failing to meet consensus guidelines) and compare health outcomes between these two groups. However, as we have shown in studies #1 through 3, this is problematic as health risk varies significantly among individuals classified as inactive due in part to differences in physical activity. Thus, one of the key points to be taken from this thesis is that the benefits of physical activity occur along a continuum - a continuum that could be defined in terms of either physical activity intensity or physical activity duration. Further, the benefits may start to accrue at a very low level and/or intensity of physical activity.
We also recognize that within this thesis, when considered in light of the many factors that influence or contribute to the relationships between physical activity and SED with obesity and the associated health complications, we were only looking at a small component of a large and intricate web such as that outlined by Kumaniyika 188. With the exception of study #3 where we included a measure of caloric intake, we only examined factors contributing directly to energy expenditure or energy output. It is possible that some of the many other factors previously shown to impact the relationships considered within the three studies, including but not limited to genetics, stress levels, and the home or built environment, may explain some of the unknown variance in the regression models used. Further, acknowledgement of the many other contributors to obesity and related complications may help to rationalize why physical activity only explains a relatively small proportion of variance within the regression models.

6.2 Reconciling Disparities and Addressing Limitations

As was noted within the individual studies in chapters 3 through 5, our findings were at times inconsistent with some previous literature. Reasons for the disparities are indicated in the respective chapters and therefore will not be repeated here. However, it is also important to acknowledge that within populations or samples, normal variation exists. Previous studies have shown that the response (CRF) to a given stimulus (physical activity) varies from almost no change to a 100% change. Thus, it is very likely that a given amount of IPA or MPA will affect health outcomes differently in different
individuals. This may be particularly relevant to our sample as our inclusion criteria were quite stringent, specifying that participants must be inactive, abdominally obese men and women between the ages of 35 to 69 who were located in Kingston, Canada and did not smoke. Further, the population of Kingston is primarily Caucasian and this was reflected in our participants. Thus, in terms of the characteristics listed above, our sample was relatively homogeneous and it is possible that for this reason, our results differed from those of Healy et al. 12, 13 who examined similar associations in a sample representative of Australia. As was previously mentioned however, the sample examined in this thesis represents a group that is highly prevalent in Canada and at substantial health risk. Thus, it is important to refine our understanding of the relationships between physical activity/inactivity, obesity, and the associated health complications in this particular population.

Lastly, the sample utilized in the present thesis was a convenience sample recruited to participate in a 6-month randomized controlled trial examining the effects of exercise dose and intensity on the reduction of 2-hour glucose and other cardiometabolic risk factors. Although participation in the trial did not influence the results in this thesis per se, individuals drawn to commit to a 6-month trial may possess characteristics that are not representative of the Kingston community as a whole (e.g., motivational characteristics).
6.3 What is our Public Health Message?

Results from study #1 support the first key guideline for adults outlined in the 2008 *Physical Activity Guidelines for Americans*, which states that *some physical activity is better than none*, and adults who participate in any amount of physical activity gain *some health benefit* \(^{78}\). Conversely, studies #2 and 3 suggest that there is an intensity threshold that must be reached to experience benefit. More specifically, MPA is more strongly associated with various health outcomes than LPA. However, as was mentioned within the individual studies, it is important to point out that on average, the physical activity accumulated was at an intensity comparable to a comfortable walking pace and was sporadic in nature. For those individuals who do not habitually participate in substantial physical activity, who are constrained by time or who find bouted, higher intensity physical activity daunting or too difficult, this is indeed a positive concept to reinforce. A prescription of lower intensity and/or sporadic physical activity may be one that improves adoption and adherence rates as it is easier to incorporate into daily routines, does not require knowledge of exercise or gym routines, and does not necessitate exceptional co-ordination or motor skills associated with sporting activities or gym-based routines. Of note, the newly released Canadian guidelines for adults \(^{10}\) focus solely on participation of 150 min/wk in bouted moderate and vigorous physical activity and do not mention the importance of accumulating physical activity throughout the day. This is unfortunate as these guidelines may not seem achievable to some and may deter inactive individuals from incorporating physical activity into their day.
With respect to SED, it is difficult to derive a clear public health message from our results given that we did not find SED to be a significant predictor of any cardiometabolic risk factor. However, we did find a strong inverse relationship between SED and IPA \((r = -0.82)\), suggesting that SED may displace time that could be spent in IPA. Thus, if individuals were encouraged to decrease SED, and thereby increase IPA, (especially that of moderate intensity) positive health benefits may ensue.

A principle message from the findings of this thesis is that individuals should be encouraged to increase participation in IPA of all intensities for health benefit however, for more substantial health benefit the accumulation of physical activity that is of at least moderate intensity should be recommended.

### 6.4 Objective Measurement of Physical Activity – What Next?

Technological advances in physical activity measurement devices are being made at a phenomenal rate. Numerous additions are being added to the devices currently being used to improve our ability to correctly identify activity across the movement continuum and provide context or meaning to the acquired data. For example, inclinometers are being incorporated into accelerometers to overcome limitations associated with capturing activity at the lower end of the movement continuum and global positioning systems are able to provide environmental context to physical activity participation. Thus, I have no doubt that our ability to acquire both
physical activity and SED will improve drastically in the upcoming years and will allow us to refine our understanding of how these behaviours impact health.

Availability of various physical activity measurement devices outside of the research setting has also increased drastically in recent years (e.g., Garmin) and similarly to the research tools, the complexity of these products has also increased. For example, the Forerunner® 310XT can track distance, pace, and heart rate in multiple sports modes (land, bike, and swimming) and send this information wirelessly to a home computer. It can also be used to track body weight, body fat, body water, and various other indicators of body composition. Thus, the technology currently available allows interested individuals to track physical activity patterns (and limited changes in health outcomes) very closely. Given that self-monitoring is a critical behavioural component to lifestyle change \(^{189}\) and that technology-based monitoring systems are successful in aiding positive behaviour change for at least a 6-month period \(^{190}\), technology has the potential to aid tech-savvy individuals in their attempt to make lifestyle changes.

6.5 Future Research Directions

In the broad field of physical activity, SED and health, we have barely scratched the surface in terms of our understanding of how and why certain factors are related or not and what causes the relationships. Thus, there are a limitless number of research questions yet to be answered. Given the heightened interested in SED and LPA, this will be a ripe area of research in upcoming years. A few potential research questions
include: What is the effect of an increase in incidental physical activity on cardiometabolic risk factors in an inactive population? Does the implementation of an intervention of light intensity and/or sporadic moderate physical activity improve adherence rates compared to a traditional intervention prescribing bouted MVPA? What is the effect of decreasing SED, by for example incorporating standing work stations in offices, on health outcomes?
Chapter 7
Summary and Conclusions

While it is well-established that individuals who meet consensus physical activity guidelines experience a reduced risk of mortality and many chronic health conditions compared to individuals who do not meet physical activity guidelines, the results from this thesis, along with many recent publications highlight the importance of considering the effects of physical activity (that which is accumulated below the recommended guidelines), SED, and sleep patterns on health risk. Although our results do not support the belief that SED is associated with increased health risk, our findings do support the concept of an active lifestyle; that all physical activity is associated with health benefit. This notion is especially relevant to the sample examined within the present thesis as it provides more options to those inactive individuals interested in beginning a lifestyle change program to decrease health risk. Importantly, these options will likely be more favourable than the traditional higher intensity, structured exercise interventions as they can be more easily incorporated into daily routines (eliminating time barriers), do not require specific knowledge of exercise or sport (eliminating knowledge barriers), and are not associated with substantial cost (eliminating financial barriers). The next step will be motivating these individuals to make and maintain the positive changes and experience the health benefits.
References


96. Dunn AL, Marcus BH, Kampert JB, Garcia ME, Kohl HW 3rd, Blair SN. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. *JAMA* 1999; 281: 327-334.


147. Taheri S. The link between short sleep duration and obesity: we should recommend more sleep to prevent obesity. Arch Dis Child 2006; 91: 881-884.


172. Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA* 2007; **297**: 2081-2091.


133


Appendix A
Consent Form

CONSENT TO VOLUNTEER FOR PARTICIPATION IN A STUDY

TITLE: Dose-response effects of exercise on abdominal obesity and risk factors for cardiovascular disease in women and men

PRINCIPAL INVESTIGATOR:

Robert M.J. Ross, Ph.D.
Queen’s University
School of Kinesiology and Health Studies/ Medicine, Division of Endocrinology and Metabolism
Kingston, Ontario, K7L 3N6
(613) 533-6583

CO-INVESTIGATORS:

Robert Hudson, M.D., Ph.D., FRCPC
Kingston General Hospital
Medicine, Division of Endocrinology and Metabolism
Kingston, Ontario, K7L 3N6
(613) 533-2973

Miu Lam, Ph.D.
Queen’s University
Department of Community Health and Epidemiology
Kingston, Ontario, K7L 3N6
You are invited to participate in a research study on the influence of different doses (amounts) of exercise on abdominal fat and related health risk. The following brief is intended to provide you with the details you should be aware of prior to your consent as a participant in this study. Please read the following information carefully and feel free to ask any question that you may have.

BACKGROUND INFORMATION

Obesity is a major risk factor for disease and a public health problem. Recent information suggests that body fat located in the upper body region (abdominal fat) conveys a very strong health risk. Exercise is thought to be a good treatment option for reducing both abdominal fat and cardiovascular risk factors (e.g., blood fats (cholesterol), blood sugar and blood pressure). However, the specific exercise strategy or program required to achieve optimal benefit continues to be the source of considerable debate. At present, health professionals are unsure of the specific type, amount, pattern, and intensity of exercise that provides optimal health benefits. Therefore, you are invited to participate in a study to assess the relationships between exercise dose (how much) and intensity (how hard) on abdominal fat, and cardiovascular risk factors (e.g., blood sugar and fats). The results of the study may have important implications for development of public health messages and clinical guidelines for prevention and treatment of obesity and associated health risks through exercise.

EXPLANATION OF PROCEDURES

Pre-participation screening
You will be required to complete a medical questionnaire and make an appointment with your family physician prior to participation in this study. Your physician will also complete a medical questionnaire and may perform a medical examination on you. If your family physician charges you for completion of this exam, an invoice can be faxed to the Project Coordinator 613-533-2580 for payment or, the study investigators will reimburse you fully. In addition to the medical exam, you will have a fasting blood test to
measure your blood fat and sugar levels. We will also measure your waist circumference. These measures are explained in further detail on pages four (4) and five (5) of this form.

**Study Protocol**

The exercise study will be approximately 7 months in duration. The 6-month exercise period will begin and end with a 1 to 2 week weight maintenance period. By volunteering to participate in this study, your name will be selected by chance and placed into one of the following four groups: (1) Control - no exercise, (2) Low volume-Low intensity exercise, (3) High volume- Low intensity exercise, (4) Low volume-High intensity exercise. You will have a 1 in 4 chance of being placed in one of the four study groups. You will not be able to choose which group you will be in.

The follow-up study will take place during Months 7-13. During this part of the study, you will be asked to continue the same exercise routine that you followed for the first six months. The reason for the 6-month follow-up is to find out whether you have been able to maintain the exercise level prescribed at start of the study.

**Expectations**

You will be expected to:

1. Accept your group assignment
2. Participate fully in your assigned groups for the duration of the study
3. Keep all testing appointments
4. Provide accurate answers on all questionnaires

You can expect:

1. Full disclosure of all procedures required for participation in this study
2. To be treated fairly and with respect
3. Any information that is disclosed will be private and confidential
4. No one will be coerced or forced to do anything they wish not to do
5. To have all your questions answered fully and as promptly as possible
6. To not be penalized for choosing to withdraw from the study for any reason

**Control Group:** For the entire study the men and women in this group will consume a healthful diet. Thus there will be no weight loss or exercise.
**Low volume-Low intensity group:** As a participant in this exercise group you will be asked to perform walking type exercise on a motorized treadmill for around 30 minutes, 5 times per week, at about 50% of your maximum fitness level (e.g., low-to-moderate paced walking) for the duration of the 6 month treatment period. During each exercise session we will measure your heart rate every 5 minutes using an automated heart rate monitor. All of your exercise sessions will be by appointment and performed under supervision of a trained professional within our laboratory at Queen’s.

**High volume-Low intensity group:** As a participant in the aerobic exercise group you will be asked to perform walking type exercise on a motorized treadmill for around 60 minutes, 5 times per week, at about 50% of your cardiovascular fitness level (e.g., low-to-moderate paced walking) for the duration of the 6 month treatment period. During each exercise session we will measure your heart rate every 5 minutes using an automated heart rate monitor. All of your exercise sessions will be by appointment and performed under supervision within our laboratory at Queen’s.

**Low volume-High intensity group:** As a participant in the aerobic exercise group you will be asked to perform walking and/or jogging type exercise on a motorized treadmill for around 30 minutes, 5 times per week, at about 75% of your cardiovascular fitness level (e.g., brisk walking) for the duration of the 6 month treatment period. During each exercise session we will measure your heart rate every 5 minutes using an automated heart rate monitor. All of your exercise sessions will be by appointment and performed under supervision within our laboratory at Queen’s.

**Diet Program:** All participants in each group will eat the same type of foods. The diet will consist of regular foods that you will buy and prepare yourself. All aspects of the diet plan will be explained to you by a nutritionist. The session will take place at the beginning of the study, with several additional sessions planned throughout to help you follow the diet plan. If someone else shops for your food or prepares your meals, or if you share those tasks with someone else that person is invited to meet with the
nutritionist as well. You will be required to record the food you eat each day for the duration of the study. All of your meetings with the nutritionist will be in Dr. Ross’s laboratory within the School of Kinesiology & Health Studies at Queen’s.

At the beginning of the study, using the diet records that you complete, the number of calories required to maintain your body weight will be determined. During the study the nutritionist will work with you to help you to maintain this caloric (number of calories) intake. In other words, the nutritionist will help you eat an amount of food that would normally maintain your body weight. Thus any weight loss you experience will be the result of an increase in exercise.

**Magnetic Resonance Imaging**

Magnetic resonance imaging (MRI) is a method for creating pictures of body structures or organs. MRI gives pictures (images) in slices comparable to those produced by x-ray tomography (e.g., CT scan). One of the primary advantages of MRI is that it does not use x-rays or other forms of radiation. Instead, a large magnet, a radio transmitter/receiver and a computer are used to gather information from the body, and to produce pictures of internal anatomy. No harmful effects have been associated with MRI under existing conditions of use. However, if you feel claustrophobic during the scan you can end the test immediately.

As mentioned, the MRI procedure is very similar to a scanner examination. You will be placed on a table and moved smoothly into the scanner. A loud-speaker within the magnet makes it possible for you to keep in constant contact with the staff. At all times the operator can see and hear you and if you need help or have questions, you can be removed from the machine if necessary. The whole procedure takes about 30 minutes and will be performed by appointment at Kingston General Hospital once at the beginning of the study and one at the end of the exercise study (week 24).

**Anthropometry (Skinfolds and Circumferences)**

Many circumference measurements will be taken at numerous places on your body. These measurements can be used to derive estimates of body composition. Skinfold callipers (skinfold thickness) will be measured at 4 different places on your body.
Circumferences measurements using a measuring tape will also be obtained at different places on the body. These measurements require about 45 minutes to complete and will be obtained at Dr. Ross’s laboratory within the School of Kinesiology & Health Studies at Queen’s.

We will collect these measurements five times throughout the study: at the beginning (week 0), then after two months (week 8), four months (week 16), at the end of the exercise training period (week 24), and at follow-up (week 48, six months after the end of the exercise training period).

**Assessment of Cardiovascular Fitness**

We will measure your cardiovascular fitness (endurance) using a treadmill (VO₂) test. The test will begin at a level you can easily accomplish and will be advanced in stages, depending on your capacity to do so. We may stop the test at any time because of signs of fatigue or you may stop the test because of personal feelings of fatigue or discomfort.

The treadmill test involves risks comparable to any strenuous exercise situation. They include very rare instances of abnormal blood pressure, fainting, disorders of the heartbeat, and heart attack. Every effort will be made to minimize your risk by preliminary medical examination and observation during the test. A Research Assistant at Hotel Dieu Hospital, with a trained paramedic or medical doctor on-site, will conduct your fitness test. You will perform the exercise test 6 times: at the beginning (Week 0), after one month (week 4), after two months (week 8), after four months (week 16), at the end of the exercise training period (week 24), and at follow-up (week 48, six months after the end of the exercise training period).

**Assessment of Daily Physical Activity**

How physically active you are throughout the day will be measured by two small devices known as accelerometers: one is worn on your arm (armband) and one is worn on your hip (Actigraph). The armband involves wearing a monitor that is worn on your upper right arm that will track the amount of energy you burn and the amount of physical activity that you perform. The Actigraph is a small unit that you wear on your belt at the
level of your hip and this device also measures the amount of physical activity that you perform. You will wear these monitors during all of your waking hours and will remove the monitor when you sleep or participate in water activities such as showering, bathing, or swimming. You will wear this device for 7 consecutive days at 0, 8, 16, and 24 weeks.

**Laboratory measurements (blood glucose (sugar) and lipid (fat) tests)**

The measurement of how much sugar and fat are in your blood will be done at Dr. Ross’s laboratory within the School of Kinesiology & Health Studies at Queen’s. To determine your ability to manage blood sugar you will be asked to perform an Oral Glucose Tolerance Test. You will be asked to arrive at the lab in the morning after an overnight fast (no eating after 7pm the night before). The first step of this test will be the insertion of a saline lock into a vein in your arm. This allows the nurse to take blood at different times without having to re-puncture each time. She will then remove about 30 ml (3 tablespoons) of blood. The only risk from this procedure is possible local pain and bruising at the time of the blood test. In addition, you will be asked to drink a fluid that contains 75 grams of sugar (like an orange drink). At 30-minute intervals for 2 hours after drinking the sugar solution, a small amount of blood will be taken (through the saline lock) for the purpose of measuring the amount of sugar in the blood. This test will be performed four times during the study: at week 0, after four months (week 16), at the end of the exercise period (week 24) and at the end of the follow-up (week 48).

**Summary of Appointments and Time Requirements**

All appointments will be scheduled at a time that is convenient for you. For the testing you will be required to make six 45-minute appointments at the Hotel Dieu Hospital to complete the cardiovascular fitness (VO2 max). We will also arrange two 30-minute appointments to complete the MRI (Kingston General Hospital). The other testing will be done at Dr. Ross’s laboratory in the School of Kinesiology & Health Studies at Queen’s. This includes: four 2.5-hour appointments for the oral glucose tolerance test and blood lipid/cholesterol tests (fasting blood draw); and five 45-minute anthropometric measurement appointments. In addition, we will ask you to make
appointments for dietary counselling and for exercise (if you are randomized into one of the exercise groups). The total time commitment for all testing appointments and exercise sessions over the total 13-month study will be between 86 and 149 hours.

### Time commitment per participant

<table>
<thead>
<tr>
<th>Measure/Task</th>
<th>Time per session</th>
<th>Number of sessions</th>
<th>Total time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometrics</td>
<td>1 hr</td>
<td>5</td>
<td>5 hr</td>
</tr>
<tr>
<td>Fitness (VO$_2$) test</td>
<td>1 hr</td>
<td>6</td>
<td>6 hr</td>
</tr>
<tr>
<td>OGTT</td>
<td>2.5 hr</td>
<td>4</td>
<td>10 hr</td>
</tr>
<tr>
<td>MRI</td>
<td>0.75 hr</td>
<td>2</td>
<td>1.5 hr</td>
</tr>
<tr>
<td>Dietary Counsel</td>
<td>0.5-1 hr</td>
<td>6-12</td>
<td>3-6 hr</td>
</tr>
<tr>
<td>Exercise</td>
<td>0.5-1 hr</td>
<td>120</td>
<td>60-120 hr</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
<td><strong>86-149 hours</strong></td>
</tr>
</tbody>
</table>

### Benefits of Participation

You will gain no direct benefit through participation in this study.

### Risks of Participation

Participation may involve some risks. The known risks are:

1) Insertion of a catheter in your arm or hand vein may cause bruising, bleeding, soreness or infection.

2) For MRI, there are certain conditions that would exclude you from participating in this study. These include cardiac pacer, aneurysm clip, cochlear implant, intra-uterine device (IUD), shrapnel, neurostimulators or other metal devices. Metal objects present in the body could be moved by the large magnet involved in the MRI, and such movement could cause serious injury. Fear of closed spaces (claustrophobia) is also a reason you would be excluded from the study. No serious biological effects have been reported from being in a magnet. If you experience a fear of the confined space while in the magnet, you can terminate the study. Trained personnel are always in attendance during these studies.

3) The exercise test may cause muscle soreness or fatigue. In any individual, there is a minute risk of a heart attack or death from the exercise test. A trained
paramedic or medical doctor will be on-site. If you develop chest pain, the test will be stopped immediately.

4) **Risk of Wearing the Activity Monitor:** Some people may experience mild skin irritation at the site where the activity monitor is worn. One cause of skin irritation has already been identified in people who wear the armband for extensive periods of time (i.e., more than 24 hours). Specifically, the build-up of sweat that can be trapped between the skin and the armband can cause pink pustules or pimples to appear. This condition is named miliaria, or prickly heat. This condition is common and occurs in 10% to 25% of people (10 to 25 out of 100 people) that wear the armband. To help to prevent this condition you should clean your arm using rubbing alcohol before putting on the activity monitor. Also, you should use soap and water to clean the elastic strap that attaches the monitor to your arm before each use. You should also wipe off the monitor using rubbing alcohol and allow this to dry before putting it on your arm.

You should inform the investigators if you have participated in any other research study during the previous year. This will help to ensure that you have not been exposed to a procedure in another study that may influence your ability or eligibility to participate in this one. You should understand that this study is a research study and may not be of direct benefit to you. If requested, a report will be generated for your medical record, which will include any information important for your medical care.

**CONFIDENTIALITY**

All information obtained during the course of this study is strictly confidential and your anonymity will be protected at all times. Your information will be kept in locked files and will be available only to Dr. Robert Ross and those working within his laboratory. Your identity will not be revealed in any description or publication.

In the event you that you are injured as a result of the study procedures, medical care will be provided to you until resolution of the medical problem. By signing this consent form, you do not waive your legal rights nor release the investigator(s) and sponsors from their legal and professional responsibilities.

Financial remuneration ($100) for parking, gas, and other costs associated with participation in the study will be provided to you.
VOLUNTARY CONSENT

I have been given an opportunity to ask any questions concerning the procedures. All of my questions regarding the research project have been satisfactorily answered. I understand that my test results are considered confidential and will never be released in a form that is traceable to me, with the exception of my family physician or myself. I understand that all my lab results will be sent to my family physician. I do understand that I am free to deny consent if I so desire, and may withdraw from the study at any time without prejudicing current or future medical care.

Should I have any questions about the study, I know that I can contact any of the following: Dr. Robert Ross (613 533-6583), Dr. Jean Coté, Head, School of Kinesiology and Health Studies (613 533-6601), or Dr. Albert Clark, Chair, Queen’s Health Sciences & Affiliated Teaching Hospitals Research Ethics Board (613 533-6081). A copy of this consent form will be provided me for my records. My signature below means that I freely agreed to participate in this study.

_________________________  ____________________
Volunteer’s Signature         Date:

STATEMENT OF INVESTIGATOR

I, or one of my colleagues, have carefully explained to the subject the nature of the above research study. I certify that, to the best of my knowledge, the subject understands clearly the nature of the study and demands, benefits, and risks involved to participants in this study.

_________________________  ____________________
Principal Investigator’s Signature  Date
Appendix B
Medical Questionnaire

School of Kinesiology and Health Studies

MEDICAL QUESTIONNAIRE FOR RESEARCH STUDY

DOSE-RESPONSE EFFECTS OF EXERCISE ON ABDOMINAL OBESITY AND RISK FACTORS FOR CARDIOVASCULAR DISEASE IN WOMEN AND MEN

To the study participant: Please answer all questions in sections 1 and 2 of this form. Have your family doctor fill out section 3.

To the physician: Please fill out section 3 of this form (pages 4-6). Completing this form may not require a medical re-evaluation of your patient. If the results of recent tests are readily available that might prove useful to study personnel while dealing with the participant, please include that information in this questionnaire.

Please return sections 1 to 3 to the Project Manager via fax at (613)533-2580 along with an invoice for any costs associated with completing the form.
SECTION 1: PERSONAL DATA (please print)

Name: ________________________________

Date of Birth: ________________________

Date: ________________________________

SECTION 2: MEDICAL HISTORY

A. Has your doctor ever said you have heart trouble?  ____  ____

B. Do you get pains, pressure or tightness in your chest?  ____  ____

C. Do you often feel faint or experience dizziness?  ____  ____

D. Has your doctor ever told you that you have high blood pressure?  ____  ____

E. Is there a good reason, not mentioned above, why you should avoid exercise?  ____  ____

F. Have you ever had blood taken? ________________________________

G. Have you ever had any negative experiences with a blood draw?
   If yes, please describe:
   ____________________________________________________________
   ____________________________________________________________

H. Do you have any allergies (i.e. latex, medications, etc)?
   ____________________________________________________________
   ____________________________________________________________

I. Do you have diabetes?  YES □  NO □
If yes, please indicate:

Type I Diabetes ☐  Type II Diabetes ☐  Unsure ☐
(Also known as Adult Onset)
☐ Diet Controlled  ☐ Oral Diabetic Medication  ☐ Insulin Required

J. Do you have, or have you ever had, problems with any of the following?

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. Heart or blood vessels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ii. Nerves or brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iii. Breathing or lungs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iv. Hormones, thyroid, or diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>v. Muscles, joints, or bones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vi. Other (please list)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

K. Please list any serious injuries suffered, or surgeries you have had.

____________________________________________________________________
____________________________________________________________________

L. If you have had surgery, was any metal (e.g., pins or screws) left in your body?

____________________________________________________________________
____________________________________________________________________

M. Are you presently taking any medications? If yes, please list.

____________________________________________________________________
____________________________________________________________________

N. Are you presently undergoing physiotherapy, or any other sort of treatment? If yes, please list.

____________________________________________________________________
I hereby authorize my family physician to complete Section 3 of this medical questionnaire and to fax or send to the SERENA exercise study researchers at Queen’s University.

Signature   Witness

SECTION 3: MEDICAL REFERRAL

Physician: The applicant is considering participation in a research study that is investigating the effects of exercise dose (amount) on abdominal obesity and related cardiovascular disease risk factors. A brief summary of the study objectives is provided (see pages 8-10). As a participant in this study, your patient would undergo a cardiorespiratory fitness appraisal (see explanation on page 7) and a number of other tests to assess body composition and metabolic health risk. We will forward any test results to you with your patient’s consent.

Should you have any questions regarding the participation of your patient in this project, please contact Robert Ross Ph.D., School of Kinesiology and Health Studies, Queen’s University (613-533-6583). Please return completed sections 1 to 3 to the Project Manager via fax at (613-533-2580) along with an invoice for any costs associated with completing this form.

1. Review of Systems - please include diagnoses.
   a) Cardiovascular
   b) Respiratory
   c) Neurological
   d) Gastrointestinal
   e) Genitourinary
   f) Endocrine
   g) Musculoskeletal

149
h) Skin

i) Gynecological

II. Physical Examination

Blood Pressure: _____________  Pulse: _______________
Cardiovascular: __________________________________________
Respiratory: _______________________________________________
Head and Neck _____________________________________________
MSK: _____________________________________________________
Abdomen: ___________________________________________________
12-lead ECG (not mandatory): ________________________________
Neurological: _______________________________________________

III. Laboratory findings (not mandatory)  Date of Test(s): ________________
Hb ____________  WBC ____________  Plts ____________
Total Cholesterol ___________  HDL ___________  Chol:HDL ratio __________
LDL _____________  Triglycerides ____________  Uric Acid _____________
TSH _____________  Glucose _____________ fasting ☐  random ☐
75 g OGTT @ 120 min _______________

IV. Additional abnormalities of which you are aware

_________________________________________________________________
_________________________________________________________________

V. Current medications and doses

_________________________________________________________________
_________________________________________________________________
VI. On the basis of your knowledge and medical evaluation of the applicant, you would recommend (mark the appropriate answer):

_____ Participation in a fitness appraisal supervised by a physical education graduate, or
_____ Participation in a fitness appraisal only when a physician or paramedic is present, or
_____ Participation in a fitness appraisal is not recommended

Note: An explanation of the fitness appraisal protocol, as well as absolute and relative contraindications to exercise testing, is provided on page 7 of this form.

Physician’s Name: _________________________________________
Physician’s Signature: _________________________________________
Date: ____________________________
Phone Number: ____________________________
Address: _________________________________________
                                   _________________________________________
                                   _________________________________________
                                   _________________________________________

Thank you very much for your help. We hope that this study and its results will be beneficial to you and your patient.
Appraisal of Cardiorespiratory Fitness (VO$_2$max)

Cardiorespiratory fitness is assessed using a maximal oxygen uptake (VO$_2$max) test, which is routinely employed within the laboratory of the study investigators. The treadmill test begins at a level the study participant can easily accomplish (comfortable walking pace with no incline) and is slowly increased in intensity (by increasing treadmill incline) until the participant reaches volitional fatigue. We may stop the test at any time because of signs of fatigue or the subject may stop the test because of personal feelings of fatigue or discomfort.

The maximal oxygen uptake test involves risks comparable to very strenuous aerobic exercise. Every effort is made to minimize the risk by preliminary medical examination and close observation during the test by physical education graduate students and a physician.

American College of Sports Medicine Contraindications to Exercise Testing

Absolute Contraindications

A recent change in the resting ECG suggesting infarction or other acute cardiac events
Recent complicated myocardial infarction
Unstable angina
Uncontrolled ventricular dysrhythmia
Uncontrolled atrial dysrhythmia that compromises cardiac function
Third-degree A-V block
Acute congestive heart failure
Severe aortic stenosis
Suspected or know dissecting aneurysm
Active or suspected myocarditis or pericarditis
Thrombophlebitis or intracardiac thrombi
Recent systemic or pulmonary embolus
Acute infection
Significant emotion distress (psychosis)

Relative Contraindications

Resting diastolic blood pressure $>120$ mm Hg or systolic blood pressure $>200$ mm Hg.
Moderate valvular heart disease
Known electrolyte abnormalities (hypokalemia, hypomagnesemia)
Fixed-rate pacemaker (rarely used)
Frequent of complex ventricular ectopy
Ventricular aneurysm
Cardiomyopathy, including hypertrophic cardiomyopathy
Uncontrolled metabolic disease (e.g., diabetes, thyrotoxicosis, or myxoedema)
Chronic infectious disease (e.g., mononucleosis, hepatitis, AIDS)
Neuromuscular, musculoskeletal, or rheumatoid disorders that are exacerbated by exercise
Advanced or complicated pregnancy
STUDY DETAILS

Hypothesis or Aim

Current knowledge does not provide an understanding of the separate effects of dose and intensity of exercise on abdominal obesity and related cardiovascular risk factors. This represents a major gap in knowledge with implications for the development of public health messages and clinical guidelines as recognized by leading health authorities. We will randomize abdominally obese men and women at increased health risk to one of the following 4 conditions:
1) No-exercise, wait list controls (C),
2) Low volume, low intensity exercise (LVLI),
3) High volume, low intensity exercise (HVLI),
4) Low volume, high intensity exercise (LVHI).

The primary aim of the trial is to determine the effects of varying exercise dose (energy expenditure, kcal) or intensity (relative to VO$_2$ max) on waist circumference and glucose tolerance. We will test the following hypotheses:
1) That the reduction in waist circumference and improvement in glucose tolerance in response to all treatments will be greater than controls.
2) That reduction in waist circumference and improvement in glucose tolerance in HVLI and LVHI will be greater than LVLI.
3) That hypotheses 1 and 2 are true independent of gender.

The secondary aim is to distinguish between varying exercise dose (energy expenditure, kcal) or intensity (relative to VO$_2$ max) on abdominal subcutaneous fat, visceral fat and insulin resistance. The driving hypothesis is that the attenuation of health risk with exercise is largely explained by associated reductions in abdominal obesity, in particular visceral fat. Specifically, we will test the following hypotheses:
1) That by comparison to controls, all treatments will be associated with reduction in abdominal subcutaneous, visceral fat, liver fat and insulin resistance.
2) That reduction in abdominal subcutaneous, visceral and liver fat and insulin resistance in HVLI and LVHI will be greater than LVLI.
3) That hypotheses 1 and 2 are true independent of gender.

Summary of Study Protocol

We will perform a randomized, controlled trial designed to study the separate effects of habitual exercise differing in dose (energy expenditure, kcal/session) and intensity (relative to VO$_2$ max) on abdominal obesity and glucose tolerance. We will recruit, assess and randomly assign 320 sedentary, abdominally obese men (N=160) and women (N=160) at increased health risk to one of the following 4 conditions: 1) No-exercise, wait list control (C), 2) Low volume, low intensity exercise (LVLI), 3) High volume, low intensity exercise (HVLI), 4) Low volume, high intensity (LVHI). All exercise
sessions regardless of group assignment will be performed within the laboratory of the principal applicant and will be supervised by trained exercise specialists. Each exercise session will be strictly controlled for both dose and intensity using continuous monitoring of heart rate combined with knowledge of individual oxygen consumption capacity as measured and adjusted throughout the trial.

**Control group** participants will receive diet composition advice similar to that received in the exercise (intervention) groups and will be asked to complete dietary records for 3 weekdays and one weekend day every week for the duration of the 6 month intervention period. Control group participants will be asked not to participate in any planned exercise, or change exercise habits for the duration of the 6 month intervention. However, all control group participants will be wait-listed for participation within the exercise intervention group of their choice after completion of all 6 month outcome measures. Previous experience in 3 successfully completed RCTs confirms that wait-listing minimizes drop-out and encourages adherence. That wait-list control subjects remained sedentary in prior trials was confirmed using doubly labelled water and/or measurements of maximal oxygen consumption.

**Experimental Conditions:** The experimental conditions are illustrated in Figure 1 (above).

**Rationale for selection of exercise dose:** The underlying assumption that guides the study design is that exercise time (duration in minutes) for all treatment (exercise) groups is governed by the respective exercise dose (volume, kcal per session). In other words, we calculate that it will take approximately 30 minutes for those in the low volume, low intensity exercise group (LVLI) (40 to 50% VO₂ or ‘light effort’ exercise according to Canadian Guidelines) to achieve the prescribed dose or energy expenditure target (e.g., 180 kcals for women, 300 kcals for men). Similarly, we calculate that it will take approximately 60 minutes for those in the high volume, low intensity exercise (HVLI) group to achieve the prescribed dose or energy expenditure target (e.g., 360 kcals for women, 600 kcals for men). It is extremely important to note that the exercise dose calculations presented here (see Figure 1) for both men and women are based on data previously obtained from our assessment of exercise capacity (e.g., VO₂ max) in sedentary, abdominally obese individuals similar to those that will be recruited in the proposed study. However, we appreciate that the time required to achieve the exercise dose will vary individually and that improvement in cardiorespiratory fitness (exercise capacity) will improve throughout the study; thus, on average the number of exercise minutes will likely decrease over the 6 months for all groups.

**Rationale for selection of exercise intensity:** Health Canada, in association with the Canadian Society for Exercise Physiology, currently recommends (*Canada’s Physical Activity Guide to Healthy Active Living*) that Canadian adults should “accumulate 60 minutes of light-intensity activity or 30 minutes of vigorous intensity physical activity as capability improves most days of the week”. In *Canada’s Physical Activity Guide*,
exercise intensity is presented in qualitative terms in that ‘light effort’ (~60 min) is presented as light walking, volleyball, easy gardening and stretching whereas vigorous effort (20-30 min) is presented as, for example, jogging, fast swimming, aerobics, hockey. In this proposal, exercise intensity is derived relative to the person’s capacity, (e.g., relative to the individuals VO₂ max) and thus, low intensity or light effort represents approximately 50% of VO₂ max whereas high intensity or vigorous exercise represents approximately 75% of VO₂ max. It is generally accepted that low intensity exercise represents about 40 to 50% VO₂ max and that vigorous exercise represents about 75% of individual VO₂ max.

**Exercise Protocol:** Regardless of exercise group, all men and women will be asked to perform walk/jog type exercise on a motorized treadmill for the time required to expend the desired energy (kcal/session) according to group assignment, 5 times per week at the required intensity (relative to VO₂) for the duration of the 6 month treatment period. Using the heart rate and oxygen consumption data obtained from the baseline graded exercise test (see below), the heart rate associated with a VO₂ of ~ 50% (Group LVLI and HVLI) and ~75% (LVHI) will be determined and prescribed for each subject. A second and third graded exercise test will be performed on all subjects at weeks 4, 8, 16, and 24 (see Figure 2) to verify the relationship between heart rate and oxygen consumption. Thus we will continually adjust the heart rate-oxygen consumption relationship for each individual thereby adjusting for improvement in cardiorespiratory fitness which will alter the time required to achieve the prescribed exercise dose (e.g., energy expenditure in kilocalories). Heart rate will be monitored every 5 minutes each exercise session using an automated heart rate monitor (Polar Electro Oy, Kempele, Finland). As per established procedures in the laboratory of the principal applicant, all exercise sessions will be by appointment and performed under supervision.

**Monitoring of Non-exercise energy expenditure levels:** Non-exercise (e.g., excluding prescribed exercise performed under supervision) energy expenditure levels will be monitored using Accelerometers for 1 week periods throughout the trial (see schedule in Figure 2) to determine daily physical activity levels for all subjects including Controls. Accelerometers have the potential to overcome many of the problems associated with self-report measures while providing robust and detailed physical activity information. Daily activity levels will be used to interpret conformance with waist loss expectations given prescribed energy deficits induced by the respective exercise regimens. They will also be used during the post-intervention follow-up period to interpret physical activity behaviour.

**Dietary Regimen:** The volunteers will be free-living and all foods consumed will be store bought and self-selected by the participants. No vitamins or other nutritional supplements will be prescribed. Each subject will participate in a series of educational seminars designed to teach proper food selection and preparation as designed by the study Nutritionist. These sessions will be consistent with those established within our laboratory. For all subjects the diet composition will provide energy as follows: approximately 50 to 55% carbohydrate, 15-20% protein and 30% fat. Subjects will be asked to submit daily diet records for the duration of the program. Our experience
suggests that while cumbersome, submission of daily food records is a critical step in the design of individual success strategies for compliance to the dietary (caloric and composition) requirements of the study. Submission of daily diet records have been a fundamental procedure in three previously completed RCTs in our laboratory. Computer analysis of diet records in prior trials confirm that our procedures ensure that diet quality is not different between groups, and that energy intake values are as prescribed in all treatment groups.

At the beginning of the run-in period, the number of calories required to maintain body weight will be determined using each subject’s resting metabolic rate (see below) and multiplying that number by a factor of 1.5. The value derived will be prescribed for each subject and followed for the 1 to 2 week baseline period. During this period body weight will be monitored to determine the accuracy of the prescribed daily energy requirement. The caloric intake required to maintain weight will be maintained throughout the 6 month treatment period. Thus the negative energy balance induced will be a consequence of the increase in energy expenditure respective to the individual exercise treatment. This is an important characteristic of the proposed study as, combined with a healthful diet, it will allow us to isolate the effects of exercise dose and intensity on the primary outcomes. In other words, we are not prescribing a caloric restriction. Following the treatment period, isocaloric requirements will be determined and prescribed for a 2-week weight stabilization period. These procedures are well established in our laboratory and are published in several directly relevant manuscripts. Confirmation that subjects in prior trials adhered to the prescribed energy intake for the duration of the trial was confirmed by the simultaneous use of doubly labeled water combined with computer analysis of daily dietary intake records as well as daily body weight measurements.

The intervention will be six months and the negative energy balance will be induced by the increase in exercise alone (e.g., no caloric restriction). In our experience, given the volume of exercise performed within each treatment group, we estimate that substantial reductions in the primary outcome variables (e.g., abdominal obesity and glucose tolerance) will occur within the first 4 to 6 months. Although further improvement would likely occur in subsequent months, in view of the increased logistical and participant burdens (perhaps leading to poorer adherence) and costs of running a highly controlled, laboratory-based study for a longer period, we limited the length to 6 months.
Appendix C
Accelerometry Protocol

List of Measured Variables

- Average daily intensity (counts per minute; cpm)
- Sedentary behaviour (duration and intensity)
- Light physical activity (duration and intensity)
- Moderate to vigorous physical activity (duration and intensity)
- Bouted (accumulated in ≥ 10 consecutive minutes) activity
- Sporadic (accumulated in < 10 minutes) activity
- Total physical activity (duration and intensity)
- Incidental physical activity (duration and intensity)
- Sleep duration (minutes)

Measurement Device

- GT3X Actigraph Activity Monitor (Pensacola, FL)

Measurement Procedure

The accelerometer was given to the participant either immediately before or after the anthropometric appointment and was worn for 7 consecutive days. Participants were encouraged to wear the accelerometer for the full 7 days (except when participating in water-based activities such as showering or swimming) including at night. However, the participants were reassured that if the device was disruptive to normal sleep habits or if they were uncomfortable wearing the device to bed, it would be sufficient to wear the accelerometer for the full waking period of the day only (i.e., the
participant was asked to put the accelerometer on as soon as they woke up in the morning and remove it immediately before returning to bed in the evening).

**Preparing the Accelerometer for Data Collection**

1. Ensure the battery is fully charged before being given to a participant. The accelerometer can be recharged via a standard 2.0 USB connection plugged into a computer.

   Note: When the battery is plugged in and recharging a red light will flash. When this red light stops flashing and stays on, the battery is fully charged.

2. When the accelerometer is charged it can be initialized to begin collecting data in 60 second epochs on midnight of the day data collection begins and end exactly 7 days later at midnight. When initializing also include the participant ID and check off the boxes for: 1) Activity, 2) Step Count, 3) Enable Stop Time, 4) Dual Axis, 5) 3rd Axis, and 5) Inclinometer. Finally, ensure that the **GT3X Mode** is selected.

   Note: after the accelerometer has been initialized the red light will flash until it hits the programmed start time. The red light will start flashing again once it reaches the stop time until the data is downloaded.

3. Attach the accelerometer to an elastic band and record the serial number of the accelerometer on the **Accelerometer Wear Spreadsheet**.

**Preparing the Participant**

1. There are no guidelines the participant needs to follow prior to getting the accelerometer.
2 The accelerometer will be attached to an elastic band to be worn around the waist next to the skin (or over a light, tight-fitting top if it is too itchy) to minimize extra motion and will be situated directly over the right hip.

3 The participant will be wearing the accelerometer for a 7 day period and removing it only for water activities (e.g., swimming, showering, or bathing).

4 The participant will also be given a log (see next page) where they will record when and why the accelerometer was removed, when sleep started and stopped, and provide comments.
# Activity Monitor Log

<table>
<thead>
<tr>
<th>Participant ID:</th>
<th>Monitor ID:</th>
<th>Return Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dates</th>
<th>Day One</th>
<th>Day Two</th>
<th>Day Three</th>
<th>Day Four</th>
<th>Day Five</th>
<th>Day Six</th>
<th>Day Seven</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Awake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time Asleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor Off</td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
</tr>
<tr>
<td>Why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor Off</td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
</tr>
<tr>
<td>Why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitor Off</td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
<td><strong>:</strong> to <strong>:</strong></td>
</tr>
<tr>
<td>Why?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any problems?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Please explain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you have any questions or concerns please call or email Ashlee McGuire at 613-533-6000 x: 75118 or 7kam1@queensu.ca.

Thank you for your participation!
**Retrieving Data**

1. Download raw data and then using proprietary software from Actigraph, convert the raw file into an excel file (which gives a minute-by-minute recording of the data and a graphical representation of each day) to visually examine the data for compliance with wearing instructions and to ensure the accelerometer was functioning properly.

2. When saving the file use the following format: IDVisit_startday, where Monday = 1, Tuesday = 2, and so on. For example: S001V00_2

3. Wash the elastic band in a hypo-allergenic formula and hang to dry.

**Data Analysis**

1. Using both the sleep log and the excel file, determine sleep stop (i.e., wake time) and sleep start (i.e., sleep time) for each day and record in a separate excel spreadsheet. The following formula will calculate the exact epoch when each sleep stop time occurs: =IF((AND(D8<>"",D8>=0)),((($C8-1)*60*24)+D8*60+E8),"""). A similar formula was used for sleep start times. The Table below is an example of what the log should look like for each participant. This spreadsheet will then be used by custom designed software to separate daytime and nighttime, and calculate all daytime activity variables.

<table>
<thead>
<tr>
<th>ID</th>
<th>Visit</th>
<th>Weekday</th>
<th>Sleep Stop Hour</th>
<th>Sleep Stop Min</th>
<th>Sleep Stop Hour</th>
<th>Sleep Start Hour</th>
<th>Sleep Start Min</th>
<th>Sleep Start</th>
</tr>
</thead>
<tbody>
<tr>
<td>S001</td>
<td>V00</td>
<td>1</td>
<td>7</td>
<td>59</td>
<td>479</td>
<td>1</td>
<td>23</td>
<td>55</td>
</tr>
<tr>
<td>S001</td>
<td>V00</td>
<td>2</td>
<td>6</td>
<td>40</td>
<td>1840</td>
<td>2</td>
<td>22</td>
<td>48</td>
</tr>
<tr>
<td>S001</td>
<td>V00</td>
<td>3</td>
<td>4</td>
<td>25</td>
<td>3145</td>
<td>3</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>S001</td>
<td>V00</td>
<td>4</td>
<td>4</td>
<td>57</td>
<td>4617</td>
<td>4</td>
<td>23</td>
<td>40</td>
</tr>
<tr>
<td>S001</td>
<td>V00</td>
<td>5</td>
<td>5</td>
<td>29</td>
<td>6089</td>
<td>5</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>S001</td>
<td>V00</td>
<td>6</td>
<td>7</td>
<td>32</td>
<td>7652</td>
<td>6</td>
<td>23</td>
<td>59</td>
</tr>
<tr>
<td>S001</td>
<td>V00</td>
<td>7</td>
<td>8</td>
<td>13</td>
<td>9133</td>
<td>7</td>
<td>23</td>
<td>59</td>
</tr>
</tbody>
</table>

162
Custom designed software was used to determine whether participants met inclusion criteria for accelerometry. Participants were required to wear the accelerometer for 4 full days (defined as at least 10 hours of wear during the waking hours), including at least 1 weekend day. This was determined by the software after extended periods of zeros (i.e., 60 minutes) were removed from the data. To be included in the 3rd manuscript, participants were required to wear the accelerometer for a full 4 days (day and night), including 1 weekend day. The software also calculated all variables necessary for statistical analysis.
Appendix D
Cardiorespiratory Fitness Protocol

List of Measured Variables:

- Maximal oxygen consumption (L/min)
- Maximal oxygen consumption per kg body weight (ml/kg body weight/min)

Measurement Devices

- Sensor Medics Vmax29 Metabolic Cart
- Laptop computer
- Treadmill
- Calibration gas tanks (with sufficient gas)
- Polar HR monitor
- USB stick

Measurement Procedures

Cardiorespiratory fitness tests were performed at Hotel Dieu Hospital at the beginning of the study for each participant.

The VMax system (used to measure breath-by-breath gases) was turned on 30 minutes in advance of attempting system calibration. Flow-volume and gas calibration took approximately 30 minutes. The test took approximately 45 minutes per participant. The participants changed into comfortable athletic attire which included a pair of comfortable shoes suitable for brisk walking or jogging (they were reminded to bring all items on the day of the test). Participants wore a Polar heart rate monitor throughout the test so that heart rates could be obtained every 20 seconds for the duration of the test. The protocol used was the Modified Bruce Treadmill Test. On average, the test lasted
between 8-12 minutes, beginning with a relatively brisk pace at level grade, increasing grade to 5% at the third minute, and then further increasing the grade by 2% every 2 minutes thereafter. If after 2 minutes at the maximal incline of 15% the subject had not reached exhaustion, the speed was increased (generally by 0.2 mph). Heart rates were observed and recorded on the VO₂ Data Collection Sheet by a Research Assistant. Breath-by-breath analysis of respiratory gases was recorded throughout the test.

**Criteria for a successful VO₂ max test**

There are a number of popular criteria in the literature which are to be used to assess whether the participant being tested has actually achieved VO₂ max.

- **Plateau in VO₂** (oxygen uptake) with increasing work rate (increasing treadmill incline, speed or both). For our purposes we defined plateau in VO₂ as ∆VO₂ < 0.05 L/min at VO₂ peak and the data point 40 seconds above or below, with increases in external work.
  - **Note:** This criteria is often criticized as it has been shown that approximately 50% of individuals undergoing VO₂ max testing never reach a true plateau.

- **Respiratory Quotient > 1.10:** This suggests non-metabolic production of carbon dioxide and reliance on anaerobic metabolism.

- **Heart rate (beats per minute or bpm) exceeding age predicted max heart rate (220-age) minus 12bpm.** For example, for a 20 year old, the heart rate to be exceeded = 188 bpm (220 - 20 -12)

- **Borg scale = 10.** This gives the perception of effort by the participant during the test.
A successful test was required to meet at least 3 of the above criteria.

**Familiarization**

Measuring cardiorespiratory fitness requires a comparison of maximal performance on a graded exercise test. For people who have never been on a treadmill and are unaccustomed to pushing themselves physically, obtaining meaningful results can prove difficult. Thus, for each participant unfamiliar with walking on a treadmill, time was allotted during the accelerometry appointment to allow a familiarization period. Additionally, the warm-up for all participants was long enough for them to feel comfortable on the treadmill. The more they comprehend the test and what is required of them, the better the participants responded when encouraged to exercise “to fatigue” during the test.
Appendix E
Protocol for Glucose Metabolism, Blood Lipids and Lipoproteins

List of Measured Variables

- Fasting glucose
- Fasting insulin
- 2-hour glucose
- 2-hour insulin
- Serum total cholesterol
- High density lipoprotein cholesterol
- Total triglycerides

Measurement Equipment

- 2 X 6 mL mauve, 3 X 6ml red, 1 X 3ml gold/yellow and 1 X 3ml grey top tubes: labelled 0
- 1 red and grey top 3 mL tubes labelled 30, 60, 90 and 120. These are the times you need to take the blood.
- 20-gauge angio
- 1 interlink cap used to put on the end of the angio
- 1 X 4.4cm X 4.4cm Tegaderm
- 1 X10 mL normal saline flush
- Alcohol swab
- 4 x 4 gauze
- 7 blunt cannulas
• 6 BD Vacutainer Multiple Sample Luer Adapters
• 1 Vacutainer
• 1 x 5 mL syringe with blunt plastic cannula attached to end for discarded blood
• 1 op-site to apply over angio
• Tape
• COLD Glucodex (75 g 300 mL) with glass
• Timer
• Paper and pen to keep record of times for blood draw

Measurement Procedures

The 2-hour oral glucose tolerance test (OGTT) was acquired at our laboratory facilities in the Kinesiology and Health Studies Building on Queen’s campus. At the time of the OGTT, blood lipids were also measured.

Preparing the participant: Participants were instructed to eat a normal meal the evening before, followed by a 12-hour fast prior to testing. Upon arrival to the laboratory, participants were introduced to the study nurse, who would seat them and briefly explain the test.

OGTT Procedure: The participant was asked when they last had something to eat or drink. If they had not fasted for at least 12 hours the test was not completed. The procedure for taking blood was then explained to the participant.

1. Start IV with 20 angio with Interlink (cap) in the antecubital vein.
2. Have a 10mL syringe of flush ready.
3. The order of blood draws were as follows: Gold/yellow, red, mauve and grey
4 Take your first blood sample (time 0) with the multiple adapter and blunt cannula attached to the vacationer. Gently invert the tubes 5 to 10 times to enhance the clotting or anticoagulation.

5 Inject 2.5mL of flush in the angio to keep the line patent.

6 Give the participant Glucodex 75g 300mL in a cup. They have only 5 minutes to drink it. They must drink ALL of it within the 5 minutes.

7 As soon as they are finished start the timer for 30 minutes. This will start the OGTT. From this point onwards, blood samples will be taken every 30 minutes.

8 Allow the yellow/gold and red top tubes to sit at room temperature for 30 minutes to clot.

9 Prepare centrifuge to spin mauve, grey and red top tubes. These tubes should be put in the centrifuge immediately after blood is taken.

10 After each blood draw follow #8’s instructions.

11 When you have taken your last sample (at 120 minutes), offer juice, crackers and cheese or peanut butter.

12 Explain to the participant the importance of having some food after the OGTT.

13 Explain hypoglycaemia and the symptoms to the participant. Explain there might be a small chance of feeling weak after the OGTT.

14 Each mauve 6 mL top tube requires two aliquots (4 in total) and the 3 mL requires one aliquot for each time taken.
15 Make sure blood tubes are labeled with code number and times (0  30  60
90  120).

16 Store blood in -80°C freezer.

Storage and Handling of Blood Samples

Preparing the Blood for the Lab and Centrifuge:

1 All blood tubes should be kept in a vertical position in a blood tray. This
position promotes complete clot formation and reduces agitation of the tube
contents, which in turn reduces the potential for hemolysis.

2 The yellow and red top tubes should remain at room temperature for 30 - 60
minutes to allow for clotting. The mauve top tubes should be put in the
centrifuge at 16°C immediately.

3 Once the yellow top has clotted, prepare to send to the lab by making sure the
tube has been labeled and there is a requisition. The tube must be
transported in a Biohazard bag. The tube should reach the final lab within 2
hours sitting at room temperature.

4 The mauve top tubes should be spun and separated within 2 hours. (The
sooner the better). The tubes should be stored in a –80°C freezer labeled with
the code and study.

Operating the Centrifuge:

1 Keep the centrifuge temperature at 20°C.

2 The speed (rpm) should be at 4000 - 4250.
3 The blood should be spun for 10 minutes.

4 When putting the tubes in the centrifuge the tubes must be balanced for size and volume. If the volume is not equal you must fill an empty tube of the same size with water to match the volume. BALANCE IS A MUST.

5 Close the lid and hit the start button.

6 When the centrifuge is done a green light will come on.

**Separating the Blood:**

1 Remove the tubes from the centrifuge VERY carefully to a test tube rack.

2 Fill out the required aliquots with the proper study and code number.

3 Very carefully separate the serum from the whole blood making sure no blood cells enter the pipette. Distribute the serum evenly amongst the aliquots.

4 If some red blood cells enter the pipette the tubes must be spun again.

5 Put the proper coloured caps on the aliquots that match the study.

6 Dispose the blood tubes in the proper biohazard bucket or container.

7 Store aliquots immediately in the -80°C.

**Analysis of Blood**

After separating out the plasma by centrifugation, blood samples from the OGTT were sent to the Kingston General Hospital CORE Lab for analysis. Plasma glucose was determined using enzymatic methods on the Synchron LX® Systems (Beckman Coulter, Inc., Brea, CA, USA). Serum total cholesterol, triglyceride, and high density lipoprotein levels were determined using standard enzymatic methods on the Synchron LX® Systems (Beckman Coulter, Inc., Brea, CA, USA). Insulin was determined with a
chemiluminescent immunoassay using the Beckman Coulter UniCel Dxi 800 Access® Immunoassay System (Beckman Coulter, Inc., Brea, CA, USA).

The two most important samples for diagnosing Type 2 diabetes are the fasting or “0-time” sample and the sample taken 120 minutes after ingestion of the glucose drink. Fasting samples which are greater than 7.0 mmol/L or a 2-hour glucose level greater than 11.1 mmol/L are diagnostic of diabetes, according to the 1999 World Health Organization diabetes criteria. The blood lipids were also measured with the fasting blood samples.
Appendix F
Blood Pressure Protocol

List of Measured Variables

- Systolic Blood Pressure (mmHg)
- Diastolic Blood Pressure (mmHg)

Measurement Device

- BP Tru Blood Pressure Monitor (BPTru Medical Devices, Coquitlam, BC)

Measurement Procedures

The blood pressure was acquired at our laboratory facilities in the Kinesiology and Health Studies Building on Queen’s campus.

1. Seat participant in a comfortable chair with left arm resting on armrests and feet flat on the floor.

2. Place blood pressure cuff on upper left arm so that the brachial artery lines up with the lower edge of the cuff proximal to the antecubital area of the arm.

3. Check to make sure that the cuff is the right size. If it falls outside the range indicated on the cuff, use a smaller or larger cuff as needed.

4. Test fit by placing two fingers between the cuff and the person’s arm. If unable to place fingers inside, fit is too tight. If you can fit more than two fingers inside, fit is too loose. Adjust accordingly before proceeding.

5. Explain to the participant that the BPTru will take 6 readings, 2 minutes apart, and will take an average of the last 5.

6. Explain that the cuff does inflate quite tightly and to not be alarmed. You will stay with them for the first reading to make sure that everything works properly. Note:
the cuff will usually inflate to about 182 mmHg systolic and then gradually inflate less and less as it adjusts throughout the readings. In persons with very high blood pressure, the cuff may inflate to 220 mmHg. However, if cuff seems to inflate abnormally high, immediately stop the test and restart.

7  Make sure BPTru is turned on and press start. Remind participants to keep legs uncrossed.

8  Once the first reading has finished leave the room and allow the participant to relax in order to reduce the “white coat syndrome” effect.

9  Once the test has finished, record the average and then scroll through the previous readings by pressing the review button.
Appendix G
Anthropometry Protocol

List of Measured Variables

- Weight
- Standing Height
- Waist (iliac crest)

Measurement Devices

- Anthropometric tape (Gullick II) - contains a tension indicator device
- Detecto Weight Scale
- Stadiometer

Measurement Procedures:

Anthropometric measurements were completed at one of two locations: 1) In our
laboratory in the School of Kinesiology and Health Studies building on Queen’s campus
or 2) In our space at Hotel Dieu Hospital.

Weight (kg): measured on the Detecto scale with shoes removed, wearing the ‘Greys’
clothing provided.

Standing Height (cm): measured with shoes removed, standing with heels close to the
wall, feet together, eyes looking straight ahead, back, and buttocks touching the back
rest of the stadiometer. The head may or may not touch the back rest, depending on the
size of the participant. Some participants may have to lean back in order to have the
head touch; this would result in an inaccurate height measurement. Instruct participant to
stand tall and take a normal breath in, record measurement given on dial.
**Waist Circumference**

The iliac crest landmark is used.

1. Clear the participant’s abdomen of all clothing and accessories. If you find resistance to the suggestion to fully remove shirt, roll up the shirt to allow free access to measurement sites and hold in place with a clip (i.e., hair clip).

2. Position the participant with feet shoulder width apart and arms crossed over the chest in a relaxed manner.

3. Take a position to the right side of the participant’s body on one knee.

4. Position the tape directly around the abdomen so that the inferior edge of the tape is at the level of the landmarked point. Use a cross-handed technique to...
bring the zero line of the tape in line with the measuring aspect of the tape. Ensure that the measuring tape is positioned in a horizontal plane around the abdomen. Apply tension to the tape to ensure it is snug, without causing indentation to the skin. Walk around the participant to ensure the tape is straight all around the abdomen. Alternatively, if a mirror is available – use this to ensure proper tape alignment.

5 At the end of a normal expiration, take the measurement at the top of the iliac crest. To find this landmark, palpate the upper right hipbone and draw a line where you locate the uppermost lateral border of the iliac crest.
Appendix H
Magnetic Resonance Imaging Protocol

List of Measured Variables

- Total abdominal adipose tissue
- Visceral adipose tissue
- Abdominal subcutaneous adipose tissue

Measurement Device

- General Electric 1.5 Telsa magnet (Milwaukee, WI)

Measurement Procedures

Data acquisition occurred with MRI technicians at Kingston General Hospital (KGH) outside of the normal hours of medical use on the magnet (e.g., Saturday mornings).

Preparing the participant

A graduate student met the participant at the main entrance of KGH and escorted them to the imaging department. The participant changed into hospital gowns to eliminate clothing-related artefact in the images and removed all items containing metal (e.g., earrings). Following this, the graduate student and MRI technician reviewed a safety checklist with the participant to ensure participant safety.

Image Acquisition

The data acquisition process generally took 15 to 20 minutes. During this time, the MRI technician performed at least 11 scans (including scouts) to acquire cross-sectional images of each participant (see figure below).
Initially, the participant laid face down and entered the MRI machine feet first. The L4-L5 disk was landmarked, and then images were acquired from L4-L5 down to the toes at 50 mm intervals. Once this sequence was completed, the participant was removed from the MRI machine and asked to change orientation so that they entered the MRI machine head first (still face down) with arms extended over their head. Again, the L4-L5 disk was landmarked, and then images were acquired from L4-L5 to the finger tips at 50 mm intervals. There were two sets of 7 images taken from L4-5 to the arm. Each time a set of 7 images in the abdomen was acquired, the participant was asked to hold their breath for approximately 20 seconds to reduce movement and minimize in the resulting image.
Data Analysis

The acquired images were burned to compact disk and taken to an image analysis computer at Queen’s University. For each set of scans, the images to be used for analysis were identified and arranged sequentially from inferior (foot images) to
superior (finger images). A program (script file) for the computer to retrieve the images in sequence for tissue analysis was then created and saved.

Determination of tissue area (muscle, fat, organ, et cetera) on each image was accomplished using specially-designed image analysis software called Slice-O-Matic, a product of Tomovision (Montreal, Canada). For each cross-sectional image, the various tissues were identified, tracing the gray-level image and tagging (i.e., colouring) the visible tissue area with specific colors (see below for example).

**Figure.** Comparison of grey-level image and a tagged image from magnetic resonance imaging

A completely analyzed L4-L5 image, for example, would have tag colours identifying subcutaneous adipose tissue, muscle, lean tissue (large veins, nerves, et cetera), intramuscular fat, and visceral adipose tissue, and bone. The voxel area of the tag labeling each tissue could be quantified, indicating the volume of tissue found in that cross-section of the body that was 1 cm thick. If the images were contiguous, simply
adding the voxels of a specific tissue tag throughout the body would yield whole body tissue volume.

Since the images are not contiguous, but rather placed at 5 cm centers, the 4 cm of body tissue between images was interpolated mathematically using data from adjacent images. This is called the truncated cone formula. See figure below for a visual representation of inter-image interpolation and formulas used for the volume calculations. Using voxel summary data from the images on each whole body scan, a stand-alone program to run interpolation formulas and calculate whole body tissue volumes was used. Each tissue varies in density therefore tissue-specific conversions were employed to express volumes as masses (in kilograms). For example, skeletal muscle and adipose tissue volumes were converted to masses by multiplying them by 1.04 and 0.92, respectively.
The images utilized to quantify abdominal adipose tissue in the present thesis consisted of one image below L4-L5 to three images above L4-L5. Below is an example of the five images used.
Figure: Magnetic resonance imaging slices utilized to calculate abdominal obesity
Appendix I
Examples of Statistical Tests

A. Example of normalization of data.

Manuscript 1: Histogram of IPA duration not-normally distributed.

IPA Duration tests of normality. Significant Shapiro-Wilk Test ($p < 0.001$); IPA duration not normally distributed.

Tests of Normality

<table>
<thead>
<tr>
<th></th>
<th>Kolmogorov-Smirnov&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Shapiro-Wilk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statistic</td>
<td>df</td>
</tr>
<tr>
<td>IPAduration</td>
<td>.089</td>
<td>135</td>
</tr>
</tbody>
</table>

<sup>a</sup> Lilliefors Significance Correction
Histogram of IPA Duration after square-root transformation.

IPA Duration tests of normality. Significant Shapiro-Wilk Test ($p > 0.05$); IPA Duration normally distributed.

<table>
<thead>
<tr>
<th>Tests of Normality</th>
<th>Kolmogorov-Smirnov$^a$</th>
<th>Shapiro-Wilk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statistic</td>
<td>df</td>
</tr>
<tr>
<td>SqrtIPAduration</td>
<td>.046</td>
<td>134</td>
</tr>
</tbody>
</table>

a. Lilliefors Significance Correction

* This is a lower bound of the true significance.
### B. Examples of Linear Regression Analyses

**Manuscript 1, Table 2, Model 3:** Association between square-root transformed IPA Duration and CRF, control for sex (gender) and BMI.

<table>
<thead>
<tr>
<th>Model</th>
<th>Variables Entered</th>
<th>Variables Removed</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BMI, Gender</td>
<td></td>
<td>Enter</td>
</tr>
<tr>
<td>2</td>
<td>SqrtIPAduration</td>
<td></td>
<td>Enter</td>
</tr>
</tbody>
</table>

- **a.** All requested variables entered.
- **b.** Dependent Variable: CRF

<table>
<thead>
<tr>
<th>Model</th>
<th>R</th>
<th>R Square</th>
<th>Adjusted R Square</th>
<th>Std. Error of the Estimate</th>
<th>R Square Change</th>
<th>F Change</th>
<th>df1</th>
<th>df2</th>
<th>Sig. F Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>.710(^a)</td>
<td>.504</td>
<td>.496</td>
<td>3.1344</td>
<td>.504</td>
<td>64.951</td>
<td>2</td>
<td>128</td>
<td>.000</td>
</tr>
<tr>
<td>2</td>
<td>.724(^b)</td>
<td>.525</td>
<td>.513</td>
<td>3.0800</td>
<td>.021</td>
<td>5.561</td>
<td>1</td>
<td>127</td>
<td>.020</td>
</tr>
</tbody>
</table>

- **a.** Predictors: (Constant), BMI, Gender
- **b.** Predictors: (Constant), BMI, Gender, SqrtIPAdura
<table>
<thead>
<tr>
<th>Model</th>
<th>B</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>Sig.</th>
<th>95.0% Confidence Interval for B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bound</td>
</tr>
<tr>
<td>1</td>
<td>(Constant)</td>
<td>43.067</td>
<td>2.093</td>
<td>20.574</td>
<td>.000</td>
<td>38.925</td>
</tr>
<tr>
<td></td>
<td>Gender</td>
<td>-5.777</td>
<td>.587</td>
<td>-9.842</td>
<td>.000</td>
<td>-6.938</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>-.371</td>
<td>.062</td>
<td>-5.987</td>
<td>.000</td>
<td>-.494</td>
</tr>
<tr>
<td>2</td>
<td>(Constant)</td>
<td>37.972</td>
<td>2.983</td>
<td>12.730</td>
<td>.000</td>
<td>32.070</td>
</tr>
<tr>
<td></td>
<td>Gender</td>
<td>-5.921</td>
<td>.580</td>
<td>-5.842</td>
<td>.000</td>
<td>-7.069</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>-.357</td>
<td>.061</td>
<td>-5.842</td>
<td>.000</td>
<td>-.478</td>
</tr>
<tr>
<td></td>
<td>SqrtIPAduration</td>
<td>.275</td>
<td>.117</td>
<td>.146</td>
<td>2.358</td>
<td>.020</td>
</tr>
</tbody>
</table>

a. Dependent Variable: CRF
Manuscript 2, Table 2, Model 1: Association between SED and 2-hour glucose, control for time accelerometer worn.

<table>
<thead>
<tr>
<th>Variables Entered/Removed&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

a. All requested variables entered.

b. Dependent Variable: 2HRGlucose

<table>
<thead>
<tr>
<th>Model Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

a. Predictors: (Constant), SEDduration, AvgWakeTimePerDay

<table>
<thead>
<tr>
<th>Coefficients&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

a. Dependent Variable: 2HRGlucose
**Manuscript 3:** Test of sex interaction for the association between MPA and VAT. No sex interaction present. SexIntMPA = interaction term.

### Variables Entered/Removed

<table>
<thead>
<tr>
<th>Model</th>
<th>Variables Entered</th>
<th>Variables Removed</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SexIntMPA, Sex, MPA</td>
<td>.</td>
<td>Enter</td>
</tr>
</tbody>
</table>

**a.** All requested variables entered.

**b.** Dependent Variable: VATwt

### Model Summary

<table>
<thead>
<tr>
<th>Model</th>
<th>R Square</th>
<th>Adj. R Square</th>
<th>Std. Error of Estimate</th>
<th>Change Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>.637a</td>
<td>.391</td>
<td>1.273591282</td>
<td>R Square Change</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F Change</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>df1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>df2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sig. F Change</td>
</tr>
<tr>
<td></td>
<td>.406</td>
<td>.279</td>
<td>1.273591282</td>
<td>27.794</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>122</td>
<td>.000</td>
<td></td>
</tr>
</tbody>
</table>

**a.** Predictors: (Constant), SexIntMPA, Sex, MPA

### Coefficients

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>95.0% Confidence Interval for B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
</tr>
<tr>
<td>1</td>
<td>(Constant)</td>
<td>1.453</td>
<td>.642</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
<td>2.085</td>
<td>.442</td>
</tr>
<tr>
<td></td>
<td>MPA</td>
<td>-.329</td>
<td>.282</td>
</tr>
<tr>
<td></td>
<td>SexIntMPA</td>
<td>.088</td>
<td>.172</td>
</tr>
</tbody>
</table>

**a.** Dependent Variable: VATwt