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**THE INFLUENCE OF FREE-LIVING ACTIVITY AND INACTIVITY ON
HEALTH OUTCOMES AND RESPONSIVENESS TO EXERCISE TRAINING**

A Dissertation Presented
by
SARAH KOZEY KEADLE

Submitted to the Graduate School of the
University of Massachusetts Amherst in partial fulfillment
of the requirements for the degree of

DOCTOR OF PHILOSOPHY

May 2012

Department of Kinesiology

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by

SARAH KOZEY KEADLE

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Dedicated to my husband and our growing family

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quals, comps, proposing, the challenge grant, and all the ups and downs in between.

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ABSTRACT

THE INFLUENCE OF FREE-LIVING ACTIVITY AND INACTIVITY ON HEALTH OUTCOMES AND RESPONSIVENESS TO EXERCISE TRAINING

MAY 2012

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On average, starting an exercise training program decreases one's risk for chronic disease. However, there is remarkable individual variability in physiologic responses to exercise training. The activity and inactivity during the remaining 95% of the day (when the individual is not training) is rarely considered. The overall objective of this dissertation was to apply validated sedentary behavior (SB) and physical activity (PA) measurement techniques during an exercise training study to determine if time spent in SB and PA outside of training influences the physiological response to training. Twenty subjects participated in a pilot study to determine the feasibility of reducing SB and the validity of PA monitors for measuring SB compared to direct observation (DO). Participants completed a 1-week baseline period and a 1-week intervention period, where they were instructed to decrease SB. The correlation between the AP and DO was $R^2=0.94$ and the AG100 and DO sedentary minutes was $R^2=0.39$. SB significantly decreased from 67% of wear time (baseline period) to 62.7% of wear time (intervention period) according to AP. Only the AP was able to detect reductions in SB and was more precise than the AG. Study Two was a 12-week randomized controlled study. There were 4-groups that were instructed to: 1) CON: maintain habitual PA and SB 2) rST: reduce and break-up SB and increase daily steps 3) EX: exercise 5-days per week for 40-minutes per session at moderate intensity 4) EX-rST: combination of EX and rST. Cardiovascular disease risk factors were assessed pre-and post-

intervention. The AP was used to verify AP between-group differences in activity at four time-points. EX-rST had improvements in insulin action variables that EX did not. All other physiologic responses to training were similar between EX groups and rST has less robust changes than either EX group. These data provide validation of activity monitors for measuring SB and present preliminary evidence that activity outside of exercise training may influence the metabolic response to training. This dissertation shows that what is done outside of exercise training can and should be quantified using objective monitors that assess daily exposure to activity and inactivity behavior.

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CHAPTER 1

INTRODUCTION

Statement of the Problem

There is a clear association between physical activity (PA) and a reduced risk of chronic disease (22). Specifically, the 2008 Physical Activity Guidelines recommend 150 minutes of moderate and/or 75 minutes of vigorous PA each week to reduce risk of obesity, cardiovascular disease (CVD) and type II diabetes (22). On average, when non-exercising individuals begin exercise training they reduce disease risk factors and improve overall metabolic health (2). However, exercise training studies have reported large individual variability in the increase in cardiorespiratory fitness (CRF) and in the reduction of disease risk factors (e.g. insulin sensitivity) following the training period (2, 23). To date, research has primarily focused on identifying genetic factors to explain the individual variability in responsiveness to training (1). Limited research has focused on the possible role of modifiable behavioral factors contributing to individual differences in responsiveness to exercise training (3, 15). A training regimen lasting for 60 minutes per day fails to account for more than 95% of an individual's day; therefore time spent in activity or inactivity outside of exercise training may be an important modifiable factor to consider in understanding individual differences in physiological response to exercise training.

There is variability among individuals in their levels of spontaneous physical activity (SPA) (14, 28). SPA is defined as the energy expended during activities of daily living, fidgeting, spontaneous muscle contraction, and maintaining upright posture (13). Individual differences in SPA have been linked to obesity, and changes in energy availability have been linked to changes in SPA (14). A growing body of literature suggests that individuals may compensate for the energy expended during exercise training by decreasing SPA and increasing their sedentary behavior (SB), defined as time spent sitting or reclining (5, 15, 20). However, results have been inconsistent across studies (12, 19, 27). Two recent studies have provided preliminary evidence that individual variability in SPA may affect weight loss and blood lipid changes in response to

exercise training (3, 15). In addition, a growing body of evidence suggests that SB and exercise are distinct behaviors with independent effects on health (17). Recent studies show that SB and insufficient PA are *independently* associated with obesity, metabolic health, metabolic syndrome, type II diabetes, and mortality (9-11, 25). However, this evidence is based on prospective surveillance (26) or lab-based studies that use short-term (i.e., 1-day) experimental designs in humans or animal models (7, 24). No intervention studies have been designed to examine the long-term effects of reducing SB on health outcomes.

In summary, no study has quantified time spent in SB during an intervention study. Time spent in SB is a modifiable behavior that could explain inter-person variability in response to exercise. The feasibility of reducing SB and the effects of reducing SB on health outcomes have not been previously examined. A key limitation to understanding the role of non-exercise SB and SPA on exercise training responsiveness is a paucity of measures providing detailed and accurate assessment of usual SB and SPA throughout the training intervention (8). ***Therefore, the overall objective of this dissertation was to apply validated SB and PA measurement techniques during an exercise training study to determine if time spent in SB and PA outside of training influences the physiological response to training.***

Experimental Approach

To address the overall dissertation objective, two studies were conducted that contribute to an understanding of how SB and PA affect responsiveness to exercise training in previously non-exercising individuals. In the first study direct observation was used as a criterion measure to validate tools for measuring sedentary behavior (Chapter 3). Recommendations to reduce free-living SB were developed and implemented among non-exercising overweight office-workers to determine the feasibility of reducing SB. In addition, the ability of existing measurement tools to quantify behavior change was assessed following the intervention (Chapter 4; aim 2). In the second study, (Chapter 5; aims 3 and 4) the validated activity monitors and the sedentary time

reduction strategies from Study One were applied during an exercise training trial to determine if variation of time spent in SB and PA contributes to individual differences in responsiveness to training.

Aims and brief summary of experimental designs

Study One: Validation of objective measures of free-living PA and SB

Although there is accumulating and promising evidence that SB is detrimental to health, a primary limitation in the field is in measurement of SB and light-intensity PA (8). No objective activity monitors have been validated for assessment of SB and light intensity PA in a free-living environment using direct observation as the criterion measure. Furthermore, it is not known if existing technologies can capture subtle changes in patterns of behavior or if it is feasible for individuals with sedentary occupations to reduce their sedentary time. Therefore, the first study employs a novel study design where daily activity and SB were experimentally manipulated. This design allowed us to address two important aims within a free-living environment.

Specific Aim 1: To determine the validity of two activity monitors for measuring SB in a free-living setting using direct observation as the criterion measure.

Hypothesis 1: Both the activPAL and ActiGraph will accurately measure free-living activity and SB compared to direct observation.

Experimental Design: Twenty overweight (mean (SD)) BMI = 33.7 (5.7) kg·m⁻², inactive, office workers aged (mean(SD)) 46.5(10.7) yrs were directly observed for two, 6-hour periods while wearing an activPAL monitor and an ActiGraph GT3X (AG) activity monitor. During the second observation period, participants were instructed to reduce sedentary time. The validity of the commonly used cut-point of 100 counts·min⁻¹ (AG100) (16) and several additional AG cut-points for defining SB was assessed. Direct observation (DO), using focal sampling with duration coding was used to record either sedentary (sitting/lying) or non-sedentary behavior. The

accuracy and precision of the monitors and the sensitivity of the monitors to detect reductions in sedentary time were assessed using mixed model repeated measured analyses.

Specific Aim 2: To determine the feasibility of reducing free-living sedentary time and determine the sensitivity of the of activity monitors to detect change in patterns of light-intensity activity and SB.

Hypothesis 1: Participants will successfully reduce free-living SB during the intervention period compared to the baseline period.

Hypothesis 2: The ActiGraph and activPAL will accurately detect decreases in SB.

Experimental Design: The study included 20 overweight, inactive office-workers. Participants wore the activPAL and AG (AG; both 100 and 150 counts·min⁻¹ cut-points to define SB). Participants received a simple intervention targeting free-living SB reductions and wore activity monitors during the 7-day intervention period. They recalled sedentary time on two questionnaires (ST-Q) following the each 7-day period.

Study Two: Influence of activity and inactivity on cardiovascular disease risk factors

There are well established health benefits of PA including decreased risk of mortality, increased physical fitness and improved metabolic health in active persons compared to those who are less active (22). However, when a previously non-exercising individual initiates an exercise training program, there is remarkable variability in the response to training (2). There is a great deal of individual variability in levels of SPA performed outside of training and it is not well understood if SPA changes in response to training (4). During a 16-hour waking day, a 30 minute exercise session leaves over 15.5 hours of one's day that is spent in non-exercise behaviors at varying intensities and postures. Some evidence suggests individuals may compensate for exercise energy expenditure by decreasing SPA, thus increasing SB (15). Since accumulating evidence suggests exercise and SB may have independent effects on health (18), it may be important to consider time spent in inactivity and activity during the times the individual

is not exercising. In addition, the existing body of literature demonstrating a detrimental association between SB and risk for chronic diseases is based on cross-sectional and prospective studies (17, 26). No known intervention study has examined the effects of reducing SB on health outcomes.

Specific Aim 3: To examine how the amount of activity and inactivity performed outside of exercise training affects responsiveness to exercise training. CRF, insulin sensitivity, blood lipids and body composition outcomes will be examined.

Hypothesis 1: Individuals who receive an intervention targeting decreases in SB and increased time in light-intensity activity outside of exercise training time will have greater improvements in CRF, body composition, blood pressure, blood lipids, insulin action and triglycerides compared to those who are sedentary outside of exercise training time.

Specific Aim 4: To examine the effect of an intervention focused on reducing sedentary time on selected chronic disease risk factors compared to a control group and a traditional exercise training group. CRF, insulin sensitivity, blood lipids and body composition outcomes will be examined.

Hypothesis 1: Individuals receive an intervention targeting decreases in SB and increased time in light-intensity activity will have greater improvements in CRF, body composition, blood pressure, blood lipids, insulin action and triglycerides compared to the control group.

Hypothesis 2: Individuals receive an intervention targeting decreases in SB and increased time in light-intensity activity will not have as large improvement in CRF, body composition blood pressure, blood lipids, insulin action and triglycerides compared to the exercise training group.

Experimental design:

Study Two was a four-arm, 12-week randomized controlled study. Free-living activity and SB were measured using the activPAL monitor that was validated in Study One. The control group was instructed to maintain their habitual active and inactive behaviors. The sedentary time reduction group received recommendations to reduce and break-up sedentary time, increase light-

intensity activity, and increase daily step count. The other two groups were exercising training groups. Participants in both groups exercised 5-days per week for 40 minutes per session at 50-65% of heart rate reserve. In addition to the training protocol, half of the exercising participants received a prescription to reduce and break-up sedentary time, increase light-intensity activity and increase daily step count. Selected cardiovascular disease risk factors were assessed pre-and post-intervention including CRF, insulin sensitivity, blood lipids and body composition outcomes.

Summary and Significance

Although activity monitors have been validated for measuring SB in laboratory settings (6, 21), Study One is the first known investigation to validate activity monitors to assess SB in a free-living setting using direct observation as the criterion measure (Chapter 3; Aim 1). The ability of the existing measurement tools to detect changes in free-living sedentary time over a 7-day period was also assessed, which is important to determine prior to utilizing the monitors in an intervention study (Chapter 4: Aim 2). In addition, the first study provides a framework for an intervention to reduce sedentary time among non-exercising individuals with inactive employment. Identifying a valid and precise tool for measuring SB will allow for a detailed characterization of non-exercise SB and PA to determine if there are durations or patterns of SB that are associated with poor outcomes.

The validated measurement tools from Study One were used in a randomized controlled trial that examined the influence of free-living activity and inactivity on responsiveness to exercise training. Study Two provides additional evidence for the value of exercise in modifying risk factors for chronic diseases. This study also provides detailed information about total-daily activity exposure during an exercise training study, both with and without recommendations to modify non-exercise activity behavior. Lastly, this study presents preliminary evidence linking changes in SPA and SB to selected cardiovascular disease risk factors. These results have the potential to impact how clinical exercise trials are conducted (e.g. need for monitoring activity

outside the trial) and how exercise is prescribed (e.g. both reducing sedentary time *and* increasing PA).

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CHAPTER II

REVIEW OF LITERATURE

Introduction

Insufficient PA clearly correlates with cardiovascular disease (CVD); however, large individual variability in CVD risk reduction is consistently reported following exercise training of previously non-exercising individuals (11). This variability in individual responsiveness to exercise training has been observed in numerous trials and across a broad range of physical activity (PA) doses (18, 85). For example, 23% of women who completed 6-months of exercise training at an amount equal to the current public health recommendations did not improve or decreased their cardiorespiratory fitness (CRF) following the training period (84). Similarly, in a sample of over 500 individuals who trained for 20 weeks, 42% did not improve or decreased their insulin sensitivity (14). All participants in both trials attended over 90% of the exercise sessions (14,84). Researchers suggest numerous demographic and genetic factors as possible causes for large individual differences in the magnitude of CVD risk reduction (11). However, the role of PA and/or time in sedentary behavior (SB) during the intervention should be considered as a possible mechanism to explain inter-person variability in response to exercise training. The health benefits of exercise training may be negated if individuals compensate for structured exercise training by increasing time spent in SB (60). A large body of literature demonstrates that SB and insufficient PA correlate independently with obesity, metabolic health, metabolic syndrome, type-2 diabetes, and mortality (41, 45-46). This review of the literature will address three main areas of research that will be addressed in this dissertation. First, the results of previous exercise training trials will be presented, along with evidence that considering time outside training may be an important factor to understand the high prevalence of non-response to training. Second, the association between SB and compromised metabolic health will be evaluated to explain why focusing on time spent in SB outside training is of particular importance. Third, the importance of

accurate measurement of spontaneous physical activity (SPA) and SB to elucidate the relationship between exercise, SB, and reductions in disease risk factors will be discussed.

Non-response to exercise in cardiorespiratory fitness and disease risk-factors

For decades, researchers have studied the variability in CRF improvements following an exercise training protocol (13, 56). The HERITAGE study was a large trial designed to examine the variability in response to exercise training that included men and women, different race/ethnic groups and a broad age range (9). Over 600 previously non-exercising individuals completed a standardized 20-week exercise training protocol. The average increase in CRF (measured by a VO_2 max test) following the training period was 17%. However, individual changes in VO_2 max ranged from -5% to 56% (7). Similarly, the dose response to exercise in women (DREW) trial included previously non-exercising, overweight women who trained at an energy expenditure of 4 $\text{kcal}\cdot\text{kg}\cdot\text{week}^{-1}$, 8 $\text{kcal}\cdot\text{kg}\cdot\text{week}^{-1}$ or 12 $\text{kcal}\cdot\text{kg}\cdot\text{week}^{-1}$ for 6-months (73). In all exercise groups participants increased their fitness levels on average (18). However, 32% showed no improvement or *decreased* their CRF following the exercise training (84). Even among the group who exceeded current public health recommendations by 50% (training volume of 12 $\text{kcal}\cdot\text{kg}\cdot\text{week}^{-1}$), 19% of the women showed no improvements in fitness. In the DREW trial, the investigators attributed the high prevalence of non-response to age, initial fitness level and amount of exercise (84). This is in contrast to the HERITAGE study which showed age, initial fitness level, race and sex had no effect on the CRF response to the standardized exercise stimulus (85). In the HERITAGE study, the maximal heritability was 47% and there was 2.5 times more variance in fitness response between families than within families, suggesting a genetic component for response to training (7). The genetic component to fitness response to training has been verified in numerous twin studies (10, 12-13, 56). However, family members may have more similar activity behavior outside of training than unrelated individuals, which is not accounted for in the heritability figures. In addition, heritability accounts for less than half of

the variability in response to training and is not changeable. From a public health perspective, it is important to identify modifiable factors that contribute to non-response in CRF consequent to training. The HERITAGE study did not assess activity outside training, while the DREW trial did assess steps per day during the intervention (18). However, DREW did not examine activity outside the intervention as a contributor to non-response (i.e. if those participants who took more steps per day were the individuals who responded to the exercise stimulus). In addition, total steps per day do not provide an indication of intensity, energy expenditure, activity type, or time spent in SB.

Although CRF is an important predictor of all-cause mortality and metabolic disease progression (4-5), there are numerous additional risk factors that are important indicators of risk for CVD and type II diabetes. These include blood pressure, high LDL and triglycerides, low HDL, insulin sensitivity, and body composition. The HERITAGE study reported that, following 20 weeks of training, body composition, total cholesterol, HDL, systolic blood pressure, resting insulin and glucose-peak all significantly improved *on average*. However, similar to the CRF response, there was a high variability in response for each risk factor (93). Remarkably, for all of the 30 outcome measures some participants “got worse” or increased their disease risk despite attending a *minimum* of 57/60 training sessions over the 20-weeks. An important risk factor that warrants further mention is insulin resistance, a metabolic disturbance that predicts the onset CVD and type II diabetes (61). In the HERITAGE trial, insulin sensitivity was assessed 24 hours following the last exercise session using an intravenous glucose tolerance test (IGVTT). All insulin-derived variables improved, on average (14). However, there was a high prevalence of non-response ranging from 42% (insulin sensitivity index) to 55% (acute insulin response to glucose) (14). Furthermore, HDL and body composition were the only risk factors that were significantly correlated with CRF (93). Despite statistical significance, these correlations were very small in magnitude ($r= 0.19$ was the highest correlation, for fat-free mass). The lack of correlation among changes in risk factors with CRF highlights the need to consider response of

multiple outcome measures, including but not limited to CRF. To date the HERITAGE trial is the only known trial to examine the non-response of numerous disease risk factors following exercise training.

In summary, the HERITAGE and DREW studies illustrate the high prevalence of non-response to exercise training (14, 84). However, the mechanisms that contribute to the non-response are not well-understood. The disease burden and prevalence of chronic diseases such as type II diabetes are rising at epidemic rates (15). On average, there is a strong association between PA and reduced risk of developing chronic diseases; therefore public health strategies have been developed to increase PA (78). However, due to the high prevalence of individuals who do not improve health outcomes following an exercise training trial, it is critical to identify modifiable factors that are associated with individual variability. If one can target and change factors that contribute to non-response, a higher prevalence of individuals who begin an exercise training program may achieve the health benefits of exercise, perhaps reducing the prevalence of some chronic diseases.

Evidence that physical activity contributes to non-response to exercise

There is confusion in the literature regarding the influence of age, sex, race, initial fitness, and exercise dose on fitness non-response (11, 84-85). Although there appears to be a genetic component, genetic factors do not fully explain the variability in response of fitness and biomarkers to exercise training (7-8). Furthermore, one's genetics, age, sex and race are not changeable. Therefore, it is critical to identify modifiable behaviors that may reduce the high prevalence of non-response to training. There is a gap in the understanding of how activity behavior outside training contributes to non-response to training. The following sections will review the evidence suggesting that activity outside of training may be an important factor that may contribute to non-response to exercise training. Specifically, evidence will be presented that non-exercise PA is highly variable between individuals and contributes to metabolic health (65,

94). Furthermore, daily SPA may decrease in response to a negative energy balance such as exercise (64), which is partially supported in evidence from weight loss trials (81). Lastly, some evidence will be presented that individuals who are less active and decrease SPA during training may not respond as well to the training as those who are more active outside of training time (23, 51, 68).

Evidence of Individual Variability in Levels of Spontaneous Physical Activity

There is evidence of large individual variability in SPA, defined as the energy expenditure of activities of daily living, fidgeting, spontaneous muscle contraction, and maintaining posture when not recumbent (64). SPA does not include other components of total daily energy expenditure (TDEE) such as resting metabolic rate, thermic effect of food or exercise energy expenditure (64). SPA is the most variable component of TDEE and has been postulated to account for 10-50% of an individual's daily activity (67). Zurlo and colleagues reported large individual variability in SPA among Pima Indians, ranging from 4-17% of TDEE (94). Zurlo et al. also concluded SPA is a familial trait that may contribute to the pathogenesis of obesity, primarily in men, as differences in SPA predicted weight gain after 33 months (94).

Levine and colleagues have linked differences in levels of SPA to obesity. For example, obese, non-exercising individuals spend 164 more minutes seated and expended 350 Kcal less in SPA per day than lean non-exercising individuals (65). Among 16 individuals who were overfed by 1000 Kcal \cdot day⁻¹ and did not exercise, weight gain was directly linked to differences in SPA but not basal metabolic rate or thermic effect of food (64). Levine suggests that varying levels of SPA are linked to energy status, whereby increased energy availability results in increased SPA and vice versa (64).

Based on the individual variability in SPA, one could reasonably expect a range of SPA among participants in an exercise training study, which may influence response to training. However, limited studies have assessed whether SPA outside of training affects an individual's

response to training, and in those studies, the measurement of free-living activity is a limitation (23, 68). Therefore, to provide additional rationale for examining activity and in activity outside of training, evidence will be presented that individuals compensate for the increased energy expenditure of exercise training by decreasing SPA and thus TDEE, which may contribute to the non-response of health outcomes to exercise.

Energy Balance during Exercise Training Trials

In adults, few studies have examined non-exercise activity during an exercise training study. Free-living PA is difficult to measure; therefore an indirect method to determine if an individual is decreasing his/her energy expenditure outside of exercise training is to use the energy status. If an individual is in energy balance, his/her energy intake is equal to his/her energy expenditure. For weight loss to occur an individual must be in energy deficit, whereby they must expend more energy than is consumed. Initiation of an exercise program will cause an energy deficit, thus an individual will lose weight, *if* the individual maintains non-exercise energy expenditure and energy intake. Although some trials have reported exercise alone will induce weight loss (82), others have reported exercise training without dietary restriction does not consistently result in weight loss (26). If an individual begins exercising and does not lose weight, the individual either takes in more calories and/or expends less outside of training time. Unfortunately, both energy expenditure and energy intake are difficult to measure in a free-living environment, therefore limited data directly assesses compensation of energy expenditure or intake during exercise training.

For over 25 years, researchers have suggested that individuals increase energy intake in response to exercise training (32). A recent review concluded there is evidence for partial compensation (i.e. individuals eat ~30% of the calories they expended from exercise) (59). King and colleagues categorized individuals based on whether they lost as much weight as predicted (non-compensators) or if they did not lose as much weight as predicted (compensators) following

12-weeks of supervised exercise training (60). They showed the compensators increased intake by 300 Kcal·day⁻¹ during the training period based on a test-meal intake (60). In the DREW trial, the high amount of exercise group had a high prevalence of compensators for weight loss. However, in contrast to the King study, participants reported a reduction in energy intake following training on a food frequency questionnaire (19). Further complicating matters, there is evidence women may increase energy intake in response to exercise more than men (88). It is prudent to mention the effects of sex, macronutrient content and the energy status on appetite regulating hormones, and consequently, ad libitum feeding (37). Hagobian et al. found sex differences in appetite regulating hormones in response to an acute exercise stimulus (38). Turner and colleagues (94) measured EE using the actiheart, a device that combines heart rate and accelerometry, for one-week before and during weeks two, nine, and 18 of a 6-month exercise training program among middle-aged men. They reported a significant increase in PAEE at week 18 of the intervention. However, they calculated the “expected” weight loss based on the estimated calories expended during exercise and conclude that men only lost ~40% of the “expected” weight. Because men increased PAEE during the intervention, they suggest a compensatory increase in energy intake, although it is important to note there was no measure of energy intake during this study. Regardless, this study highlights the complex interactions between both diet, energy expenditure and weight loss. The influence of energy intake on energy balance during exercise training is beyond the scope of this review. However, due to the confusion in the literature, it was necessary to consider studies where diet was carefully monitored during the training period to determine if decreases in SPA are prevalent.

Redman and colleagues (81) compared the TDEE of overweight individuals (BMI >25 and <30 kg·m²) in a control group (n=12) to a group who reduced caloric intake and initiated exercise (CR+EX). Participants in the CR+EX group were instructed to reduce their baseline energy intake by 12.5% and increase their expenditure through exercise by 12.5%. To enhance compliance to the caloric restriction, all meals were provided to the participants for the first 3

months. The energy expenditure increase was achieved through supervised exercise training five days per week, equivalent to 2015 Kcal·week⁻¹ for women and 2845 Kcal·week⁻¹ for men. In both groups, doubly labeled water was used to measure TDEE at months three and six. Despite the increase in expenditure from exercise, the individuals in the CR+EX did not increase TDEE compared to the control group at either time point, suggesting that reductions in SPA outside of training accounted for the lack of increase in TDEE. However, since energy intake was also reduced, one cannot say whether the compensation was due to the increased expenditure from exercise or the caloric restriction. Heymsfield et al. (49) fed overweight individuals a standard formula of 900 Kcal·day⁻¹ for a 5-week period. Half of the individuals were also prescribed a walking protocol to expend ~350 Kcal·day⁻¹. The individuals in the exercise group did not lose more weight than the control group despite the increase in exercise energy expenditure. Although this study eliminates the confounding effect of diet since both groups were in caloric restriction, the degree of energy restriction (900kcal/day) may limit its generalizability to free-living situations.

The studies by Redman et al. and Heymsfield et al. suggest behavioral compensation for energy expenditure. However, both included restriction of energy intake, therefore the reductions in SPA cannot be conclusively linked to exercise (49, 81). In contrast, in the Midwest exercise trial, exercise energy expenditure, energy intake and TDEE were all carefully measured using doubly labeled water, but only exercise energy expenditure was manipulated (25, 79). This trial was a 16-month randomized controlled study in previously non-exercising individuals. The exercise training protocol was gradually increased until month six when participants exercised 5-days per week for 45 minutes at 75% of their VO₂ max for the remaining ten months. On average, the participants improved fitness, and the men lost weight and improved insulin sensitivity while the women did not (79). The results provide evidence that individuals may compensate for exercise energy expenditure by decreasing TDEE. Every four months, exercise energy expenditure was verified using indirect calorimetry and energy intake was directly measured for a

2-week period. In addition, TDEE and energy balance was measured in 44 participants using doubly labeled water. Despite an increase in energy expenditure from exercise of approximately 400kcal per session, and a slight but non-significant increase energy intake of 22 Kcal·day⁻¹, women gained 0.6 kg on average at 16 months, suggesting a reduction in SPA outside of exercise training. Women in the exercise group expended only 97 Kcal·day⁻¹ more than the control group despite expending a minimum of 400 Kcal·day⁻¹ from exercise. Similarly, males were in negative energy balance of approximately 350 Kcal·day⁻¹, despite consistent energy intake and expending 600 Kcal per exercise session (25). Therefore, it is reasonable to speculate that a portion of the 250-300 Kcal·day⁻¹ difference between the expected energy deficit from exercise and the actual measured deficit is a conservation of energy through an increase in SB and/or reduction in activity outside training. Furthermore, improvements in insulin sensitivity were directly linked to changes in weight status (79). Encouraging individuals to maintain or increase energy expenditure outside training may increase the energy deficit and maximize health benefits.

Few studies have directly measured SPA using accelerometer-based devices, which have two advantages over doubly labeled water. First, accelerometers provide time-stamped information on the duration of time spent in different intensity categories (i.e., sedentary, light, moderate), and second, because the data are time-stamped, it is possible to examine the exercise time separate from the non-exercise time. The STRRIDE trial used RT3 accelerometers in two phases of an intervention trial. In the first phase, described in detail below, they compared different doses (intensity and duration) of exercise on health outcomes. They measured PA in a subset of participants and reported an increase in both TDEE and non-exercise EE in all exercise groups (50). In the second phase, they compared aerobic exercise to resistance training and again found an increase in TDEE but found no change in non-exercise EE (80). Notably, in both phases there was large inter-individual variability in the changes in TDEE and non-exercise energy expenditure, thus indicating that some individuals compensated by decreasing SPA (50, 80). The results of the STRRIDE trial are in contrast to other studies that reported a decrease in SPA in

response to exercise (34, 58, 68, 72) and are in line with some previous work (92), highlighting the need for more work in this area. In particular, few studies measure activity or TDEE at multiple time points within the exercise training period, which may provide more insight into the temporal adaptations and variability in SPA.

Evidence that health benefits are linked to activity outside of training

Two recent studies have directly assessed whether compensatory decreases in SPA during an exercise training study contribute to non-response to exercise training. Manthou et al. (68) studied 34 overweight or obese, non-exercising women who began an 8-week supervised exercise intervention. For the week prior to the intervention and the last week of the intervention, participants wore a heart rate monitor for all waking hours and recorded all activities in an activity log. Using an individually calibrated HR x VO₂ equation they estimated EE for all inactive, active, and sleep time. They classified individuals as ‘responders’ (those who lost at least as much weight as predicted) and ‘non-responders’ (those who lost less weight than predicted). The non-responders expended significantly less energy during non-exercise times than the responders. This was the first study to link changes in SPA and individual variability in weight loss. However, the combined HR and activity log method to measure EE has not been validated and did not allow for an examination of sedentary time as a distinct behavioral component.

Di Blasio et al. (23) examined the effect of changes in SPA on response to training including plasma lipids, body mass, fasting glucose and insulin, and adipokines among 34 women. They used the Sensewear Pro2 armband (Body Media, Pittsburg, PA) to evaluate TDEE. Participants wore the armband for 3-days prior to initiating training and 3-days at the end of the study period, including one training day and two non-training days. The exercise dose was four days per week of moderate walking for a 13-week period. The intensity was set based on rating of perceived exertion (RPE) and was multiplied by exercise duration to estimate weekly exercise

volume. They classified individuals into two distinct sub-groups- those who increased TDEE and those who decreased TDEE during the intervention period. Participants who increased TDEE showed improvements in cholesterol and LDL, while those who decreased TDEE did not. Changes in all other outcome variables were not different between the groups. This study has important limitations including the use of RPE to estimate exercise volume rather than a physiologic measure such as heart rate, limited days of monitoring of TDEE (including only one training day), and a sample that included only postmenopausal women. However, it is the first known study to link changes in SPA with a biomarker (plasma lipids). In addition, this study showed that over half of women who started the exercise training program *decreased* total daily EE. The authors conclude additional intervention may be necessary to ensure behavioral compensation does not take place outside of exercise training in effort to enhance the health benefits of exercise training.

The STRRIDE trial compared the effect of three different exercise groups and a control group on CVD risk reduction (63). The prescribed dose of exercise for each group is listed in Table 1, and participants were instructed to maintain body weight throughout the trial. Outcome measures included fitness, blood lipid profiles, insulin sensitivity, and body composition measures. As expected, insulin sensitivity, measured via 3-hour intravenous glucose tolerance test 16 to 24 hours after the final exercise bout, improved in the three exercise groups compared to the control group.

Surprisingly, however, the low/mod and high/vig group significantly improved insulin sensitivity compared to the low/vig group (51). In addition, the metabolic syndrome, a clustering of risk factors including insulin sensitivity, blood lipids, and visceral adipose tissue was assessed using a continuous z-score measure. Both the low/mod and high/vig groups significantly improved their z-score compared to the control group, while the low/vig group did not (55). In this study, the duration of exercise rather than changes in fitness or body mass predicted improvements in health outcomes. Specifically, the low/mod and high/vig groups exercised 60-

minutes more each week than the low/vig group, time that could be spent in SB. The investigators estimated TDEE using RT3 accelerometers in a sub-set of participants. The TDEE for the low/mod group was higher than the low/vig despite no difference in energy expenditure prescribed for exercise, further suggesting the low/vig group spend time in SB's while they were not exercising (50).

In conclusion, there is strong evidence that variability in individual responses to an exercise stimulus (11) in SPA during exercise training studies (65, 94). Evidence from the Midwest exercise trial suggests individuals may conserve energy by decreasing energy expenditure outside of training (25), and evidence from the STRRIDE trial suggests duration of exercise may be an important predictor of response to training (51). Two recent trials provide preliminary evidence that behavioral compensation (decrease in SPA) is widespread during exercise training trials, with nearly 50% in each study sample showing a decrease or no change in TDEE (23, 68). In addition, these studies linked decreases in SPA to changes in body composition and plasma lipids. In combination with the indirect evidence from other trials, there is a growing body of literature that supports the importance of measuring daily SPA during a training trial and examining the impact of changes in SPA on health outcomes. For example, although duration of exercise was more important for health benefits than intensity, it is not known if the STRRIDE participants in the low/vig group spent more time in SB. Future work is needed that assesses and manipulates activity and inactivity outside of training to adequately examine how the activity and inactivity outside training affects responsiveness to training. In the next section evidence will be presented that SB, independent of exercise is an important determinant of metabolic health. The literature on SB and health could explain some of the variability in responsiveness to training, particularly if, as Levine suggests (67), SPA is decreased and SB, increases in response to any energy deficit (i.e. initiating exercise).

Sedentary behavior and health outcomes

Simultaneously, epidemiological evidence has emerged that 1) sitting is ubiquitous in the modern environment and 2) sitting is associated with an increased risk of obesity, chronic disease and mortality (75). The majority of occupational, transportation, and discretionary time is spent in SB defined as energy expenditure between 1-1.5 METs while sitting or reclining (76). Specifically, in the National Health and Nutrition Examination Survey Matthews et al. reported that 54% (7.7 hrs) of waking hours are spent in sedentary activities (71). Among healthy, predominantly overweight individuals an average of 62-68% of waking hours or 9.7 hrs/day, are spent in sedentary pursuits (70). Epidemiological studies have shown increased TV viewing time has been associated with obesity, elevated glucose levels following an oral glucose tolerance test, metabolic syndrome and mortality (2, 27-29, 36, 45, 86). In a large prospective cohort, sitting “a lot of the time” is associated with a 50% increased risk of CVD mortality compared to sitting “most of the time” over 14 years (57). Objectively measured SB is associated with poor metabolic profiles, and mortality (43-44, 47). After nearly 6 years of follow-up, time spent in SB predicted higher levels of fasting insulin independent of the amount of time spent at moderate/vigorous PA (48). However, the same group reported moderate/vigorous PA but not SB was associated with insulin sensitivity at one-year follow-up (48), suggesting more prospective and experimental studies are needed to elucidate dose-response relationships between SB, PA and health outcomes. A recent review by Thorp et al. (90) concluded there is prospective evidence that supports relationships between SB, mortality, and health outcomes. Studies have shown that sedentary time is associated with increased risk for type II diabetes (48, 52-53) and mortality (27). Other studies report no association or suggest reverse causality between sedentary time, obesity, and insulin resistance (30-31). Studies often failed to adjust for PA and BMI, which may explain the disparate results (90). In addition, the majority of these studies used surrogate measures of

sedentary time (e.g., TV viewing) and self-report measures, which may not accurately measure sedentary time.

In addition to association studies, a number of studies in animals and humans investigated biological mediators between inactivity and risk for disease (78). SPA, which includes the energy expenditure from fidgeting, short walks, and standing is the most variable component of daily energy expenditure is a potential mediator. SPA has been hypothesized to explain inter-individual differences in weight gain and to decrease in response to an energy deficit (64). This is consistent with epidemiologic literature showing that an increased risk of obesity among the most sedentary individuals (65, 89) and data showing changes in metabolic health (primarily obesity status), are linked to differences in SPA (65). A study by Stephens et al. (87) showed that one day of sitting decreased insulin sensitivity by 18% compared to a day with high amounts of SPA and low-sitting. Sedentary time is associated with two biological processes associated with CVD and type II diabetes. Specifically, SB decreases lipoprotein lipase (LPL), a lipoprotein that regulates triglyceride uptake, HDL production and glucose uptake (3, 39-41). Notably, it has been suggested that the biological processes underlying inactivity are different from the processes underlying adaptations to structured exercise (40).

Previously “sedentary” was a default label applied to those who are not meeting PA recommendations (77). However, Dietz argued SB’s are not the inverse of PA, but each behavior (activity and inactivity) has independent health associations (24). This has been confirmed in numerous studies, where SB and insufficient PA are independently associated with obesity (89) metabolic syndrome (29), type II diabetes (54), and mortality (57). A detrimental dose-response association between TV viewing and waist circumference, systolic blood pressure and 2-hr plasma glucose persists among adults who are sufficiently active (45). The literature suggests that high levels of SB may negate the beneficial responses to exercise training; however this has not been experimentally tested.

The epidemiological and mechanistic evidence strongly suggest that sitting too much is a health risk (16). However, the majority of the evidence in the SB literature is cross-sectional or from prospective cohorts and therefore causation cannot be inferred (30). Few studies have examined how changing SB will impact health. Advances in technology and the industrial revolution have reduced occupational, transportation and domestic demands for PA (17). Our physical and social environment creates a ubiquitous sitting environment, which makes prescribing reductions in SB difficult. Promising evidence suggests “breaking up” sitting time is associated a better metabolic profile, independent of total sitting time (44). In addition, researchers have identified potential areas of intervention including reduction of discretionary sedentary time (such as watching television), utilizing active workstations, and promoting active transportation to reduce SB (16, 66). To date, only two published intervention trials targeting sedentary time reductions are available in adults (33, 74). Otten et al. (74) targeted TV viewing among overweight and obese individuals who watch TV > 3 hours per day and showed a 3.8% per day decrease in sedentary time. Their study targeted only one sedentary domain (TV viewing) and the primary outcome was percent of time in sedentary activities according to the Sensewear arm-band (74). Gardiner et al. (33) designed an intervention for older-adults who completed a 7-day baseline period followed by a 7-day intervention targeting sedentary time. They reported a 3.2% per day decrease in sedentary time (33). They did not exclude participants who were participating in MVPA at baseline, and occupational sitting was not a target for their intervention since many participants were retired. The primary outcome measure was the AG100 estimate of sedentary time (33). While both studies provide preliminary evidence that reducing sedentary time is possible, they did not include a population that is inactive at work, nor did they exclude participants who were active at baseline. Future research should determine the feasibility of reducing sedentary time among an at-risk population of overweight, non-exercising office-workers.

Measurement of physical activity and sedentary behavior

The Physical Activity Guidelines Advisory Committee recently identified poor measurement of PA exposure as a primary limitation to understanding the dose-response relationship between PA and chronic disease (78). Although there are limitations in the field of PA measurement, techniques specific to SB are far behind the PA measurement field (77). Research shows an association between SB and risk for disease, however, a major limitation is a lack of validated instruments to measure features of SB (77). The majority of research on SB has used self-report questionnaires (21). Few studies (i.e. 3 of 48 included in the Thorp review) have used activity monitors for SB research (90). The most common self-report measure of SB is time spent watching television (TV) (27, 53-54). In observational studies, robust positive relationships have been reported between TV viewing and poor health outcomes including risk of diabetes and premature mortality (36). However, TV viewing is also associated with increased energy intake and markers of poor health that may confound the association between SB and metabolic health (6, 22). Furthermore, while TV viewing is correlated with sedentary time among unemployed individuals, it is not for those who are employed. This suggests that TV viewing may be a poor surrogate measure for overall sedentary time (20). Other self-report measures include occupational sitting time (1), and global sitting time (54). However, no known self-report measure can comprehensively assess all SBs, self-reports have not been validated for measuring “breaks” or changes in SB, and they are subject to bias. Reviews assessing the validity and reliability of existing self-report measures concluded “reasonable” reliability and validity (21, 42, 69). Recently Healy and colleagues (42) concluded that self-report tools may be acceptable for establishing cross-sectional associations with health outcomes. However, due to variability and poor absolute agreement they may not be appropriate for assessing changes over time in cohort and intervention studies (42).

In response to the limitations of self-reports, researchers have used objective measures including pedometers and accelerometers to define SB. The pedometer definition of “sedentary”

as less than 5,000 steps per day does not provide any information on the quality or intensity of the steps and does not consider the independent association between PA, SB and risk for disease (91). Using an accelerometer-based activity monitor, SB is defined as an ActiGraph (Pensacola, FL) output of less than 100 counts·min⁻¹ (71). Studies utilizing ActiGraph accelerometers have shown a positive relationship between objectively measured SB and poor health outcomes (43). Although widely used, the pragmatic 100 counts·min⁻¹ cut-point was not empirically derived, and this monitor is not designed to distinguish postures. The ActiGraph monitor output for activities where an individual is standing including folding laundry and washing dishes is near or below 100 counts·min⁻¹ (62).

A promising tool engineered to quantify these low intensity activities and different postures (e.g. sitting vs. standing) is the activPAL (PAL Technologies, Glasgow, Scotland). This accelerometer has been validated in the laboratory to measure steps and time in various postures (35, 83). The device has not been evaluated in a free-living setting nor has it been shown to be sensitive to changes in time spent in sedentary activities in a natural setting. To date, no objective monitor has been validated for measuring sedentary and light intensity activity in a free-living situation.

Summary

Previously non-exercising individuals reduce their risk for disease on average following an exercise intervention; however there is remarkable variability in the response to exercise training (11). There is also large individual variability in SPA (94). Therefore, one could reasonably expect a range of SPA among participants in an exercise training study. There is preliminary evidence that differences in SPA during exercise training are linked to health outcomes (23, 68). Furthermore, strong evidence shows SB is associated with negative health outcomes (41); thus it is possible that SB during training negates the benefits of exercise. However, the influence of activity/inactivity level outside of training on an individual's responsiveness to training has not been examined. Furthermore, the robust associations between

SB and health outcomes in epidemiologic studies are promising (23). However, before public health recommendations targeting reductions in sedentary time are issued, more experimental studies are needed that compare reductions in sitting time with the benefits of moderate-to vigorous PA across a range of risk factors for chronic diseases. This dissertation addresses this knowledge gap by comparing changes in health outcomes of participants who receive a 12-week intervention to reduce sedentary time to those who are engaging in a traditional exercise intervention and those who receive both the exercise intervention and sitting time intervention (Chapter 4).

A primary reason that free-living activity and inactivity has not been adequately assessed during randomized-controlled trials is that is difficult measure free-living PA and SB accurately with existing measurement techniques. In chapter 2, evidence is presented that the activPAL is an accurate and precise measure of sedentary time compared to direct observation. In addition, Chapter 3 presents evidence that free-living reductions in SB are possible among non-exercising overweight office-workers and additional evidence is given that the activPAL tool is sensitive to measuring these changes.

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		Low/Mod	Low/Vig	High/Vig
Intensity (% VO ₂ max)		40-55%	65-80%	65-80%
Dose		14 kcal/kg/week	14 kcal/kg/week	23 kcal/kg/week
Equivalency (90kg)		Walk 12 mi/week	Jog 12 mi/week	Jog 20mi/week
Exercise time (min)		176 ± 36	117 ± 26	174 ± 35
VO ₂ max % change		6.9 % *	16.7%*	17.8%*
Body weight change		-0.55 ± 1.80 kg *	-0.17 ± 1.79 kg *	1.52 ± 2.16 *
VAT (95cm baseline)		-1.6 (3.1)cm*	-1.4 (2.8)cm*	-3.4 (3.4)cm**
TG (change in mg/dl)		-51 *	-14	-20
Insulin sensitivity (mU/L/min)	Baseline	3.0 ± 2.3	3.9 ± 2.2	3.7 ± 2.7
	Change	1.6 ± 2.1 *	0.5 ± 1.7	1.5 ± 2.2 *
Metabolic syndrome z-score	Baseline	-0.5 ± 2.4	-1.0 ± 2.5	-0.9 ± 3.0
	Change	-0.8 ± 1.6 *	-0.3 ± 1.4	-1.4 ± 1.7*
RT3: total daily EE		74.9 kJ/hr	49.4 kJ/hr	137.3 kJ/hr *

Table 1 Exercise doses and results from STRRIDE trial.

CHAPTER III

VALIDATION OF WEARABLE MONITORS FOR ASSESSING SEDENTARY BEHAVIOR

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Introduction

Sedentary behavior, defined as energy expenditure between 1 and 1.5 METs while sitting or lying, is detrimental to one's health (15). Independent of physical activity status, there are positive associations between sedentary behavior and risk of obesity, (20) metabolic syndrome (2), type II diabetes (9), and mortality (3, 11). Despite these observations, we lack validated instruments to measure sedentary behavior (16). The majority of sedentary behavior research uses self-report questionnaires including surrogate measures such as time spent watching TV (1). However, no self-report measure comprehensively assesses all components of sedentary behavior. In particular, patterns of inactivity such as breaks <5 minutes or changes in sedentary behavior are challenging to measure with a self-report instrument.

In response to the limitations of self-report instruments, researchers have begun to use objective measures, including pedometers and accelerometers, to quantify sedentary behavior. Five thousand steps per day defines the upper boundary for sedentary behavior using a pedometer, but this definition does not distinguish between sitting and standing time, nor does it describe patterns of inactivity within a day (22). As a result, researchers primarily use accelerometer-based activity monitors to assess sedentary behavior. In studies that use the ActiGraph (AG) (ActiGraph LLC, Pensacola, FL) activity monitor, a sedentary minute is defined as one when the monitor output is less than $100 \text{ counts} \cdot \text{min}^{-1}$ (14). Such studies have shown a robust relationship between objectively measured sedentary behavior and health outcomes (7-8). Although widely used, the $100 \text{ counts} \cdot \text{min}^{-1}$ cut-point (AG100) was not empirically derived. Additionally, the AG monitor is a single hip-mounted device that may not be able to distinguish

postures (e.g. sitting vs. standing). For example, the AG monitor output for standing activities, such as folding laundry and washing dishes, can be near or below 100 counts·min⁻¹ (13), and these activities are not sedentary. In general, the ability of this monitor to distinguish between sedentary time and light-intensity activity time is not known. The activPAL (AP) (Physical Activity Technologies, Glasgow, Scotland) is a promising tool designed specifically to measure free-living activity. It has the ability to differentiate among postures and classify an individual's activity into time sitting, standing and stepping. This device has been validated in the laboratory compared to a criterion measure (direct observation (DO)) and was recently found to be 100% accurate for measuring sitting, standing, and walking (5, 18). However, the AP has not been validated in a free-living setting compared to DO. A recent study examined the convergent validity of the AG and the AP and reported that on average, the AG recorded 132 minutes more sedentary time than the AP over 15 hours (6). In this study a criterion measure was not used and thus, it cannot be determined which monitor was more accurate.

These activity monitors have not been validated for assessment of sedentary behavior in a free-living environment compared to a criterion measure. Therefore, the primary aim of this study was to validate the AG100 and the AP monitor for assessing sedentary behavior. We validated the monitors in two ways: 1) assessing the difference between monitor estimates and DO measures of sedentary behavior, 2) examining monitor performance in detecting reductions in sedentary behavior among inactive individuals. A secondary aim was to determine if the AG100 is the most appropriate cut-point for the AG. We compared the validity of the AG100 to other count cut-points ranging from 50 counts·min⁻¹ (AG50) to 250 counts·min⁻¹(AG250) using DO as the criterion method.

Methodology

Eligibility and Recruitment: Participants were recruited from the University of Massachusetts, Amherst and local communities via fliers and word of mouth. Eligible participants were at least 25 years old, overweight or obese (body mass index (BMI) > 25 kg·m⁻²), and

inactive, which was defined as participating in less than three days per week of moderate physical activity for 20 minutes per session over the preceding six months. Participants were employed in an occupation where the majority of the work day was spent sitting.

Eligible participants reported to the University of Massachusetts and signed an Informed Consent Document that was approved by the University of Massachusetts Institutional Review Board. Participants then completed a physical activity readiness questionnaire (PAR-Q), a health history questionnaire, and a physical activity status questionnaire. Following the consenting process, height and weight (to the nearest 0.1kg) were measured using a floor scale/stadiometer (Detecto; Webb City, MO) while participants wore a thin layer of clothing and no shoes. The sample included five males and 15 females. The average age of the participants was (mean (SD)) 46.5(10.7) years. The average BMI was 33.7(5.7) kg·m⁻².

Procedures: Participants completed two, 7-day conditions. The first condition was a baseline measurement where participants were asked to maintain their current level of activity and were specifically directed not to initiate any exercise programs (sedentary condition). In the second condition participants were prescribed strategies to reduce sitting time (active condition). During both study conditions participants concurrently wore the AG monitor and the AP. Participants were instructed to wear the activity monitors during all waking hours each day. During both conditions, participants were directly observed in their free-living environment for one, 6-hour period.

Strategies to reduce sitting: At the end of the 7-day sedentary condition, participants were given recommendations to increase their time standing and decrease their time sitting. They were provided with detailed information about the health risks associated with sedentary behavior and the benefits associated with increasing light-intensity activity. They were given examples and strategies for decreasing sedentary time and accumulating light intensity activity (e.g., standing during all commercials while watching television, taking a 5-minute ‘standing/walking’ break each hour at work). To help facilitate compliance, participants were given daily and hourly

checklists of tasks to complete. The checklists helped participants self-monitor their compliance and also served as regular reminders for participants to break up their sitting time. During the active condition, participants were given a pedometer step goal of at least 7500 steps per day. This step goal has been designated as the lower boundary of “somewhat active” behavior (22).

Criterion measure, direct observation: Participants were observed for six consecutive hours, once per condition. The majority of observations took place during participants’ working hours. A custom DO program was developed for a personal digital assistant (PDA) (Palm Tungsten E2, Palm Inc., Sunnyvale, CA). The PDA was synchronized with the activity monitors prior to each data collection session. Three researchers completed DO training that included review of a training manual, two hours of training videos and DO practice sessions with the PDA for a minimum of 12-hours. Following the training, trainee’s completed a testing video that was 25 minutes in duration and included 20 different video clips, each containing various postures and activities. Prior to data collection, researchers were required to correctly classify 90% of the body positions, intensity levels, and duration of activities throughout the training video.

Focal sampling and duration coding were employed, with trained data collectors coding the real-time occurrence of the five activity categories, body positions and intensities described below:

- 1- **Lying:** the individual was flat on their back (horizontal)
- 2- **Sitting:** the individual had some of their body weight supported by the buttocks or thighs. The upper body was not parallel to the ground. If the person was kneeling they were coded based on the thigh position (i.e., if the thigh is parallel to the ground sitting was selected).
- 3- **Standing still:** the individual was standing with little or no contribution from the upper body. The individual was not carrying a load greater than 1 kg. Standing still included talking with hand gestures, looking at something or waiting in a line.
- 4- **Standing still with upper body movement:** the individual was upright with some contribution from the upper body that causes an increase in energy expenditure (holding a load greater than

1kg, filing papers or doing a task that requires the arms). The purpose of the activity had to include the upper body.

5- **Standing/moving**: the individual was engaging in activities that are of light intensity (<3 METs) (e.g., walking at a speed less than 2.5mph and not be carrying a load). These activities included movements around an office or a home but not for locomotion (e.g. travelling between one place and another).

6- **Moving Moderate**: the individual was engaging in activities greater than 3 METs.

Examples include walking faster than 2.5 mph, gardening, vacuuming, and carrying a load.

7- **Moving Vigorous**: the individual was engaging in activities greater than 6 METs.

Typically involves purposeful exercise including jogging, walking briskly uphill, and sporting activities. Total sedentary time was determined by summing/totaling the amount of time spent in lying and sitting body positions from the DO coding system. Any other body positions or postures were not considered sedentary behaviors.

Activity Monitors: The AP is a small (2.0 x 1.4 x 0.3 inches) and light (20.1 grams) single unit accelerometer device worn on the mid-right thigh (attached by non-allergenic adhesive tape), and uses accelerometer-derived information about thigh position to estimate time spent in different body positions (horizontal = lying or sitting; vertical=standing) in 15 second epochs. When the participant was stepping, the device measured step cadence and number of steps. The AP output of time spent sitting/lying was defined as sedentary behavior.

The AG (model GT3X) is a small (1.5 x 1.44 x 0.7 inches) and light (28 grams) triaxial accelerometer that was secured to the right hip using an elastic belt. Firmware version 2.1.0 was used and the low-frequency extension was selected. The monitor was initialized to record vertical acceleration in one second epochs. Sedentary time was defined as the sum of the minutes where the monitor output was below a specific count threshold (e.g., time below $100 \text{ counts} \cdot \text{min}^{-1}$ was sedentary for AG100). We examined the following five count thresholds for sedentary behavior;

50 counts·min⁻¹ (AG50), 100 counts·min⁻¹ (AG100), 150 counts·min⁻¹ (AG150), 200 counts·min⁻¹ (AG200), and 250 counts·min⁻¹ (AG250).

Data Cleaning: To be included in the analysis a participant was required to have simultaneous AG, AP and DO data. Two participants wore the AP monitor upside down during one of the observation periods and for one participant the AP stopped recording prematurely (data not included). One participant used a chair at work that supported her lumbar spine and resulted in a vertical thigh position (perpendicular to the floor) while she was seated. As a result, the observer was unsure how this should be coded and sitting time was recorded as standing by the AP, thus the data from this participant was not included in the analysis. Of the 20 enrolled participants 16 had valid data for both DO sessions and 19 participants had valid data for at least one DO session. This resulted in a total of 12,132 observation minutes with corresponding monitor data. On average each participant was observed for 346 minutes (5.8 hours) per observation.

Statistical Analyses: To determine the validity of the AG100 and AP monitors, we performed two analyses. First, we compared the monitor estimates to the DO measures of sedentary time, and second, we evaluated the ability of the monitors to detect reductions in sitting time. We used a repeated measures linear mixed model to determine the ability of the AG100 and AP to estimate sedentary time in free-living subjects compared to DO. Both accuracy (i.e., bias: The extent that each monitor overestimated or underestimated sedentary time) and precision (i.e., variability or random error: How far the estimate of sedentary minutes randomly fluctuate above and below its average value for each person on each day) were evaluated. We measured bias in units of minutes (*monitor sedentary minutes – DO sedentary minutes*) and as a percentage ($((\text{monitor sedentary minutes} / \text{DO sedentary minutes}) - 1) * 100$). In both cases, positive biases indicated overestimates of sedentary behavior and negative values indicated underestimates of sedentary behavior. The percentage bias is useful because, for instance, a 10% bias could be applied to an observation time of 10 hours (a one hour overestimate) or an observation time of 70

hours (a seven hour overestimate). We used correlation and confidence intervals as measures of precision. Higher precision was indicated by higher correlations and smaller confidence intervals.

The second method for validating the monitors was to evaluate if the monitors could detect changes in sedentary behavior between a sedentary and an active condition. Using the DO data, a subset of participants (n=11) were identified who reduced their sitting time in the active condition compared to the sedentary condition. A repeated measures linear mixed model was used to compare the differences in mean sitting time between conditions and separate models were fit for DO, AP, and AG. Likelihood ratio tests were used to determine if there were statistically significant differences across conditions within subjects. The likelihood ratio test examined if the addition of condition as an independent variable resulted in a significantly better fit. If it did not, then the variability in the measurements was too large to statistically discern the changes in sedentary time within subjects. All statistical analyses were performed using R- software packages (www.r-project.org) (21). Significance levels were set at $p < 0.05$.

The secondary aim of the study was to determine if the AG100 was the most accurate and precise cut-point to assess sedentary behavior. The AG100 cut-point was compared to cut-points of 50, 150, 200, and 250 counts·min⁻¹. The analyses described above were repeated for each count cut-point.

Results

The directly observed data for time spent sedentary was normally distributed over the days and subjects within each condition. The mean (SD) percent of directly observed time sedentary during the sedentary condition was 78.1% (16.5%), which is equivalent to 269.5 (60.9) sedentary minutes. For the active condition, the average percent of observed time spent sedentary was 69.5% (11.2%), which is equivalent to 242.9 (43.0) sedentary minutes.

On average, both the AP and the AG100 underestimated sedentary time compared to DO. Figure 1 shows the bias in minutes and as a percentage. The AP bias was -7.7 min and standard error (SE) was 2.5 min (95% Confidence Interval (CI) -12.5 to -2.9 min). The AG100 bias was -

16.9 min and SE was 8.5 min (CI -33.6 to -0.3 min). Using percent bias, the AP underestimated sitting time by 2.8% (SE 1.0%; CI -4.7 to 0.9%) while the AG100 underestimated sitting time by 4.9% SE of 3.4%; CI -11.6 to 1.8%). The results of the secondary aim analysis illustrate that the AG cut-point with the lowest bias was AG150 (bias =-0.9 minutes; SE = 7.7 minutes [95% CI – 15.9 to 14.1]) (Figure 1). The AG150 also had the lowest percent bias of 1.8% (95% CI –5.3 to 8.9). The percent biases and bias in minutes for AG50, AG200 and AG250 were higher than the commonly used AG100 (range: -22% to 17.8%; -60 minutes to 32 minutes) (Figure 1). Figure 2 is a modified Bland-Altman plot to illustrate the relationship between the DO and the AP percent of time sedentary $R^2= 0.94$, the DO and the AG100 $R^2= 0.39$, and the DO and AG150 percent of time sedentary $R^2= 0.40$.

Of the 16 participants with valid data at both observation periods, 11 reduced their sedentary time during the active condition compared to the sedentary condition. The smallest change in sitting time among the responders was a 2% reduction in sitting time during the active condition compared to the sedentary condition. In this sub-set of participants the average percent of time sedentary was significantly different between conditions based on DO ($p<0.01$) (Figure 3). According to DO, sedentary time was 83.7% (11.2%) of the sedentary condition and 68.5% (11.4%) of the active condition. Sedentary time was significantly different between conditions ($p<0.01$); according to the AP, it was 79.5% (13.8%) of the sedentary condition and 66.5% (10.2%) of the active condition. The AG100 estimate of sedentary time was not significantly different between conditions ($p=0.2$) it was equal to 70.5% (17.8%) of the sedentary condition, and 66.9% (11.9%) of the active condition. Although the AG150 had the lowest bias for the AG monitor, it was not sensitive to reductions in sitting time between conditions ($p=0.3$), nor were any other AG count cut-points (Figure 3).

Discussion

As evidence accumulates that sedentary behavior is associated with premature mortality and chronic disease it is imperative we have accurate measures of the time spent in sedentary

behaviors (3, 15). The major finding of the current study was that the AP is an accurate and precise monitor for measuring sedentary behavior and is sensitive to reductions in sitting time. Our results support the use of the AP in studies designed to determine the effects of sedentary behavior and changes in sedentary time on health outcomes. Another important finding was that the AG count cut-point of 150 counts·min⁻¹ was the most accurate AG cut-point to define sedentary behavior. Using the previously defined sedentary cut-point of 100 counts·min⁻¹ for the AG monitor resulted in a significant underestimation of sitting time in our sample.

In this study we report the bias and precision validation for each estimate of sitting time. Bias is the average difference between the estimate (monitor prediction) and the criterion (DO). The bias is commonly reported as it reflects the accuracy of the monitor and whether the monitor over or under-estimates sitting time. The AP had a slightly smaller bias (-2.8%) than the AG100's bias (-4.9%), but these were not statistically different. Although bias is an important measure, when differences in sitting time pre and post intervention are considered the biases cancel each other. Thus, bias does not impact the sensitivity of the monitor to detect changes following an intervention. In contrast, precision (i.e. variability or random error) is of vital importance in the application to intervention trials. The higher precision of the AP compared to the AG (smaller standard error, higher correlation) results in higher statistical power, more reliability, and smaller sample size requirements. This was illustrated in this study when we examined the sensitivity of the monitors to detect changes between conditions where only the AP could detect the reductions in sedentary behavior (Figure 3).

Large bias and low precision also impairs the ability to identify a dose-response relationship between a sitting time and health outcomes. Data from the National Health and Nutrition Examination Survey (NHANES) using the AG100 to define sedentary behavior reported that adults spend 55% of their waking hours in sedentary behavior (14). Our results suggest sitting time was underestimated in the NHANES sample by approximately 4.9%, equivalent to 35 minutes during a 14-hour day (14). Although this is a potentially important

underestimation, it is a systematic error that could be corrected. The wide confidence intervals of the AG100 are a more critical issue in our study since it reflects large random error. If we apply the estimates from our confidence intervals to the waking day (14-hours) in the NHANES sample, the random error is between a 97 minute underestimation and a 15 minute overestimation of sedentary time. This nearly two hours of random error is by definition unpredictable and leads to challenges in identifying doses of sedentary behavior that are detrimental to one's health. While the low precision of the AG monitor in measuring sedentary behavior is concerning, studies using this monitor have reported positive associations between sedentary behavior and disease risk (8). Therefore, future studies using a more accurate and precise monitor may provide more consistent and robust associations between sedentary behavior and health outcomes.

The second aim of this study was to determine if the commonly used AG count cut-point of 100 counts·min⁻¹ is the most appropriate cut-point for sedentary behavior. Our results suggest the AG150 provided a better estimate of sedentary behavior than the AG100, but there were minimal differences in precision between cut-points. Although the AG150 had a smaller estimated bias than the AP, the difference between the two (1.8% and -2.8%, respectively) is small and likely not meaningful. Additionally, as discussed above, the AP provides more precise estimates of sedentary behavior than the AG. In order to determine the source of error in the AP monitor, we examined the difference between AP standing and stepping time. Over the course of a 6-hour period, 8 minutes of sitting time were incorrectly classified as standing time, which was overestimated by 11.5 minutes (stepping time was underestimated by ~3.5 minutes). We did not examine where the error in the AG monitor was since the AG monitor output does not provide standing time.

Recently, Hart and colleagues examined the convergent validity of the AP and the AG100 and reported that the AG100 resulted in significantly more sedentary time than the AP over a 15 hour period, which is not consistent with our results (6). However, the authors did not report whether the low frequency extension was used so it is difficult to interpret the meaning of

the magnitude of the differences in sedentary time between studies. Our data were collected with the low frequency extension filter option selected. The option was added to the GT1M and GT3X monitors by the manufacturer after investigators noted that a greater magnitude of acceleration was required to elicit a non-zero count than was required for the AG 7164 (10, 12,17). Therefore, we can only generalize our results to data collected with the 7164 or GT1M/GT3X using the low-frequency extension.

Prior to selecting a monitor for a study it is important to consider the purpose of the study and the type of exposure being investigated. Based on the results of this study, investigations exclusively focused on the measurement of sedentary behavior should consider using the AP monitor. However, during non-sedentary time the AP only provides an output of stepping time and cadence of the steps, from which one cannot estimate activity intensity or the type of activity being performed. In contrast, the AG has been used extensively to measure physical activity and exercise time. Using the AG, data processing techniques have been developed to quantify time in MET intensity categories and estimate time in various activity types (e.g., locomotion, sport) (19). Therefore, an individual may consider the AG if a range of activity intensities in addition to or in lieu of sedentary behavior is required.

This study has important limitations that should be noted. First, although DO is considered a criterion measure, human error may affect the accuracy of the DO results. We minimized this by having all observers complete a training program to standardize methods between observers before the commencement of data collection. The AG monitor sampled in 1-second epochs and it is unlikely the data collector coded the exact second a change in posture occurred. Our study sample was relatively small and included participants who were overweight or obese. We selected this group because approximately seventy percent of the current US population is overweight and these individuals are most likely to be targeted for interventions to reduce sedentary behavior (4). It is also important to note that our results may not generalize to individuals whose occupation or lifestyle behaviors included a different set of activities such as a

factory employee or a restaurant worker who stands or is active the majority of the day.

Approximately 90% of the observed time was in an office environment where participants were performing employment duties such as computer work, filing papers, delivering messages and moving around the office building.

There are important strengths to this study. We directly observed participants for over 1000 hours while the monitors were worn. To our knowledge, no other study has validated both the AP and AG monitors in a free-living environment using DO as a criterion measure. An additional strength was that we assessed the monitor's sensitivity to detect change in behavior by comparing a sedentary condition to an active condition. Activity monitors are commonly used in intervention studies to quantify pre-post changes and in epidemiological investigations to distinguish patterns of sedentary behavior. Thus, it is critical to consider the sensitivity of activity monitors to changes in patterns of behavior as a standard practice for validation studies.

This paper provides the first known free-living validation of activity monitors compared to a criterion measure of sedentary behavior. The commonly used AG100 cut-point underestimates sitting time to a greater extent than the AG150 compared to DO. Researchers using the AG monitor to estimate sedentary behavior should consider using the count cut-point of 150 counts·min⁻¹. Compared to DO, the AP monitor provides a precise estimate of sedentary behavior and the AP is sensitive to reductions of sitting time. The lower absolute bias and higher precision of the AP suggest the AP is a more appropriate monitor for measuring sedentary time than the AG.

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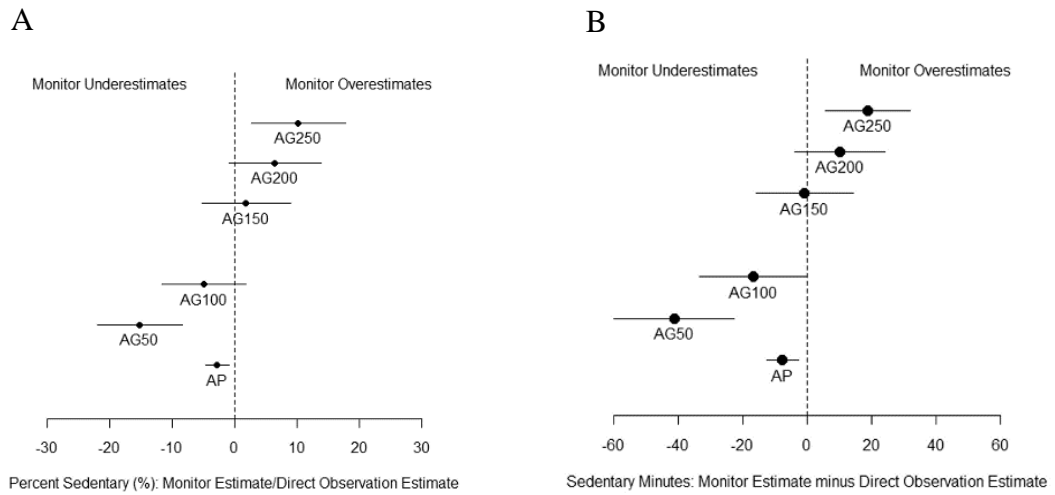


Figure 1. ActivPAL and ActiGraph under- and over-estimation of sedentary time compared to direct observation. A) percent bias and B) sedentary minutes. The closed circles are the bias and the lines illustrate the 95% confidence intervals. AP refers to the activPAL monitor. AG50 refers to the ActiGraph count cut-point of 50 counts·min⁻¹, AG100 refers to the ActiGraph count cut-point of 100 counts·min⁻¹, AG150 refers to the ActiGraph count cut-point of 150, AG200 refers to the ActiGraph count cut-point of 200, and AG250 refers to the ActiGraph count cut-point of 250.

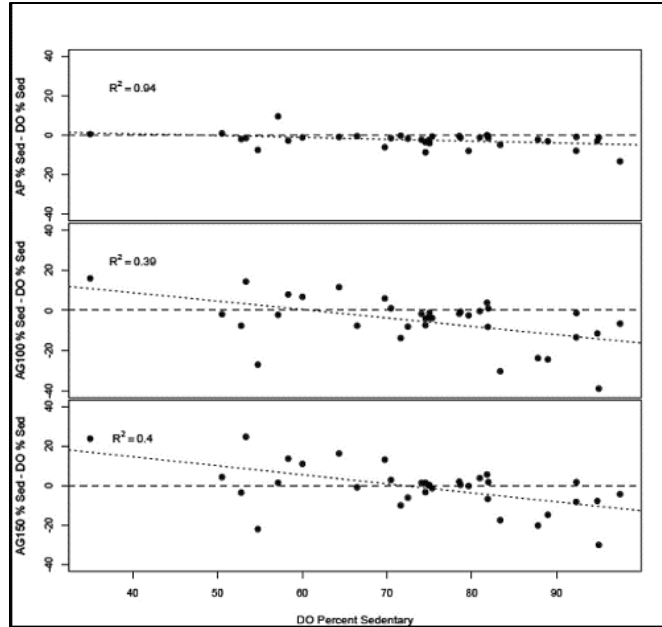


Figure 2. Modified Bland-Altman plots of the estimates of percent time sedentary. The least squares regression line is dotted and the line at zero is dashed. AP refers to the activPAL monitor. AG150 refers to the ActiGraph count cut-point of 150 counts·min⁻¹, AG100 refers to the ActiGraph count cut-point of 100 counts·min⁻¹.

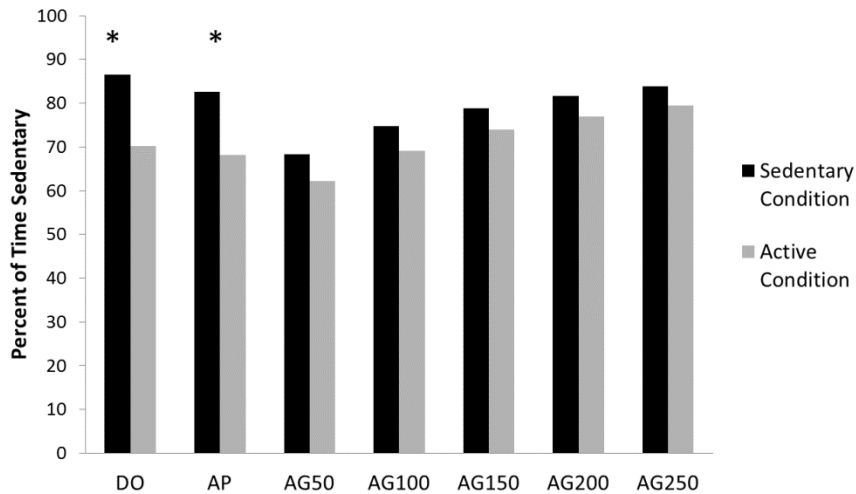


Figure 3. Sensitivity of monitors in distinguishing between sedentary and active conditions. * indicates the difference between conditions is significant at $p < 0.05$. AP refers to the activPAL monitor. AG100 refers to the ActiGraph count cut-point of 100 counts·min⁻¹, AG150 refers to the ActiGraph count cut-point of 150, AG200 refers to the ActiGraph count cut-point of 200, and AG250 refers to the ActiGraph count cut-point of 250.

CHAPTER IV

THE FEASIBILITY OF REDUCING AND MEASURING SEDENTARY TIME AMONG OVER WEIGHT, NON-EXERCISING OFFICE WORKERS

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Introduction

Sedentary behavior is defined as energy expenditure of < 1.5 metabolic equivalents (METs) while sitting or reclining (27) and accounts for the majority of occupational, transportation, and discretionary time (32). Using data from the National Health and Nutrition Examination Survey, Matthews et al. reported that 54% of waking hours were sedentary (25). Among healthy, predominantly overweight individuals, 62-68% of waking hours are spent in sedentary behaviors (24). A growing body of evidence shows that sedentary time is associated with an increased risk of obesity, chronic disease, and mortality (27). However, to date, the majority of evidence linking sedentary behavior to adverse health consequences is cross-sectional (15-16, 22), from which causality cannot be determined. A recent review by Thorp et al. (29) concluded there is some prospective evidence that supports relationships between sedentary behavior, mortality, and health outcomes. Studies have shown that sedentary time is associated with increased risk for type II diabetes (17-19) and mortality (6). Other studies report no association or suggest reverse causality between sedentary time, obesity, and insulin resistance (7-8). Studies often failed to adjust for physical activity and BMI, which may explain the disparate results (29). In addition, the majority of these studies used surrogate measures of sedentary time (e.g., TV viewing) and self-report measures, and they may not accurately measure sedentary time.

Sedentary time is frequently estimated from surrogate measurements such as time spent watching television (TV) (6, 19-20). Robust positive relationships have been reported between TV viewing and poor health outcomes including risk of diabetes and premature mortality (13). However, TV viewing is also associated with increased energy intake and markers of poor health that may confound the association between sedentary time and metabolic health (1, 3). Furthermore, while TV viewing is correlated with sedentary time among unemployed individuals, it is not for those who are employed. That suggests that TV viewing may be a poor surrogate measure for overall sedentary time (2). Self-report questionnaires, including those that measure domain specific (23) and single-item (5) sitting time, are also available. A recent review by Healy and colleagues suggests that existing questionnaires may be acceptable for establishing cross-sectional associations but may not be acceptable for prospective or intervention trials (14). The authors note a paucity of data on the absolute agreement of sedentary time estimates from self-report questionnaires, and few studies have compared sedentary time questionnaires to a valid criterion measure (14).

Activity monitors are attractive tools to measure sedentary time. To date though, few studies (3 of 48 included in the Thorp review) have used activity monitors for sedentary behavior research (29). The ActiGraph (AG), using the cut-point of 100 counts·min⁻¹ (AG100) is the most commonly used objective tool to assess sedentary time. Previous research from our laboratory showed that the activPAL (AP) activity monitor is more accurate, precise, and sensitive to detecting changes in sedentary time than AG using a number of sedentary time cut-points ranging from 50 to 250 counts·min⁻¹ (21). However, our validation results were based on two, 6-hour direct observation sessions, and do not include factors such as day-to-day variability that is important to quantify for intervention studies designed to decrease sedentary time. To date, no studies have used the AP, a criterion measure of sedentary time (12), to compare the validity of existing measurement tools over a 7-day period, or to assess the ability of existing measurement tools to detect *changes* in free-living sedentary time.

While an abundance of evidence suggests that sedentary time is associated with poor health outcomes, we do not know the feasibility of reducing sedentary time, the validity of existing measurement tools over a 7-day period, or the ability of existing measurement tools to detect changes in free-living sedentary time (14, 28). This study addressed these knowledge gaps with the following three aims. First, we determined if a simple one-week sitting time intervention decreased sedentary time as measured by the criterion AP among non-exercising, overweight/obese individuals with sedentary occupations. We compared sedentary time pre-post intervention for the total week and for weekend and weekdays. Second, we compared whether or not existing questionnaires and activity monitors detected reductions in sedentary time following the 7-day intervention. Third, we compared the convergent validity of the AP, the AG, and the questionnaires.

Methodology

Participants

Participants were recruited from the University of Massachusetts, Amherst and local communities. Eligible participants were between 20 and 60 years of age, overweight or obese with a body mass index (BMI) between 25 and 45 kg·m⁻², inactive (i.e., participating in moderate to vigorous physical activity [MVPA] < 3-days per week for < 20 minutes per session in the preceding six months), and employed in jobs where the majority of their day was sedentary (i.e. participants self-reported over 75% of their work day as sedentary). Potential participants completed a telephone screening to determine eligibility.

Study Protocol

Visit One: Eligible participants reported to the laboratory at the University of Massachusetts for an informed consent visit. Participants read and signed an informed consent document (ICD) that was approved by the Institutional Review Board at the University of Massachusetts. After signing the ICD, height and weight were measured. The average (SD) age

was 46.5 (10.8) years and BMI was 33.7 (5.6) kg·m⁻². Seventy-five percent (15/20) of the participants were female. Participants were shown the activity monitors (described below) and were provided with detailed verbal and written instructions on proper monitor placement. They were instructed to wear the monitors for a 7-day period while maintaining habitual activity levels. This was the *baseline period*.

Visit Two: After wearing the monitors for 7-days, participants returned to the laboratory and the activity monitor data were downloaded. Participants completed two self-report questionnaires (described below) with questions about sitting time during the previous 7-days (*baseline period*).

Intervention: A researcher provided the participant with information about the potential health risks associated with sedentary time and the benefits associated with increasing light-intensity activity. Participants were given a packet that contained a list of strategies to reduce sedentary time and a checklist to monitor sedentary time for each of the next 7-days. The document outlining strategies to reduce sedentary time included an extensive list of ways to replace sedentary time with light-intensity activity (Table 2). The packet also included a form asking participants about specific barriers in their free-living environment that would inhibit reductions in sedentary time. They were then counseled on specific ways to overcome those barriers. In addition, they were given a daily checklist reminding them to break-up sedentary time by reporting if they stood or walked for five or more minutes for each hour of the day. Finally, participants were provided a pedometer to wear for the next 7-days and given a goal of attaining 7500 steps/day, the lower boundary for “somewhat active” behavior (14, 31).

Participants were instructed to accumulate the steps in 5-15 minute bouts over the course of the day rather than one large bout of activity. Participants were instructed to wear the AG and AP activity monitors for another 7-day period and were asked to follow the recommendations to reduce sedentary time. This was the *intervention period*.

Visit three: Participants returned the monitors on the third visit and completed the same two self-report questionnaires completed at visit one. These questionnaires asked about time spent sedentary in the previous 7-days (*intervention period*). After completing the questionnaires, participants were asked the following questions about the intervention period: “Was the pedometer step per day goal helpful in meeting your goals? Why or why not?”, “Was the daily checklist helpful for meeting your goals?”, and “Did you fill out the checklist (circle the one that best applies)” (1) once a day (2) as you completed activity (3) every couple of days (4) once in the week.

Measurements

activPAL activity monitor (PAL Technologies, Glasgow, Scotland): This is a small (2.0 x 1.4 x 0.3 inches) and light (20.1 grams) uniaxial accelerometer-based device that was worn anteriorly on right mid-thigh, and held in place by non-allergenic adhesive tape. This device uses accelerometer-derived information about thigh position to estimate time spent in different body positions (i.e., sitting/lying, standing and stepping). Data were collected for a one-week period and processed in 15-second epochs using activPAL software (version 5.8.3). We previously validated the activPAL monitor for measuring free-living sedentary time in the same subjects as the current study (21). The activPAL was valid and precise with a bias of 2.8% and an R^2 value of 0.94 compared to direct observation (21). The monitor was also sensitive to reductions in sedentary time (21). In a laboratory-based validation, Grant et al. (12) reported a mean percentage difference between sedentary time from the monitor and direct observation of 0.19%, and the mean difference for total time spent upright was -0.27%.

ActiGraph GT3X activity monitor (Actigraph LLC, Pensacola, FL): This is a small (1.5 x 1.44 x 0.7 inches) and light (28 grams) accelerometer that was worn on the right hip, secured by an elastic belt. The monitor was initialized using ActiLife software version 4.2 and firmware version 2.1.0. The monitor was initialized to record vertical accelerations in 1-second epochs with the low frequency extension option activated. Count cut-points of 100 counts·min⁻¹ (AG100) and

150 counts·min⁻¹ (AG150) were used to define sedentary time. The Freedson cut-point of 1952 counts·min⁻¹ was used to define moderate to vigorous physical activity (MVPA) (9).

Omron Pedometer HJ720-ITC (Omron Healthcare, Bannockburn, Illinois): Pedometers have been used to provide referent goals for individuals to estimate activity levels. For example, <5000 steps/day is sedentary, 5000-7499 steps/day is low active, and >10,000 steps/day is active (31). The pedometer provided a self-monitoring tool to facilitate compliance with sedentary reduction recommendations, but since pedometer steps are not a direct measure of sedentary time, it was not considered in the primary analyses.

Total Sitting Questionnaire (T-SQ) The short-version of the International Physical Activity Questionnaire (IPAQ) was used to assess usual time sitting in total number of hours and minutes per day for both work and non-work days (5). The question reads, “How many hours did you spend sitting down while doing things like visiting friends, driving, reading, watching TV or working at a desk or computer on a typical workday in the last week.” In a sample of 744 adults, the test-retest reliabilities for the sitting items from this questionnaire ranged from $r = 0.18$ to $r = 0.95$ and criterion validity compared to the AG100 had low to moderate agreement ($r = 0.07$ to $r = 0.61$) (5).

Domain Specific Questionnaire (D-SQ) This questionnaire asks about time spent sitting in hours and minutes on a typical weekend day and weekday over the past 7-days in each of five domains: transportation, watching television, at work, using a computer at home, and leisure time not including television (e.g, visiting with friends). The test-retest reliability and convergent validity compared to the AG100 for the five sitting domains range from $r=0.31$ to $r = 0.91$ and $r=0.13$ to $r = 0.74$, respectively. Both reliability and validity were lower for weekend days compared to weekdays (23). To score the data, the sum of the sitting times from the five domains was used to estimate daily sitting time.

TV viewing (TV-Q): The TV viewing question from the DS-Q was used to determine total time watching television. The question reads “please estimate how many hours per day you spend sitting while watching television.”

Monitor log and wear time

All participants recorded details about monitor wear in a log used to determine monitor wear-time. Participants were asked to record the time they woke up in the morning, the time they put the monitors on, the time they took the monitors off, and the time they went to bed. They were also asked to indicate any times they took the monitors off during the day for greater than ten minutes. To be included in the analyses a participant was required have at least four days of monitor wear for at least ten hours each within each period (30).

Statistical Evaluation

Twenty participants completed the study protocol. One participant was excluded from all analyses because the participant sat in a seat where the thigh was perpendicular to the floor while seated. This resulted in erroneous standing time estimate from the AP tool. All statistical analyses were performed using R (www.r-project.org). Significance levels were set at $p < 0.05$. The data were graphically examined using q-q plots and histograms to confirm normality.

Effect of the Intervention: Primary outcome measure AP: To eliminate the effect of different wear times, we computed the percentage of wear time that was sedentary (i.e., (sedentary hours/total wear-time)*100) for each day. A repeated measures linear mixed model was then used to compare the differences in percent sedentary time pre- to-post intervention. A separate model was also fit for percent stepping, percent standing, breaks per day (i.e., sit-to-stand transitions), steps per day, and wear time. We also examined the differences pre- to post-intervention for week and weekend days separately. Likelihood ratio tests were used to determine if the difference in each outcome measure pre-to-post intervention was significant.

Sensitivity to Change: A repeated measures linear mixed model and likelihood ratio tests were used to analyze the differences pre-to post-intervention in percent sedentary time for the

AG100 and AG150. A paired t-test was used to examine the differences pre- to post-intervention for T-SQ, D-SQ, and the TV-Q. We also assessed the sensitivity and specificity for each measure compared to the AP. Based on the AP, an individual was classified as a responder (reduced sedentary time) or non-responder (did not reduce sedentary time) during the intervention period compared to the baseline period. There was no minimum amount of change required to count as a responder. We then identified responders and non-responders to the intervention for each of the other measures and categorized them based on the following criteria:

1. True positives: The individual was a responder according to both the AP and the measure.
2. True negative: The individual was a non- responder according to both the AP and the measure.
3. False positive: The individual was a non- responder according to the AP, but was a responder according to the measure.
4. False negative: The individual was a responder according to the AP, but was a non-responder according to the measure.

Sensitivity was calculated as the true positives/ (true positives+ false negatives)*100. Specificity was calculated as the (true negatives/(true negatives + false positives))*100. The 95% confidence intervals (CI) were calculated for both sensitivity and specificity.

Convergent Validity: For the third aim we assessed the validity of the questionnaires, AG100 and AG150 for measuring baseline sedentary time per day with the AP serving as the criterion measure. Since the questionnaires ask about weekend and weekdays separately, we examined weekend and weekdays separately for the activity monitors.

We assessed bias and precision to determine validity. Bias is the average difference of the estimate from the measure (AG100, AG150, T-SQ, and D-SQ) and the AP sedentary time (minutes). A positive bias indicates the measure overestimates sedentary time and a negative bias

indicates the measure underestimates sedentary time. Precision is the inverse of variability or random error, which was examined using confidence intervals and Pearson correlations. Higher precision was indicated by higher correlations and smaller confidence intervals. For the TV-Q we assessed the Pearson correlation between AP daily sitting and TV-Q but did not assess bias, since the TV-Q does not produce an estimate of overall sedentary time.

Results

Efficacy of the Intervention

Changes pre- to post-intervention: Participants significantly reduced sedentary time according to the AP from 67.0% of wear time in the baseline period to 62.7% of wear time in the intervention period ($p < 0.05$) (Table 3). Stepping time and steps per day significantly increased, there was a decrease in breaks per day, and there was no significant change in standing time (Table 4). Three participants wore the AP monitor upside down on four or more days of a condition which gave invalid data for those individuals. For two participants, the AP monitor stopped prematurely and recorded less than two days of data during one condition. That left a total sample of $n = 14$ with valid AP data both pre-and-post intervention.

Differences between weekend and weekdays: At baseline, participants were less sedentary, stood more, had more stepping time, and took fewer breaks from sitting on weekend days compared to weekdays according to the AP ($p < 0.01$). There was no significant difference in steps per day between weekend and weekdays. On weekdays, sedentary time decreased from 69.5% of wear time in the baseline period to 65.6% of wear time in the intervention period ($p < 0.05$). This change pre-to post-intervention is equivalent to a 37 minute reduction over a 16-hour waking day. On weekend days, sedentary time was 60.9% of wear time in the baseline period, and it was 55.9% of wear time in the intervention period. This is equivalent to a 48.6 minute reduction over a 16-hour waking day, but it was not a statistically significant change ($p = 0.2$).

Device and questionnaire sensitivity to change

Neither AG measure (AG100 or AG150) was able to detect a statistically significant difference in sedentary time between the baseline and intervention period (Table 4). None of the questionnaires detected significant differences between the baseline and intervention period either (Table 4). To allow for a direct comparison across the measures, this analysis was done for only the individuals who had valid data for all the measures (AP, AG, and questionnaires). For this analysis, only participants with valid data from the AP, AG, and the questionnaires at both time points were included. Six individuals who did not have valid AP data at both time points and were excluded. One AG monitor did not record a week's worth of data, leaving a total sample of 13 individuals for this analysis. However, since the power to detect change is smaller with the smaller sample size, we also examined the difference between conditions in all participants for the AG (n=19) and questionnaires (n=20), and the differences remained non-significant.

Of the 13 subjects with valid data for all measures, there were ten responders on weekdays and seven responders on weekend days according to the AP measure of sedentary time. The sensitivity, specificity and CI's for each measure compared to the AP are shown in Table 4. The sensitivities for the AG100 and AG150 for weekdays were 80% (CI: 50%, 100%) and 70% (CI: 43%, 97%), respectively. Specificity on weekdays was 67% (CI: 39%, 94%) for both AG100 and AG150. Sensitivity was nominally lower (67% and 57%) and specificity was nominally higher (71 and 80%) for AG100 and AG150, respectively on weekend days compared to weekdays. Those differences were not statistically significant ($p>0.05$).

The sensitivities and specificities for all questionnaires for weekdays and weekend days ranged from 20% to 80% and 33% to 100%, respectively. TV-Q had the lowest sensitivity but the highest specificity among the questionnaires. Both the DS-Q and T-SQ had higher sensitivity for weekdays. The sensitivity and specificity measures were lower for weekdays than weekend days for T-SQ, D-SQ but the opposite was true for TV-Q (Table 4). Those differences were not statistically significant ($p>0.05$).

Convergent Validity

For the monitors, we compared bias and precision overall (total week) and for weekend and weekdays separately. For the overall week the bias (95% CI) for the AG100 was -3.8 min, (-29 to 22.2 min). That is not significantly different from unbiased. The AG150 significantly overestimated sedentary time 31.7 min (7.1 to 56.3 min).

AG Weekend and Weekday: For weekdays, the AG100 significantly underestimated sedentary time by 40 min (-69.7 to -8.3 min), and there was no significant difference between the AP and AG150 with an average difference of 1.4 min, (-29 to 31.9 min). The correlation on weekdays between the AP and AG100 was ($r=0.52$) ($p<0.05$), and between the AP and AG150 it was ($r=0.55$) ($p<0.05$).

For weekend days the bias was 20.8 min (-32 to 74 min) for the AG100. The AG150 significantly overestimated sedentary time with a bias of 58.3 min (6.7 to 93.1 min) on weekend days. AP estimates of sitting were correlated with the AG150 ($r=0.68$) and the AG100 ($r=0.68$) for weekend days ($p<0.05$).

Questionnaires

The T-SQ underestimated sitting time, but it was not significantly different than the AP for weekdays, with an average difference of 40.5 min (-125.2 to 22.3). The correlation was not statistically significantly different from zero ($r=0.41$). The estimate of sitting time from the T-SQ was 147.4 min (-228.3 to -66.6) less than the AP for weekend days ($p<0.05$). The correlation between sitting time from the T-SQ and AP was significant for weekend days ($r=0.55$) ($p<0.05$).

The D-SQ significantly overestimated sitting time for both weekend and weekdays. On weekdays, the D-SQ overestimated sitting time by 176 min (96.1 to 256.9 min). Similarly, on weekend days, sitting time was overestimated by 157.6 min (22.1 to 293.0 min). The correlation between the AP and D-SQ was not significant for either weekdays ($r=0.30$) or weekend days ($r=0.17$). The correlation between the AP and TV-Q was not significant for either weekdays ($r=0.07$) or weekend days ($r=-0.11$).

Discussion

This study addressed two important knowledge gaps in the field of sedentary behavior and health. First, it provides empirical evidence that it is possible to reduce free-living sedentary behavior among overweight and obese, non-exercising adults. Participants decreased sedentary time by ~5%, which is equivalent to 48 minutes over a 16-hour waking day. Second, this study identified a measurement tool that is sensitive to change in sedentary behavior and provided a comparison of two commonly used accelerometer-based monitors and two self-report questionnaires.

Feasibility of Sedentary Behavior Intervention

To date, only two published intervention trials targeting sedentary time reductions are available in adults (11, 26). Our results are similar to these trials despite differences in the study sample demographics, intervention targets, and measurement tools. Otten et al. targeted TV viewing among overweight and obese individuals who watch TV > 3 hours per day and showed a 3.8% decrease in sedentary time (26). Their study targeted only one sedentary domain (TV viewing) and the primary outcome was percent of time in sedentary activities according to the Sensewear arm-band (26). Gardiner and colleagues (11) completed a similar study to the current one. They included older-adults who completed a 7-day baseline period followed by a 7-day intervention targeting sedentary time. They reported a 3.2% decrease in sedentary time (11). They did not exclude participants who were participating in MVPA at baseline and occupational sitting was not a target for their intervention since many participants were retired. The primary outcome measure was the AG100 estimate of sedentary time (11). To our knowledge, our study is the first to show a significant reduction of free-living sedentary time using a targeted intervention among non-exercising office-workers and the first to use the AP monitor as an objective tool to assess sedentary time in an intervention study. Participants replaced sedentary time by increasing stepping ($p < 0.01$) and standing time ($p = 0.06$). Breaks from sedentary time significantly decreased in the intervention period, which is of concern given the evidence that more breaks

from sitting may be beneficial for metabolic health (14). However, since sedentary time was replaced with standing, there will naturally be less opportunity for sit-to-stand transitions. Thus, in future research both breaks from sitting and changes in absolute sedentary time must be used as outcome measures in evaluation of effectiveness of interventions designed to reduce sedentary time.

Intervention strategies

At the end of the study, participants were asked to report which strategies were most effective for reducing sedentary time. All participants (19/19) reported that the pedometer was helpful, but participants who averaged <5000 steps per day at baseline found the 7500 goal to be too high. Future research should consider setting more modest incremental step goals based on the participant's baseline level of steps. While the intervention targeted sedentary time, participants reported that the step goal was helpful because it provided instant quantitative self-monitoring feedback. Based on these findings, a device that tracks and provides instant quantitative feedback specific to sedentary time may help participants reduce sedentary time. Approximately half (10/19) of the participants found the hourly checklist (where they reported whether they had stood for five or more minutes each hour) to be helpful, and they reported completing it as they finished activities. The remaining nine only completed the hourly checklist either daily or every few days. These simple strategies, targeting small behavioral changes and providing self-monitoring tools may be useful for future interventions targeting reductions in sedentary time.

Sensitivity of measurement tools

The AP was used as the criterion to differentiate responders to the intervention from non-responders (21). In this study, we confirmed the AP was sensitive to the reductions in sedentary time, but the AG and the self-report questionnaires were not. A novel aspect of this study was that it examined the sensitivity and specificity of the various measures for detecting changes in behavior. In intervention studies, it is important to use measures with high sensitivity and

specificity to insure that changes can be detected and to minimize sample size requirements. Sensitivity reflects the ability of a measure to correctly classify true behavior change. For example, the sensitivity of the AG100 was 67% for weekend days. That is, one-third of subjects who actually changed their behavior according to the AP were not classified as changing their behavior according to the AG100. The specificity was lowest for the D-SQ and T-SQ, indicating that participants were more likely to report they changed behavior when they were actually non-responders to the intervention (according to the AP). In addition, the misclassifications across measures were not occurring for the same individuals. For example, five individuals were misclassified according to the D-SQ, T-SQ, and AG150 for weekend days, but it was not the same five individuals for each measure (see Table 5).

The results comparing sensitivity to change of the AG and AP are consistent with our previous results which used 6-hours of direct observation as the criterion measure (21). Gardiner and colleagues previously reported the AG was modestly sensitive to change and detected a statistically significant decrease in sedentary time (3.2%) using the AG100 (10). Their study included 48 individuals, which suggests that the AG may be able to detect change in a larger sample. However, in the current study, eight minutes *more* sitting time on weekend days was recorded with the AG measures in the intervention period compared to the baseline period.

In contrast, the AP recorded 54 minutes *less* sitting on weekend days in the intervention period. Participants spent more time standing on weekends (31% of AP wear time) than on weekdays (23.4% of wear time) in the intervention period. This suggests that the AG does not distinguish standing from sitting. This is not surprising since the AG device is not designed to differentiate postures. If a person is standing still or standing with small amounts of movement, this will be interpreted as sedentary time using the AG cut-point method. This will cause measurement problems for interventions where participants are encouraged to replace sitting with standing.

Convergent validity of AG

The AG100 cut-point was more accurate than the AG150, and that differs from our previous work which used the same subjects and direct observation as the criterion measure (Figure 1). In the current study, there were differences in the accuracy of the cut-points depending on how much the participant was sedentary. When sedentary time was highest (on weekdays ~ 67%), the AG150 was not different from the AP while the AG100 significantly underestimated sedentary time. When sedentary time was lower (on weekend days ~ 62.7%), the AG150 significantly overestimated sedentary time while the AG100 was not significantly different from the AP. In our previous study, participants were directly observed while at work over a 6-hour period and the percent of time sedentary according to the AP was considerably higher for both the baseline period (79.5%) and intervention period (66.5%) relative to the current study, which may explain the discrepancy. Additionally it should be noted that following an intervention designed to increase standing and decrease sedentary time, the AG150 may misclassify standing as sedentary behavior and inflate sedentary time. In a highly sedentary population the AG100 may underestimate sedentary time.

Accuracy using the AG100 and AG150 were slightly different and both were equally precise with 95% confidence intervals of about 50 minutes. While the accuracy of a given cut-point may change depending on the level of sedentary behavior, the precision will not. Lower precision increases sample size requirements for intervention trials. It is also important to note that the AG monitors did detect significant differences pre-to-post-intervention for minutes in MVPA, which increased significantly during the intervention period from 16.1 min to 24.6 min ($p < 0.01$). To date, limited work has been done validating MVPA estimates from the AP. Therefore, intervention studies targeting both sedentary time and MVPA should consider using the AG.

Convergent validity of questionnaires

To our knowledge, this is the first study comparing questionnaire estimates of sedentary time to the AP. In contrast to the T-SQ, which underestimated sedentary time, the D-SQ overestimated sedentary time. Therefore, it is very important to consider the type of questionnaire when attempting to compare prevalence estimates across populations. Clemes et al. compared two sedentary behavior questionnaires to the AG100 (4). Similar to our results, they reported the single-item T-SQ underestimated sedentary time by over two hours on weekend days. In the current study, the difference between the T-SQ and the AP was not significant on weekdays, while Clemes et al. did report a significant underestimation of sedentary time (4). They reported no significant difference for the D-SQ compared to the AG100, which is different than what we reported when comparing the questionnaires to the AP. While participants were instructed to avoid double-reporting of time in multiple domains, it is possible that occurred. Another explanation is that participants were awake for more time than they wore the monitors, which leaves potential time for participants to be sedentary that is not captured by the monitors. In the Clemes et al. (4) study, participants reported in a diary how much they sat each day during the week, which may have improved their awareness of sedentary time. Further, while the average difference in their study was small, they reported very wide limits of agreement using a Bland-Altman analyses (weekday = -382.0 to 354.6 min; weekend day = -578.5 to 570.2 min) which is consistent with the large individual differences in the present study. Only considering one domain (TV-viewing) was not sufficient to detect change in behavior and was not correlated with overall sedentary time. While the evidence linking high levels of TV viewing to poor health outcomes is robust, a more comprehensive measure of sedentary time should be used by future studies that examine the dose-response relationships of overall sedentary time and health.

This study has important limitations that should be noted. We used a ten hour cut-off to define a valid day using the activity monitors. This is considered best practice for accelerometer studies and previous validation studies of sedentary questionnaires (23), but the 10-hour criterion

was originally designed for studies that primarily measure MVPA (30). Future work should examine if this is a valid criterion for determining minimum wear time needed in sedentary behavior studies. Future research, using a larger sample size, should examine the difference in estimates of sedentary time using different daily wear-time criteria. The second limitation is that the sample was small and homogenous, but it is worth pointing out that subjects in this study are probably similar to those who will be targeted for future intervention (overweight/obese, non-exercising, sedentary occupations). It is important to note that the results can only be generalized to a similar population of highly sedentary, overweight and non-exercising office workers. Finally this study demonstrates that short-term, free-living sedentary time reductions are possible. However, while the change we observed was statistically significant, a ~5% (48 minute) reduction in sedentary time per day may not be sufficient to elicit health benefits, even if sustained for a longer duration. Future research is needed to explore the health benefits of longer term reductions in sedentary time.

The strengths of this study are the within subject design that allowed us to explore key measurement limitations in the literature in unique ways. Particularly, the sensitivity to change analyses using sensitivity and specificity will inform researchers of sample size requirements for future intervention trials. In the current study, we used the AP as a criterion for changes in behavior and for measuring sedentary time. The AP has been shown to correctly classify free-living sedentary time over 97.2% of the time (12, 21). While this is not 100% accurate, we believe the effects on the comparisons across measures are small, though they may exist. To date, few studies have used the AP monitor, or a comparably accurate criterion measure, to assess the efficacy of interventions or to examine the convergent validity of sedentary time measures. In addition, our study is the first known sedentary behavior intervention study in adults to use the AP as the primary outcome measure. Finally, we provide a number of strategies and behavior change tools for future interventions that target reductions in sedentary time.

In conclusion, this study confirmed that the AP monitor is sensitive to change, and the AG monitor and self-report questionnaires are less sensitive. We provide data that improve our understanding of the measurement properties of devices and self-report tools. These data will help inform sample size estimates for future interventions. The AG100 was more accurate when sedentary time was lower, while the AG150 was more accurate when sedentary time was higher. This discrepancy highlights the inherent limitations of estimating sedentary time using a simple cut-point from a waist-mounted accelerometer. When possible, researchers should use a device that is specifically designed to measure posture for intervention studies that target sedentary time. In addition, we showed that a ~50 minute per day reduction in sedentary time is possible using targeted messages to replace sedentary time with standing and light-intensity activity. While there is evidence linking sedentary behavior to health, there remains a paucity of controlled trials examining the effect of reducing sitting time on health outcomes (28). In the future, long-term randomized controlled trial studies are necessary to demonstrate the effect of reducing sedentary time on the cardio-metabolic risk factors associated with chronic diseases.

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AT HOME
○ Walk while talking on the phone
○ Walk your dog an extra 10 minutes each day
○ Do dishes by hand instead of using the dishwasher
○ Stand during commercials (remain standing an extra minute after)
○ Do a little extra housework
○ When grocery shopping walk up and down each aisle, even doing it twice to walk longer and to pick up grocery items you may have forgotten the first time
○ Walk up and down stairs a couple times a day
○ When you're carrying things in from the car (for example groceries) take more frequent trips with only one bag at a time
○ Walk to get the mail, instead of driving by
○ Shovel instead of using a snow blower
○ Mow your lawn (even better get a non-motorized mower)
○ Wash your car (no drive-thru!)
AT WORK
○ Stand to answer telephone
○ Take a 5 minute walk/stand break each hour
○ Hand deliver a message to a co-worker instead of emailing
○ Take the stairs (start with walking 2 floors then taking elevator if your building is tall)
○ Use restroom on a different floor
○ Eat your lunch outside, or somewhere other than your desk
RECREATION AND TRANSPORTATION
○ Choose active recreation instead of going to a movie (bowling, pool, darts)
○ Volunteer to plant trees or start a garden at home
○ Volunteer to walk a dog, play with kids in need, or help habitat for humanity
○ Take the bus or other public transportation when possible
○ Go for a hike or a picnic instead of going for a scenic drive

Table 2. Strategies to decrease sedentary time.

	All days		Weekday		Weekend	
	Baseline Period	Intervention Period	Baseline Period	Intervention Period	Baseline Period	Intervention Period
% Sedentary	67.0 ± 13.3	62.7 ± 11.9 *	69.4 ± 11.1	65.6 ± 9.5 *	61.0 ± 16.3 ‡	55.9 ± 14.2
% Standing	23.2 ± 9.7	25.6 ± 9.7	21.4 ± 8.3	23.3 ± 8.0	27.5 ± 11.6 ‡	31.0 ± 11.4
% Stepping	9.8 ± 5.0	11.7 ± 4.3 *	9.1 ± 4.0	11.1 ± 3.7 *	11.5 ± 6.7 ‡	13.1 ± 5.2
Breaks per day	53.2 ± 21.0	49.2 ± 17.1 *	56.2 ± 22.4	53.6 ± 17.3	46.0 ± 15.4 ‡	38.6 ± 11.4 *
Steps per day	6417 ± 3366	8167 ± 3600 *	6121 ± 2495	8133 ± 3101 *	7132 ± 4871	8247 ± 4650
Daily wear time (hrs)	14.1 ± 1.9	14.1 ± 2.0	14.1 ± 1.98	14.3 ± 2.0	14 ± 1.7	13.7 ± 2.1

Table 3. ActivPAL outcome measure pre- and post-intervention. Note: % Sedentary, % Standing, and % Stepping expressed as percent of wear time. Data includes 14 participants with valid data during both the baseline and intervention period. ‡ Significantly different from weekdays during baseline period. * Significantly different in intervention condition compared to baseline condition (p<0.05)

		Baseline Period mean ± SD	Intervention Period mean ± SD	Sensitivity (95% CI)	Specificity (95% CI)
Weekday	AP (% Sedentary)	68.8 ± 8.5	65.1 ± 6.5*	-	-
	AG100 (% Sedentary)	66.4 ± 10.2	62.9 ± 10.5	80 (53, 100) †	67 (39, 94)
	AG150 (% Sedentary)	70.5 ± 9.4	67.1.4 ± 10.1	70 (43, 97)	67 (39, 94)
	T-SQ (hours/day)	9.3 ± 3.3	8.2 ± 4.4	80 (53, 100) †	33 (06, 61)
	D-SQ (hours/day)	12.6 ± 2.9	11.6 ± 2.2	70 (43, 100) †	33 (06, 61)
	TV-Q (hours/day)	2.3 ± 1.85	2.5 ± 1.75	20 (0, 47)	100 (73, 100) †
	Weekend	AP (% Sedentary)	60.4 ± 15.6	57.3 ± 12.1	-
AG100 (% Sedentary)		62.7 ± 8.9	64.4 ± 7.3	67 (38, 95)	71 (43, 100) †
AG150 (% Sedentary)		66.7 ± 9.0	69.0 ± 6.2	57 (29, 85)	80 (52, 100) †
T-SQ (hours/day)		6.2 ± 3.1	6.0 ± 3.3	57 (29, 85)	60 (32, 88)
D-SQ (hours/day)		12.1 ± 5.0	10.7 ± 3.9	57 (29, 85)	60 (32, 88)
TV-Q (hours/day)		3.4 ± 2.14	3.3 ± 1.60	43(15, 71)	100 (72, 100) †

Table 4. Monitor and questionnaire sedentary time and sensitivity and specificity. Note: AP, AG100 and AG150 are expressed as a percentage (total sedentary time/ wear time) to adjust for differences in wear time. Data included 13 participants with valid data for all measures during both the baseline and intervention period. *indicates statistically significant difference between conditions $p < 0.01$. † indicates significant sensitivity or specificity ($p < 0.05$).

Individual	Week days						Weekend days					
	AP	AG100	AG150	T-SQ	D-SQ	TV-Q	AP	AG100	AG150	T-SQ	D-SQ	TV-Q
1	+	+	+	+	+	-	+	+	+	+	-	-
2	+	+	+	+	+	-	+	+	+	-	+	+
3	+	+	+	+	+	-	-	-	-	-	-	-
4	+	+	+	+	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	+	-	-	+	+	+
6	+	+	-	+	+	-	+	+	+	+	+	+
7	+	+	+	+	-	-	*NA	*NA	*NA	*NA	*NA	*NA
8	+	-	+	+	+	-	-	-	-	-	-	-
9	-	-	-	-	-	-	+	-	-	-	-	-
10	+	-	-	-	-	+	+	+	+	-	-	-
11	-	-	-	-	-	-	+	+	+	+	+	-
12	+	+	+	-	+	+	-	-	-	-	-	-
13	+	-	-	+	+	-	-	-	-	-	-	-

Table 5. Individual responsiveness to intervention for each measure. (+) represents responder (reduced sedentary time pre-to-post-intervention) and (-) represent non-responders (did not reduce sedentary time pre-to-post-intervention) for each individual.

*NA = no valid AP data for weekend. Data included 13 participants with valid data for all measures during both the baseline and intervention period.

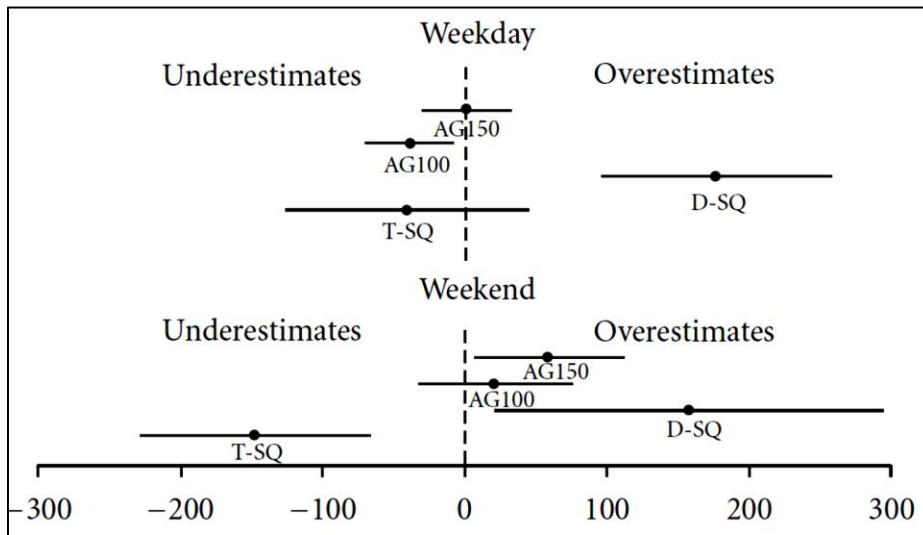


Figure 4. Illustration of the under- and over-estimation of sedentary time. Comparison of each measure to the activPAL monitor for a) weekend b) weekdays. The closed circles are the bias and the lines illustrate the 95% confidence intervals. Data includes 13 participants with valid data for all measures during both the baseline and intervention period.

CHAPTER V

THE INFLUENCE OF FREE-LIVING ACTIVITY AND INACTIVITY ON HEALTH OUTCOMES AND RESPONSIVENESS TO EXERCISE TRAINING

Introduction

There is a clear association between physical activity (PA) and a reduced risk of chronic disease (42). Specifically, the 2008 PA Guidelines recommend 150 minutes of moderate and/or 75 minutes of vigorous PA each week in order to reduce risk of obesity, cardiovascular disease (CVD) and type II diabetes (42). On average, when non-exercising individuals begin exercise training they reduce disease risk factors and improve overall metabolic health e.g., (7, 9, 26, 32). However, exercise training studies have reported large individual variability in the increase in cardiorespiratory fitness (CRF) and in the reduction of disease risk factors (e.g. insulin sensitivity) following the training period (6). To date, researchers have primarily focused on identifying genetic differences or other non-modifiable risk factors (e.g., age) to explain the exercise non-response (5, 46). Limited research has focused on modifiable behavioral factors that may contribute to individual variability in response to training.

A training regime lasting for 60 minutes per day fails to account for over 95% of an individual's waking day. Therefore, time spent in activity or inactivity outside of training may be an important modifiable factor to consider in understanding the individual differences in physiological response to exercise training. A growing body of literature suggests that behavioral compensation may take place when a previously non-exercising individual initiates exercise training that results in decreased levels of PA during the non-training hours (14, 29). However, the evidence is inconsistent with some studies reporting no change or an increase in non-exercise activity (25, 44, 52).

In addition to an inconsistency in average change across studies, there are large *individual* differences in levels of non-exercise activity (14, 28, 34, 37, 52). Recent studies

provide preliminary evidence that this individual variability in non-exercise activity may affect individual responsiveness to exercise training (10, 34). Manthou et al. (34) classified individuals as ‘responders’ (those who lost as much weight as predicted) and ‘non-responders’ (those who lost less weight than predicted) following an 8-week supervised exercise training program. Based on HR monitoring, the non-responders expended significantly less energy during non-exercise times than the responders. Di Blasio et al. (10) used the Sensewear pro2 armband (Body Media, Pittsburg, PA) to evaluate TDEE among post-menopausal women participating in a 13-week exercise training program. Participants who increased TDEE showed improvements in cholesterol and LDL, while those who decreased TDEE did not. Notably, this study showed that over half of women who started an exercise training program *decreased* TDEE, even when including energy expenditure from exercise. The authors concluded additional intervention may be necessary to ensure behavioral compensation does not take place outside of exercise training to enhance the health benefits of exercise training.

In summary, there are large individual differences in response to exercise training (6). Exercise training studies often standardize and precisely quantify the volume of purposeful exercise, however the activity and inactivity during the remaining 95% of the day (when the individual is not training) are rarely considered. Among the few studies that have quantified non-exercise activity there are large individual differences in non-exercise activity (14, 28, 34, 37, 52). Therefore, the quantification of activity and inactivity behavior of participants in an exercise training study outside of training time may be an important variable to understand individual responsiveness to exercise training. The remainder of this paper will address different aspects of this issue. Part 1 will focus on quantifying habitual activity and inactivity at multiple time-points during an intervention period. Part 2 will examine if activity and inactivity outside of exercise training affect the responsiveness to the training intervention.

Part 1: Aims

Limitations in measurement methodologies are a contributing factor to the paucity of data examining total daily activity during a training trial (42). Early studies used doubly labeled water to quantify TDEE during training studies (4, 11, 14). Doubly labeled water provides an accurate estimate of energy expenditure, but it is very expensive, it cannot separate non-exercise time from exercise time, and it does not allow for classification of activity into various intensities (i.e., sedentary, light, moderate, vigorous). Accumulating epidemiologic evidence suggests that SB (SB) and exercise are distinct behaviors with independent effects on health (21). It is well established that moderate-to vigorous activity has health benefits (42). Therefore, it may be particularly important to assess both time in SB and time in different activity intensity categories (i.e., MVPA) outside of exercise training time.

Advances in activity monitor technology have resulted in monitors that can produce accurate estimates of time in intensity categories and are relatively low-cost. For example, the activPAL monitor is a highly accurate device for distinguishing posture and measuring steps in free-living environments (15-16, 30). This monitor provides estimates of TDEE and time in MVPA, and it is sensitive to changes in sedentary time (31). Using an activPAL monitor, we are able to accurately quantify a number of PA and SB measures including TDEE, MVPA, sedentary time, steps and sit-to-stand transitions. In addition, the low participant and researcher burden allows for the measurement of PA/SB at multiple time points throughout the intervention. To date, no known study has measured time spent in sedentary behavior or quantified features of habitual activity patterns using a valid device at multiple time-points during an intervention. Therefore, the aim of Part 1 is to describe the habitual PA and SB of participants in a 12-week intervention trial to understand the patterns of PA and SB among subjects enrolled in an exercise training program. PA/SB will be measured using the activPAL at baseline and four, week-long periods during the intervention (weeks three, six, nine and twelve of the 12-week intervention).

Part 1: Methodology

Study population

Potential subjects were recruited from Amherst, MA and the surrounding area. Eligible participants were between 20-60 years of age, non-exercising (defined as exercising less than three days per week for less than 20 minutes per session for the preceding six months and employed in an inactive occupation (self-report of >75% day at work spent sedentary)). Exclusion criteria included major orthopedic limitations, wheelchair users or musculoskeletal problems that affected mobility, life-threatening illness (e.g., terminal cancer), chronic diseases (e.g., diagnosed heart disease, diabetes, and emphysema) or any condition for which a physician did not recommend exercise. Participants were excluded if they had gastric bypass or lap-band surgery within the last year, were taking medication for type II diabetes (e.g. metformin) or beta-blocker medication for high blood pressure. A variety of recruitment strategies were employed, including displaying fliers on campus and the surrounding community, listserv emails to the campus community and posting on local websites. In total, 200 individuals were screened via telephone and 103 met the initial eligibility criteria and agreed to an informed consent visit.

Screening visits

After reporting to the PA and Health Laboratory, participants read and signed an Informed Consent Document that was approved by the University of Massachusetts Institutional Review Board. They completed a health history form and questionnaires about current PA levels. In addition to the above eligibility criteria, the following measurements were taken to ensure participants met two of the three criteria for increased risk of cardiovascular disease: 1) Pre-hypertensive: resting blood pressure between 125-160 mm Hg systolic and/or 85-100 mm Hg diastolic, 2) Overweight/Obese: Body mass index (BMI) between 25 and 45 kg·m⁻², 3) High visceral fat: as defined by elevated natural waist circumference (> 102 cm [males] > 88cm [females]), a surrogate measure of visceral fat (2). Of the 103 subjects who signed informed

consent documents, 33 were ineligible based on the above criteria and the remaining 70 were scheduled for study visits.

Participants completed a VO_2 peak test as the final determinant of eligibility. The details of the test are described below. The final inclusion criterion for the study was low aerobic fitness (VO_2 peak \leq 50th percentile of age and sex specific norms) (1). A physician was present for all tests involving males >45 years and females >55 years. All participants had 12-lead ECG monitoring during the test and the ECG records were reviewed by a physician prior to final enrollment. Two participants were not given physician approval due to an abnormal ECG, and no participants were excluded for being too aerobically fit. The remaining 68 subjects were enrolled in the study.

Following the exercise test, participants were randomly assigned to one of four groups: a non-exercise control (CON), a sedentary time reduction group (rST), an exercise training group (EX) or an exercise training group plus sedentary time reduction (EX-rST) for the 12-week intervention period. To minimize differences between the groups, the study groups were matched on age, sex, race/ethnicity, and BMI. The details of the measurement protocol are described below. Participants were shown the activity monitors and provided written and verbal instructions on how to wear the monitors. They were instructed to wear the monitor for a one-week baseline measurement period while maintaining their habitual activity patterns.

Intervention period

Control (CON) Participants in the control group were asked to maintain their current level of activity for the 12-week study period. They completed the PA measurement protocols at the same time-points as the other groups. Participants in the control group were offered the opportunity to be randomized into one of the two exercise groups following the post-intervention measures.

Sedentary time reduction (rST) Participants in this group received detailed daily recommendations to decrease their time in SB. The intervention was based on a one-week pilot

intervention where participants decreased sedentary time by ~5% (31). The details of the intervention are published elsewhere (31). Briefly, participants were provided home, work, and discretionary time strategies to increase their non-exercise activity (e.g., standing during all commercials, taking a 5-minute movement break each hour at work). In addition to general instructions (e.g. take the stairs) participants were counseled on the benefits of reducing sedentary time and developed strategies tailored to their own lifestyle. Participants wore an Omron pedometer daily (HJ720-ITC, Omron Healthcare, Bannockburn, Illinois) to provide a quantitative step-goal to facilitate compliance. Steps·day⁻¹ were recorded on a step-log that was reviewed weekly with the research assistant. The steps·day⁻¹ targets were adjusted weekly and were based on the participant's baseline steps·day⁻¹. If the participant was taking <5000 steps·day⁻¹, the step goal was increased by 10% (e.g., an individual who took 4000 steps·day⁻¹ at baseline would be given a goal of 4400 steps·day⁻¹ during the first week of the intervention). Once the participant attained >5000 steps·day⁻¹ then the step goal was increased by 5% for the subsequent week. The step goals provided a quantitative target and a self-monitoring tool for the participant; however the increases were modest to encourage participants to achieve them by reducing sedentary time and increasing total daily activity rather than through one large bout of activity. Participants reported to the PA and Health Laboratory weekly to meet with a research assistant to discuss the previous weeks results. The weekly meetings followed a standard format. Briefly, participants were asked to identify the following; a) successful strategies they used in the previous week, b) barriers or challenges they faced, c) times of day or days of the week that were particularly challenging, and c) strategies to overcome barriers.

Exercise (EX) Participants exercised 5-days per week, for 12 weeks. Exercise intensity was set as a percentage of VO_{2peak} based on heart rate reserve ($HRR = HR_{max} - HR_{rest}$) and each exercise session lasted for 40 minutes (a total of 200 minutes per week). Exercise training took place on a treadmill, stationary bicycle or arctrainer (Cybex, Medway, MA). Three of the five sessions was treadmill exercise. There was a progressive increase in training volume to minimize

the risk of drop-outs and injuries. During the first week participants exercised at 40-50% of HRR for 30 minutes per session and during the second week participants exercised at 50-60% of HRR for 35 minutes per session. During weeks 3-6, participants exercised at 50-60% of HRR for 40 minutes per session. For the final six weeks (weeks 7-12) participants exercised at 55-65% of HRR for 40 minutes per session. The exercise duration exceeds the PAGAC report minimum by 50 minutes per week (42). All exercise sessions were supervised by a research assistant. The research assistant monitored exercise intensity throughout the session using heart rate (Polar RS400, Polar USA) and rating of perceived exertion. The mode, speed, duration and resistance were adjusted (when appropriate) to maintain HR within the prescribed zone. The exercise only group was instructed not to engage in any exercise outside their prescribed training time but was otherwise not given recommendations regarding non-exercise activity.

Exercise and sedentary time reduction group (EX-rST). The EX-rST received the identical exercise training dose (i.e., duration, intensity, and frequency) as the exercise only group. In addition, participants received the strategies to reduce sedentary time similar to the rST group. They were provided with and reminded of their weekly step goal at their exercise sessions. They were asked the same questions about barriers and successes as the rST group. The meetings took place during training rather than a separate lab-visit due to the high participant burden (5-days a week) for exercise sessions.

Measurement of PA and SB

The activPAL (PAL Technologies, Glasgow, Scotland) is a small (2.0 x 1.4 x 0.3 inches) and light (20.1 grams) single unit accelerometer-based device that characterizes activity patterns. The device is worn on the mid-right thigh (attached by non-allergenic adhesive), and uses accelerometer-derived information about thigh position to estimate time spent in different body positions (horizontal = lying or sitting; vertical=standing). When the wearer is standing, the device quantifies ambulatory patterns (i.e., step cadence and number of steps). At baseline, and weeks three, six, nine and 12 of the study, data were collected for a 1-week period, in 15 second

epochs. Participants were provided a monitor log to record times in and out of bed and any times the monitor was removed and put back on. They were instructed to wear the monitor for all waking hours, except time bathing or swimming.

To determine wear-time, participant's monitor logs were compared to a wear-time estimate derived from the activPAL. The wear-time algorithm was developed and validated for another commercially available monitor and the same parameters were used to objectively define wear time using the activPAL (8). The wear-time algorithm was modified from the *PhysicalActivity* package in R statistical software (43). If the log and the algorithm differed by >30 minutes, the file was visually inspected. The algorithm was used to define wear unless the file had no accelerations > 1 in the sum(abs) channel and no upright time, in which case the participant log was used.

To determine a valid day, the standard 10-hour criterion was applied (51). In addition, a day was considered valid if, based on the in/out of bed logs, participants wore the monitor > 85% of the day but wear-time totaled < 10-hours. For a week to be considered valid the participant was required to have at least 4-valid days (51). To further characterize the monitor wear-time we examined the percent of waking hours that the monitor was worn and examined changes in total wear time over the course of the intervention.

The following activity metrics were used to assess PA both for the total day and the total day with exercise training time removed (non-exercise times). For the exercise groups, separate analyses were done to eliminate the exercise time and examine changes in non-exercise activity metrics. To eliminate the effect of different wear times, we computed the percentage of wear time in each postural allocation (i.e., percent sedentary [(sedentary hrs/total hrs wear-time)*100], percent standing [(standing hrs/total hrs wear-time)*100], and percent stepping [stepping hrs/total hrs wear-time)*100] for each day. To characterize the pattern of sedentary time accumulation, breaks per day (i.e., sit-to-stand transitions), break-rate (breaks per sedentary hour) were computed. To estimate time in activity, we used the proprietary algorithm in the activPAL

software to estimate total daily EE (expressed in MET-hrs), time spent in moderate-to-vigorous PA (MVPA [> 3 METs]) and total steps per day (steps \cdot day $^{-1}$). MET-hrs were standardized to a 16-hour waking day to account for differences in wear time.

Statistical evaluation

All statistical analyses were performed using R-software packages (www.r-project.org) (43). Significance levels were set at $p < 0.05$. A repeated measures linear mixed model was used to assess within-group changes in each activity metric at weeks three, six, nine, and twelve compared to baseline. A separate model was fit for each variable and for each group. A repeated measures linear mixed model was used to test if there were significant differences in the response to training between the intervention groups. Group by time interactions were adjusted using Bonferroni corrections.

Part 1: Results

Of the 68 participants who enrolled in the study, a total of 57 completed the pre-and post-intervention measures and were included in the analysis. Three participants dropped out after randomization in the rST group (two refused to be randomized and one was diagnosed with pre-existing disqualifying disease during the screening process (cancer)). Four participants in both EX-rST and EX dropped out due to scheduling conflicts. The drop-outs were not different from the study participants in any baseline measure. Participant characteristics for the 57 individuals who completed the study are shown in Table 6. There were no significant between-group differences in age, BMI or activity/sedentary behavior metrics at baseline.

The activity/sedentary behavior measures (average time spent sedentary, standing, stepping, steps \cdot day $^{-1}$, MVPA, MET-hrs, break-rate, and breaks \cdot day $^{-1}$) for the total day ([TD] including exercise time) are shown in Table 7. Table 8 presents these measures for the total day with exercise training time removed (TD-noex).

Within-group differences in PA and SB

EX The EX-group significantly decreased TD sedentary time at weeks three and nine (Pre-to-post range: -8.4% to 4.9%) (Table 7). There was a significant increase in stepping time, MET-hrs, MVPA, and steps per day at all intervention time points relative to baseline. For TD-noex, the EX group significantly increased stepping time, MET-hrs, MVPA, steps·day⁻¹ and decreased sedentary time at week three and there were no changes at other time points (Table 8). There were no changes in standing time for TD or TD-noex. Breaks·day⁻¹ decreased at weeks six, nine, and twelve, and break-rate increased at week three only for both TD and TD-noex.

EX-rST For TD, the EX-rST group significantly decreased sedentary time at all intervention time points compared to baseline (Table 7). The range in changes between baseline and week 12 (pre-to-post range) was -28.3% to 10.9%. Steps·day⁻¹, stepping time, MVPA, MET-hrs, and break-rate significantly increased at all intervention time points. Total breaks per day and standing time did not significantly change. For TD-noex, sedentary time significantly decreased at weeks 6, 9 and 12 (Pre-to-post range: -26.7% to 13,4%) (Table 8) . Stepping time, steps·day⁻¹, MVPA, MET-hrs, and break-rate significantly increased at all intervention time-points. Breaks·day⁻¹, increased at weeks six and nine and there were no significant changes in standing time at any time point.

rST The rST group significantly decreased sedentary time at weeks six, nine, twelve relative to baseline (Pre-to-post range: -17.0% to 8.5%) (Table 7). Steps·day⁻¹, MVPA, MET-hrs, and stepping time increased at all intervention time points. Break-rate increased at week nine and there were no changes in any metrics at other time-points. The control group significant increased sedentary time and decreased standing time at all intervention time-points. No other activity metrics were significantly different from baseline.

CON The control group significantly increased sedentary time (Pre-to-post range: -0.7% to 9.6%) and decreased standing time at all time-points during the intervention compared to baseline (Table 7). There were no pre-to-post intervention changes in any other PA/SB measures for the control group.

Between group differences in PA and SB

Sedentary time EX, EX-rST and rST all significantly decreased sedentary time compared to the control group. The EX-rST group had less sedentary time than EX at week twelve only. Differences between EX and CON were not significant at weeks six and twelve for non-exercise time, while the EX-rST was lower than CON at all intervention time points for TD-noex. For TD-noex, EX-rST had lower sedentary time at weeks six and twelve than EX (Table 7 and Table 8).

Standing time rST had higher standing time than CON at weeks nine and twelve and EX was higher than CON at weeks three and nine for both non-exercise time and total day (Table 7 and Table 8). EX-rST had higher standing time than CON at all intervention time points, for both non-exercise time and total day all differences were due to significant decreases in standing by the CON group.

Stepping time EX and EX-rST significantly increased TD stepping time compared to the control group (Table 7 and Table 8). TD-noex, EX and CON were no longer different at any time-point, while EX-rST increased TD-noex stepping at all time-points compared to control. rST increased stepping time compared to the control at weeks six, nine and twelve. Stepping percentage for TD was significantly higher in the EX compared to rST at week three only, while the rST group had higher stepping time at weeks six, nine and twelve for TD-noex compared to EX. Stepping percentage for TD was significantly higher in the EX-rST compared to rST at week three, nine and twelve, there were no differences in TD-noex for EX-rST compared to rST. For TD, EX-rST had significantly higher stepping time than EX at weeks nine and twelve, and TD-noex stepping time at weeks six, nine and twelve.

Steps·day⁻¹ All trends for steps·day⁻¹ were similar to stepping percent for the intervention groups compared to the control (Table 7 and Table 8). Steps·day⁻¹ for TD was significantly higher in the EX compared to rST at week three only, while the rST group had higher steps·day⁻¹ at weeks six, nine and twelve for TD-noex compared to EX. EX-rST had higher steps·day⁻¹ at weeks six, nine and twelve and higher non-exercise steps·day⁻¹ at all intervention time-points compared

to EX. Total steps·day⁻¹ was significantly higher in the EX-rST compared to rST at all intervention time-points and there were no differences in TD-noex steps·day⁻¹ for EX-rST compared to rST.

Breaks per day and break-rate For TD and TD-noex, breaks·day⁻¹ were significantly higher in the EX-rST group compared to the EX group at weeks six, nine and twelve (Table 7 and Table 8). No other trends for between group differences were significant. EX-rST significantly increased break-rate compared to CON at all time-points. A similar trend was shown for TD-noex although the p-values were marginally significant for weeks nine and twelve (p= 0.05 and 0.07). For TD and TD-noex, EX-rST had a higher break-rate than EX at weeks nine and twelve. No other differences in break-rate were significant.

MET-hrs. For TD, MET-hrs day, all intervention groups significantly increased MET-hrs compared to control at all time points, except for week three where there were no differences between rST and CON. EX-rST increased MET-hrs compared to EX and rST at weeks nine and twelve. For TD-noex, rST and EX-rST significantly increased MET-hrs at all time points compared to the control, and at weeks six, nine and twelve compared to EX. EX increased MET-hrs at week three compared to the control, but was not different than CON at any other time-point (Table 7 and Table 8).

MVPA Minutes of MVPA for TD increased in all intervention groups at all time points compared to the control, except for week three which was not different between rST and CON (Table 7). EX-rST was higher than rST and EX at all time-points except for week three, which was not different between EX and EX-rST. For TD-noex, EX-rST was significantly greater than CON and EX at all time points (Table 8). rST was significantly greater than EX and CON at weeks six, nine and twelve. There were no differences between EX and CON at any intervention time-point.

Part 1: Discussion

The aim of this study was to quantify the habitual activity and inactivity of participants in a 12-week intervention study. A major finding of this study is that participants in an exercise training study do not reduce sedentary time without additional intervention. In addition, we showed it is possible to reduce free-living sedentary time using a targeted intervention both among individuals who initiate exercise training and among those who do not.

Participants in the EX group completed exercise 5-days per week for 40-minutes per session at 50-65% of HRR during the intervention period. All participants completed over 90% of the prescribed exercise dose. The EX group was instructed not to participate in additional exercise, but they were not given additional recommendations or restrictions on non-exercise activity. Therefore, their activity levels during non-training time should be similar to those of participants in other exercise training trials. The exercise duration is equivalent to 3% of a 16-hour waking day; therefore if participants replaced sedentary time with exercise training, we would expect a 3% reduction in sedentary time. For TD, participants in the EX group decreased sedentary time at weeks three and nine by greater than 3%, which was statistically significant. At weeks six and twelve, the change in sedentary time was < 3% and was non-significant, suggesting slight increases in non-exercise sedentary time. In addition, only 5/16 subjects decreased sedentary time by 3% or more at week twelve compared to baseline. These results support the growing evidence that exercise and SB are distinct behaviors with different attributes and determinants (19, 41).

Our results are consistent with other studies reporting exercising individuals maintain non-exercise activity during the training period, *on average* (34, 44, 52). However, there were large individual differences among the EX group in the magnitude of change in activity and inactivity measures during the intervention. For example, 43% of subjects *decreased* their non-exercise steps per day and 57% *increased* their non-exercise sedentary time during the training period. In addition, 28.5% *decreased* MET-hrs in their non-exercise time and 35.7% *decreased*

non-exercise minutes of MVPA during the intervention compared to the baseline period. This evidence supports the work of Di Blassio et al., (10) who suggested that additional intervention may be necessary to ensure behavioral compensation does not take place outside of exercise training.

There were positive initial changes in behavior at week three in the EX group, including decreases in TD-noex sedentary time and increases in stepping time, $\text{steps}\cdot\text{day}^{-1}$, break-rate, MET-hrs and MVPA. However, after week three these variables all returned to baseline levels and $\text{breaks}\cdot\text{day}^{-1}$ decreased for weeks six, nine and 12. A number of studies measure PA only at baseline and the last-week of the intervention trial, therefore comparisons of temporal adaptations are not possible (10, 25, 34, 44). Turner and colleagues (52) measured TDEE at multiple time points. They estimated TDEE using branched-equation HR monitoring and did not report any difference in non-exercise energy expenditure at week two of an intervention compared to weeks nine and eighteen. The disparate results may be due to differences in measurement methodology. To date, we are not aware of other studies that have quantified changes in non-exercise activity within the first three weeks of an intervention. More work is needed to determine the temporal nature of changes in non-exercise activity during an exercise training study.

Participants in the EX-rST group completed the same exercise dose as the EX group and received additional intervention to maintain non-exercise activity and decrease sedentary time during the intervention. All participants completed over 90% of the prescribed exercise sessions. They successfully reduced sedentary time and increased steps/day for the TD and for the TD-noex at all intervention time points. On average, TD sedentary time decreased by ~7% at weeks six, nine and twelve of the intervention and ~5% for TD-noex. Steps/day increased by ~6000 for TD and ~2500 TD-noex (Table 7 and Table 8). In addition, they increased TD and TD-noex MVPA, MET-hrs, break-rate and stepping time at all intervention time points. In the EX-rST only one participant (6.6 % of the sample) decreased steps/day, MVPA and MET-hrs during non-exercise time and two participants (13%) increased sedentary time. This is in contrast to the EX

group, where 30-60% of participants decreased non-exercise activity and increased sedentary time. This is the first known study to show that it is possible to simultaneously increase both exercise training and non-exercise activity.

Another major finding was that minutes of MVPA, MET-hrs, steps/day, percent stepping, and sedentary time were not different between EX and rST during weeks six, nine and twelve, even when exercise time was included. This is an important finding because future research can compare the health effects of a daily bout of purposeful exercise training to a similar amount of lifestyle activity (MET-hrs, steps/day, stepping time and MVPA) that is accumulated throughout the day.

The rST group received a targeted intervention to decrease sedentary time and increase steps per day. They significantly decreased sedentary time at weeks six, nine and twelve by an average of 5.0%, which is similar to the average TD-noex reduction in the EX-rST group. In addition, these values are consistent with a one-week pilot-study to determine if reductions in sedentary time were possible among overweight, non-exercising individuals (31). Our results are also similar to the other two published intervention trials among adults despite differences in study sample demographics, intervention targets and measurement tools (13, 39). Otten et. al. targeted TV viewing among overweight and obese individuals who watch TV > 3 hours per day and showed a 3.8% decrease in sedentary time (39). Their study targeted only one sedentary domain (TV viewing) and the primary outcome was percent of time in sedentary activities according to the Sensewear arm-band (39). Gardiner and colleagues (13) had a 7-day baseline period followed by a 7-day intervention targeting sedentary time in older adults. They reported a 3.2% decrease in sedentary time (13). Thus, the results from these studies suggest a ~ 5% reduction in sedentary time can be achieved by setting modest step-goals and incorporating a series of small changes into one's daily routine. Further reductions in sedentary time may require more comprehensive interventions such as the use of standing work-stations (33) or other environmental modifications.

This study has a number of important strengths. First, activity variables were measured at four time-points during the 12-week period, which allowed for a detailed and temporal description of activity and inactivity during the intervention period. Second, the activPAL was used as the measure of PA and SB. This device has been validated for distinguishing sedentary time from standing and stepping time (15-16, 30). We were able to quantify numerous activity metrics including MVPA, $\text{steps}\cdot\text{day}^{-1}$, MET-hrs, $\text{breaks}\cdot\text{day}^{-1}$, break-rate, sedentary, standing, and stepping time. Third, using an activity monitor rather than a technique like doubly labeled water, allowed for examination of non-exercise time separate from the total day.

This study is not without limitations. While the sample size is comparable to other studies in the literature (10, 34, 52), it is modest. The 16 participants who were in the EX group represented a wide range of age, BMI and included both men and women; however these results may not be generalizable to the population. Finally, the activPAL is highly accurate at measuring steps and distinguishing postures. However, Harrington et al. (20) showed the activPAL underestimates METs compared to indirect calorimetry and minutes of MVPA have not been validated.

In summary, this study showed that participants in an exercise training study do not decrease sedentary time without an additional intervention targeting non-exercise behavior. In the EX group, approximately half of the participants increased time spent in SB and decreased non-exercise $\text{steps}\cdot\text{day}^{-1}$ during the training trial. This is important as evidence accumulates that SB and PA may have independent effects on health (40). In the EX-rST individuals, on average, all activity measures improved and sedentary time decreased during non-exercise time. In addition, only 6-13% of EX-rST individuals compensated for exercise by worsening activity/inactivity measures during non-exercise time compared to 30-60% of individuals in the EX group. We confirmed previous work showing that it is possible to reduce free-living sedentary time among individuals with sedentary occupations (31). We also extended the previous findings by showing it is possible to simultaneously target reductions in sedentary time and increases in exercise

behavior. Future research should examine if changes in non-exercise activity and sedentary time are associated with physiological responsiveness to exercise training.

Part 2: Aims

Recent evidence suggests that SB and insufficient PA are *independently* associated with obesity, metabolic health, metabolic syndrome, type II diabetes, and mortality (21-22, 24, 49). Therefore, if sedentary time increases during an exercise training period, the health benefits of exercise may be negated. In addition, increases in sedentary time and decreases in activity will lower TDEE, which may inhibit weight loss and other metabolic benefits from exercise training (34). Therefore, the aim of this paper is to compare changes in health outcomes between individuals who decreased sedentary time and increased light-intensity PA in addition to exercise training (EX-rST) compared to those who exercised without reducing sedentary time (EX). Pre-to-post intervention changes in CRF, insulin sensitivity, blood lipids, and body composition were examined. We hypothesized that individuals in the EX-rST group would have greater improvements in outcome measures compared to EX. To determine if changes in health outcomes were attributable to exercise or to the changes in changing sedentary time, an additional group was included that did not exercise but reduced sedentary time and increased daily PA (rST). Additionally, we hypothesized the rST group would not have as large an improvement in the outcomes measures compared to the EX-only group.

Part 2: Methodology

Study Protocol

Study sample and screening visits are identical to those described in Part 1. A total of 57 individuals completed the pre-and post-intervention measures, which are outlined in Figure 5. Two control participants were excluded from the outcome measures (one participant changed medications, resulting in a 14 kg weight loss and the other had a minor surgery in the 9th week that

resulted in substantial weight loss). One rST participant was excluded for failure to comply with the intervention. Table 9 shows the total number of participants for each group and participants characteristics.

Participants were randomly assigned to one of four groups: a non-exercise control (CON), a sedentary time reduction group (rST), an exercise training group (EX) or an exercise training group plus sedentary time reduction (EX-rST) for the 12-week intervention period. To minimize differences between groups, study groups were matched on age, sex, race/ethnicity, and BMI. The details of the measurement protocol are described in Part 1 and shown in Figure 5.

Participants wore the activPAL monitor at baseline and weeks three, six, nine and twelve of the intervention period. At each time-point, the monitor was worn for a 7-day period. A number of PA and SB measures, including average time spent sedentary, standing, stepping, steps·day⁻¹, MVPA, MET-hrs, break-rate, and breaks·day⁻¹ were determined for each time-point. Each PA and SB measure was assessed for the total day (including exercise time; TD) and the total day with exercise training times removed (TD-noex).

Outcome measures

CRF A VO₂ peak test was used to assess CRF. Participants completed a brief (~2 minute) habituation period on the treadmill and were asked to choose a walking speed that was brisk but comfortable. They were then fitted with the metabolic measurement system (True- Max2400 Metabolic Measurement System, Parvomedics, Salt Lake City, UT) and completed an incremental, graded exercise test to maximal voluntary exhaustion. The treadmill speed was the participants' chosen walking speed and treadmill grade was increased every 2-min until the participant could no longer continue the test. Gas-exchange variables (VO₂, VCO₂ production, ventilation, and respiratory exchange ratio [RER]) were recorded every 30 seconds. Volume and gas calibrations were conducted on the metabolic measurement system before each test. Standard criteria for achievement of maximal exertion were used including RER >1.1, a plateau in VO₂,

despite an increase in work and HR within 15 beats of age-predicted maximum (9). The post-intervention exercise test was performed within 72 hours of the last exercise sessions.

Body weight and body composition Body weight (measured to the nearest 0.1 kg) and height (measured to the nearest 0.1 cm) were measured while participants wore a thin layer of clothing and no shoes using a calibrated floor scale/stadiometer (Detecto, Webb City, MO). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured at the natural waist using a plastic tape measure (Guelik II) to the nearest 0.1cm. Two measurements were taken and the average of the two measures was used. If the two measures were not within 0.5 cm, a third measurement was taken. Participants also completed a Dual X-Ray Absorptiometry Test (DEXA; GE/Lunar Corp., Madison, WI) to evaluate percent fat. Pre-intervention this test was done within 48-hours of the OGTT and post-intervention it was completed within 48 hours of the last exercise training session.

Blood Pressure Blood pressure was measured manually following a minimum of 10 minutes of quiet sitting. Two measures were taken at least two minutes apart, and the average of the two was recorded. If the values differed by $> 5\text{mmHg}$, a third measurement was taken. Pre-intervention this test was done at the initial screening visit and post-intervention it was completed within 24 hours of the last exercise training session.

Insulin action Following the baseline period, subjects reported to the laboratory following an overnight fast. A catheter was inserted into a forearm vein, and a resting blood sample was taken. Subjects ingested a 75-g glucose solution (Sun Dex, Fisher Healthcare, Houston, TX) within 5 minutes, and blood samples were collected every 30 minutes for the next 2 hours while subjects rested in a seated position. Samples of venous blood for analysis of glucose were collected in heparinized syringes and then transferred to vacutainers containing sodium fluoride. Samples for analysis of insulin were collected in heparinized syringes and then transferred to vacutainers containing EDTA. All samples were immediately centrifuged, and the plasma/serum

was transferred to cryogenic vials and frozen at -80° C until analysis. All samples were run in duplicate and pre/post samples were run concurrently. For participants in the exercise groups, the post-intervention test was scheduled 20-24 hours following the last exercise bout.

Glucose concentrations were determined using a MICRO-STAT Multi-Assay Analyzer (GM7 Analyzer, Analox InrSTuments, Lunenburg, MA). Insulin concentrations were measured using radioimmunoassay (Millipore, Billerica, MA). The composite insulin-sensitivity index (CISI) was used to estimate insulin sensitivity from the OGTT. This index uses a two-term equation to account for insulin sensitivity of the hepatic and peripheral tissue ($(10,000/\sqrt{[FPG * FPI] * [G * I]})$), where FPG is fasting plasma glucose ($\text{mmol}\cdot\text{L}^{-1}$), FPI is fasting plasma insulin ($\mu\text{U}\cdot\text{mL}^{-1}$), G is mean glucose concentration ($\text{mmol}\cdot\text{L}^{-1}$), and I is mean insulin concentration ($\mu\text{U}\cdot\text{mL}^{-1}$) during the OGTT. Glucose and insulin area under the curve were calculated using the trapezoid method. In addition, FPG, FPI, and 2-hour glucose and insulin values were assessed.

Blood Lipids Fasting blood samples were collected in heparinized syringes and then transferred to vacutainers containing sodium fluoride. All samples were immediately centrifuged, and the plasma/serum was transferred to cryogenic vials and frozen at -80° C until analysis. All samples were run in duplicate and pre/post samples were run concurrently. Triglyceride, total cholesterol and high density lipoproteins (HDL) were measured using the MICRO-STAT multi-assay analyzer.

Statistical Evaluation

All statistical analyses were performed using R-software packages (www.r-project.org) (43). Significance levels were set at $p < 0.05$. A priori power analysis was based on power to detect a 10% differences in fitness between study groups. Differences pre-to-post intervention were expressed as a percent change $((\text{post-pre})/\text{pre}) * 100$ for each outcome measure to account for baseline differences between groups. Statistical significance pre-to-post intervention in outcome measures was tested with a linear mixed model for each group. A separate model was fit for each

variable and for each group. Changes in the differences scores between groups were tested with a linear model.

Part 2: Results

Summary of PA and SB changes

EX-rST group Participants in the EX-rST group completed 12-weeks of exercise training 5-days per week for 40-min per session at 50-65% of HRR. All participants completed over 90% of the prescribed exercise sessions. In addition, the EX-rST group received a targeted intervention to increase steps and decrease sedentary time during the intervention period. On average, TD sedentary time decreased by ~7% at weeks six, nine and twelve of the intervention and ~5% for TD-noex. Steps·day⁻¹ increased by ~6000 for TD and ~2500 TD-noex. In addition, they increased TD and TD-noex MVPA, MET-hrs, break-rate and stepping time at all intervention time points. There were also significant increases in TD and TD-noex MVPA, MET-hrs, break-rate and stepping time at all intervention time points. Activity/inactivity measures are shown in Table 7 and Table 8.

EX group Participants in the EX group completed 12-week of exercise training 5-days per week at 50-65% of HRR. All participants completed over 90% of the prescribed exercise sessions. The EX group was instructed not to participate in additional exercise, but they were not given additional recommendations or restrictions on non-exercise activity. For TD-noex, participants decreased sedentary time at week three and the no other differences were significant. TD steps/day increased at all intervention time points. For TD-noex, there were initial changes in behavior at week three including decreases in sedentary time and increases in break-rate, stepping time, steps·day⁻¹, break-rate, MET-hrs and MVPA. However, after the initial change, these variables all returned to baseline levels and breaks·day⁻¹ decreased for weeks six, nine and twelve. Activity/inactivity measures are shown in Table 7 and Table 8.

rST The rST group received a targeted intervention to decrease sedentary time and increase steps per day. They significantly decreased sedentary time at weeks six, nine and twelve by an average of 5.0%. Steps per day, stepping time, MET-hrs, and MVPA significantly increased at all intervention-time points. Notably, MVPA, MET-hrs, steps·day⁻¹, percent stepping, and sedentary time were not different between EX and rST during weeks six, nine and twelve even when exercise time was included. Activity/inactivity measures are shown in Table 7 and Table 8.

CON The control group was instructed to maintain habitual activity behavior. Sedentary time significantly increased by ~5% and standing time significantly decreased by ~5% at all intervention time points. There were no changes in the control group in any other activity metric at any intervention time-point. Activity/inactivity measures are shown in Table 7 and Table 8.

Outcome Measures

CRF The average change in VO₂ peak (ml/kg/min) was (mean ± SD) 11.8 ± 8.2% for EX-rST and 9.3 ± 8.8% for EX (p<0.01) (Table 9). When VO₂ peak was expressed in L/min EX-rST increased by 7.7 ± 8.2%, and EX increased 6.0% ± 8.3% (p<0.01). There were no significant changes in VO₂ peak for rST or CON in either ml/kg/min or L/min. EX and EX-rST had a significantly greater change in fitness than CON and rST. EX-rST had a significantly greater change in VO₂ peak (L/min) than CON and rST, when expressed as L/min the difference between EX and rST was no longer significant.

Body composition BMI significantly decreased in both EX and EX-rST (3.0% and 3.2%, respectively), p< 0.01) (Table 9). There were no changes in BMI for rST or CON. EX and EX-rST significantly decreased BMI compared to CON and rST, no other group differences were significant. Similar trends were observed for TBF, with reductions of 2.7% in the EX group (p<0.05) and 4.6% (p<0.01) and no significant changes for rST or CON. EX-rST had greater reductions in TBF than rST and CON and EX had greater reductions in TBF than CON.

Blood Pressure SBP significantly decreased in all intervention groups. The percent change for EX was $-4.3 \pm 5.47\%$, for rST was $-5.4 \pm 9.3\%$ and -EX-rST $4.5 \pm 8.62\%$ (Table 9). DBP decreased in rST ($-4.7 \pm 7.2\%$). No other between or within groups were statistically significant.

Insulin action The pre-and post- intervention changes in insulin action are shown in Table 10. The primary outcome measure for insulin action was CISI, which improved by $24.2 \pm 37.9\%$ in the EX-rST group ($p < 0.05$). The change in CISI was marginally significant for the EX group, ($17.5 \pm 35.3\%$ ($p = 0.07$)). There were no significant between group differences for CISI. Insulin AUC decreased by $15.7 \pm 17.5\%$ for EX-rST ($p < 0.001$) and did not significantly decrease in EX ($p = 0.3$), rST ($p = 0.7$), or CON ($p = 0.7$). The EX-rST insulin AUC was marginally lower than for rST and CON ($p = 0.07$), and no other between group differences were significant. There were no significant changes in fasting insulin pre-to-post-intervention or between groups. Insulin concentration at 2-hours decreased for both EX-rST ($30.4 \pm 42.1\%$) and EX ($27.0 \pm 27\%$), and both EX and EX-rST significantly improved compared to CON and rST. There were no significant changes in glucose AUC or fasting glucose pre-to-post intervention or between groups. There were no significant changes in 2-hour glucose concentrations, although EX-rST had a marginally significant decrease ($7.8 \pm 23.9\%$, $p = 0.1$).

Blood lipids. There were no significant within-group or between-group differences in total cholesterol or HDL, shown in Table 11. TG decreased for both EX ($19.5 \pm 31.8\%$) and EX-rST ($18.8 \pm 25.7\%$). No other within or between group differences were significant.

Part 2: Discussion

The primary purpose of this study was to determine if the activity and inactivity outside of training contribute to the magnitude of the physiological response to exercise training. This study provides preliminary data that individuals who increase non-exercise activity in addition to exercise training may have beneficial changes in insulin action compared to those who exercise

and do not change (or decrease) non-exercise activity. In addition, this study suggests that decreasing sedentary time and increasing habitual PA for 12-weeks does not result in beneficial changes in health outcomes without exercise training.

The EX and EX-rST had comparable increases in CRF (9.3% and 11.8% respectively). Both groups increased CRF more than the other groups (rST and CON). The magnitude of the CRF changes is comparable to other training studies. For example, two moderate-intensity exercise training studies reported increases in CRF of 6.3% and 12% after 6-months of training (45, 47). The EX and EX-rST also had similar reductions in BMI, TBF, body weight and SBP. None of the groups had significant changes in total cholesterol or HDL cholesterol, which is also consistent with the findings from the STRRIDE trial (32). In STRRIDE, there were significant changes in sub-fractions of lipid particles but not those included in the traditional lipid profile. In the current study, TG decreased in both EX and EX-rST (19.5% and 18.8%, respectively).

The EX-rST group did not exhibit larger changes in blood lipids compared to the EX group, which is contrary to our hypothesis and in contrast to evidence from animal studies. Furthermore, the rST group had no change in total cholesterol or HDL pre-to-post intervention and trended towards a significant *increase* in TG (24%, $p=0.07$). A series of studies by Hamilton and Bey in rodents suggested that exercise and inactivity induce different metabolic pathways and that SB decreases lipoprotein lipase (LPL), a lipoprotein that regulates triglyceride uptake, HDL production and glucose uptake (3, 17-19). To date, these findings have not been confirmed in humans and are also not supported by data in the current study. Additional research is needed to understand if changes in LPL affect blood concentrations of TG and HDL.

The changes in glucose concentration among groups were similar. There were no changes in any group for FPG or glucose AUC. The finding that FPG did not decrease is consistent with previous training studies (7, 26). The EX-rST had a 7.8% reduction in 2-hour glucose but the change was not statistically significant, while the rST group trended toward an increase in 2-hour glucose (14.5%, $p=0.14$). Both EX and EX-rST had significant reductions in 2-hr insulin

concentrations and neither group had significant reductions in FPI. The EX-rST exhibited significant changes in CISI and insulin AUC, both measures that are highly correlated with insulin sensitivity (36), while the EX group did not. The data comparing different amounts of exercise and insulin sensitivity is sparse and is confounded by differences in training protocols and methods used to determine insulin sensitivity. For example, in the STRRIDE trial the moderate-intensity group improved insulin sensitivity by ~80%, which is higher than the ~20% increase seen in the current study. However, STRRIDE participants trained for 6-months and used an IVGTT and sampled plasma glucose and insulin 25-times over a 3-hour period to measure insulin sensitivity (26). Studies using IVGTT or the gold-standard hyperinsulinemic euglycemic clamp have reported increases in insulin sensitivity (7, 35, 38). Previous training studies that have utilized OGTT have reported modest and non-significant changes in insulin sensitivity following moderate-intensity training (27, 45). Therefore, our results showing a non-significant increase in CISI and insulin AUC among the EX group are consistent with previous studies using OGTTs. Importantly, the EX-rST group *did* significantly improve both CISI and Insulin AUC, which suggests the additional intervention targeting total day inactivity and activity may have enhanced training effects compared to EX alone.

While epidemiologic evidence supports the notion that sedentary time is detrimental to metabolic health, independent of exercise (21, 23, 50), potential mechanisms explaining the potential added benefit of sedentary time reductions to exercise response are not well understood. One explanation is that individuals who are less sedentary outside of training are expending more energy. While we did not have a gold-standard measure of TDEE, MET-hrs per day were not different between groups at weeks three and nine and were different by 0.8 MET-hrs per day at weeks six and 12, which was statistically significant but is small in magnitude. In addition, changes in body composition were not different between groups (i.e., the EX-rST did not lose more weight than EX participants), and changes in CISI and Insulin AUC were not correlated with changes in BMI for either group. This suggests that some other mechanism, rather than

simply TDEE, may mediate the relationship between sedentary time and metabolic outcome measures. Stephens et al. (48) showed that, even when controlling for energy status, one day of sitting decreased insulin sensitivity by 18% compared to a day with high amounts of low-intensity activity and little-sitting. This suggests that some feature of muscle contraction or movement, even at very low intensities (i.e., standing vs. sitting) may influence metabolic pathways. As previously mentioned, SB decreases lipoprotein lipase (LPL), which regulated glucose uptake in addition to blood lipid regulation (3, 17-19). However, there is a paucity of data supporting these mechanisms in humans. Notably, it has been suggested that the biological processes underlying inactivity are different from the processes underlying adaptations to structured exercise (18).

These data support recommendations to reduce sedentary time and increase lifestyle activity among individuals who exercise, however they do not provide any evidence that reducing sedentary time is sufficient to improve health *without exercise training*. While the rST group decreased both SBP and DBP, they did not improve body composition, blood lipid, insulin action, or CRF. The individuals who exercised (EX) and did not change habitual activity behavior had greater improvements in body composition and risk factors for chronic disease than individuals who obtain similar decreases in sedentary time and increases in MVPA, steps·day⁻¹, TDEE accumulated throughout the day (rST). This suggests that exercise accumulated in one continuous bout is more effective at improving health outcomes than activity accumulated throughout the day. While epidemiologic studies have shown that SB is associated with poor health outcomes (40), no known intervention trial has examined the health effects of changing sedentary time. More work is needed to determine if SB causes poor health or if the associations seen in prospective and cross-sectional studies are the result of reverse causality (i.e., poor health causes an increase in SB), as some have suggested (12).

A major strength of this study was the manipulation and quantification of habitual activity and inactivity at multiple time-points during the exercise training period. The majority of exercise training studies quantify the exercise volume in the training sessions but do not measure

what participants are doing during the remainder of their day. The few studies that have monitored activity outside of training and examined individual response exercise training only measured activity pre-and post-intervention (10, 34). The present results provide evidence that participants who begin exercise without additional recommendations to change non-exercise behavior may have positive initial modifications to habitual activity behavior (e.g., increasing steps·day⁻¹, and decreasing sedentary time at week three). However, by week six of the intervention the participants returned back to baseline or decreased these variables and sustained these levels throughout the remainder of the intervention. This evidence supports the work of Di Blassio et al., (10) who suggested that additional intervention may be necessary to ensure behavioral compensation does not take place outside of exercise training. The detailed activity measurements obtained in this study can be used to understand if activity/inactivity variables explain the magnitude of changes in health outcomes, which will be the subject of future analyses.

The manipulation of activity behavior outside of training was a novel feature of this study. On average, the EX-rST group successfully decreased sedentary time and increased other activity measures (MET-hrs, steps·day⁻¹, stepping time and MVPA) outside of training compared to EX. While the change in the majority of outcome measures were not significantly different between EX and EX-rST, this study does provide preliminary evidence that individuals who maintain or increase non-exercise activity in addition to exercise training may have greater improvements in insulin sensitivity and insulin AUC. The EX and rST groups were comparable in all PA/SB measures. This is an important finding because it allowed for the comparison of a daily bout of exercise training to a similar amount of habitual movement (MET-hrs, steps·day⁻¹, stepping time and MVPA) that is accumulated throughout the day rather than in a continuous exercise session. These data suggest that 12-weeks of traditional exercise training induces greater changes in body composition, CRF, and disease risk factors than a modest reduction in sedentary time over the same time period.

This study also has limitations. The OGTT is a widely-accepted clinical measure of insulin action, but is not a gold-standard measure (36). More sensitive measurement tools, such as a hyperinsulinemic euglycemic clamp may have yielded more insight into the relationship between insulin action and non-exercise activity (36). This study was designed as a preliminary examination of the influence of non-exercise activity on responsiveness to exercise training. The a priori power analysis was based on the detection of a 10% difference between groups for CRF. However, since the metabolic biomarkers (e.g., insulin action and blood lipids) are more variable than CRF response and the expected magnitude of change is lower, is it possible that the study sample was not sufficiently powered to detect between-group differences in other outcome measures. Further, the within-group variability in PA and SB may dilute the group effects. Lastly, the study population included obese, non-exercising individuals who had sedentary occupations and met criteria placing them at risk for CVD. Therefore, our results cannot be generalized to other populations.

Conclusions

These data support the use of activity monitors during exercise-training studies in order to quantify non-exercise activity. Our data showed that changes in non-exercise training activity are highly variable and that nearly half of the participants who start exercising compensate by decreasing non-exercise activity and increasing sedentary time. Precise quantification of activity behavior will allow future researchers to understand features of activity and inactivity that may be important for health, with or without exercise training. This study showed that reducing SB without exercise is not sufficient to elicit health benefits. It is possible that the magnitude of reduction in sedentary time (~5%) was not adequate or that the relatively short study duration (~3 months) was not sufficient for improvements to take place. Future studies should examine the health outcomes of reducing sedentary time by greater amounts and for longer periods of time. Based on the current study, reducing sedentary time alone is not sufficient to improve metabolic health. However, among individuals who exercise, reducing sedentary time may enhance the

metabolic benefits of exercise training. Specifically, this study provides preliminary evidence that insulin sensitivity and changes in insulin AUC may be enhanced when participants reduce sedentary time and increase lifestyle activity throughout the day in addition to exercise training. Future research should examine if individual changes in activity are linked to individual changes in health risk factors.

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	EX		EX-rST		rST		CON	
	mean	SD	mean	SD	mean	SD	mean	SD
BMI (kg/m ²)	35.2	5.3	35.0	4.2	34.8	4.3	35.3	5.2
Age (y)	43.9	9.7	42.4	10.7	44.5	9.5	42.7	10.1
VO ₂ peak (ml/kg/min)	26.0	4.6	24.3	5.1	24.4	4.8	24.5	3.1
Systolic BP mmHg	124.8	10.6	122.6	7.9	128.5	11.0	132.1	7.3
Diastolic BP mmHg	77.3	8.9	78.8	6.8	84.2	7.1	80.9	9.1

Table 6. Baseline participant characteristics by group. EX-rST is exercise and sedentary time reductions, rST is sedentary time reductions, EX is exercise only, CON is control. SD is standard deviation, BMI is body mass index. There were no significant between group differences.

	Week	EX		EX-rST		rST		CON		Between group differences
		mean	SD	mean	SD	mean	SD	mean	SD	
Percent Sedentary (%)	base	69.1	7.75	71.4	7.36	68.2	7.97	66.1	7.07	ns
	three	63.8*	5.03	66.6*	5.6	66.2	6.49	71.2*	5.37	rST, EX-rST, EX < CON
	six	66.7	5.24	64.2*	5.42	64.8*	6.49	70.9*	5.69	rST, EX-rST, EX < CON
	nine	65.5*	5.03	64.6*	5.6	61.5*	6.73	73.2*	5.37	rST, EX-rST, EX < CON
	twelve	67	5.2	64.1*	5.6	63.4*	6.24	70.4*	5.4	EX-rST < EX; rST, EX-rST, EX < CON
Percent Standing (%)	base	22	6.2	20.2	6.58	23	5.89	25	5.37	ns
	three	23.1	4.65	20.5	4.4	23.8	5.05	20.5*	4.24	EX > CON
	six	21.1	4.86	22.3	4.65	23.8	5.05	21.2*	4.43	EX-rST > CON
	nine	22.3	4.65	21.9	4.4	26.2*	5.24	18.9*	4.24	rST, EX-rST, EX < CON
	twelve	21.2	4.8	22.2	4.4	25	4.85	21.4*	4.5	rST, EX-rST < CON
Percent Stepping (%)	base	8.9	2.71	8.4	2.71	8.7	3.12	9	2.26	
	three	13.1*	1.94	12.9*	2	10*	2.16	8.3	1.7	EX, EX-rST > rST, CON
	six	12.3*	1.87	13.5*	1.94	11.4*	2.16	7.9	1.9	EX-rST > rST; EX-rST, rST, EX > CON
	nine	12.2*	1.94	13.6*	2	12.3*	2.24	8	1.7	EX-rST > EX; EX-rST, EX, rST > CON
	twelve	11.9*	2	13.7*	2	11.6*	2.08	8.2	1.8	EX-rST > rST, EX; EX-rST, EX, rST > CON
Step per day	base	6108	2138	5892	2576	5689	2491	5818	1513	ns
	three	10179*	1778	10657*	1828	6955*	1550	5512	1151	EX, EX-rST > rST, CON
	six	9659*	1796	11272*	1813	7841*	1586	5381	1217	EX-rST > rST, EX; EX-rST, EX, rST > CON
	nine	9449*	1785	11322*	1848	8797*	1594	5405	1182	EX-rST > rST, EX; EX-rST, EX, rST > CON
	twelve	9548*	1792	11392*	1828	8855*	1528	5243	1194	EX-rST > rST, EX; EX-rST, EX, rST > CON

Table 7. Total day changes in activity/inactivity measures. * denotes significant change from baseline. EX-rST is exercise and sedentary time reductions, rST is sedentary time reductions, EX is exercise only, CON is control. Total day includes exercise time. SD is standard deviation. Between group differences are significant at $p < 0.05$ after Bonferroni correction.

	Week	EX		EX-rST		rST		CON		Between group differences
		mean	SD	mean	SD	mean	SD	mean	SD	
Breaks per day	base	43.8	12.78	43.5	14.33	41.8	8.66	44	12.73	ns
	three	44.8	6.58	45.3	7.2	42.7	7.21	42.9	7.07	ns
	six	40.1*	6.36	47.7*	6.97	39.4	7.21	43.6	7.59	EX-rST > EX, rST
	nine	39.2*	6.58	48.8*	7.2	43.8	7.11	48.3	7.35	rST, EX-rST, CON > EX
	twelve	40*	6.4	45.4	7.2	44.3	6.93	41.2	7.5	ns
Break-rate (breaks·sed.hour⁻¹)	base	4.6	1.55	4.4	1.55	4.6	1.39	4.9	1.7	ns
	three	5.1*	0.77	4.9*	0.8	4.8	1.08	4.5	0.85	EX-rST > CON
	six	4.5	0.75	5.1*	0.77	4.8	1.08	4.4	0.95	EX-rST > CON
	nine	4.5	0.77	5.3*	0.8	5.3*	1.12	4.8	0.85	EX-rST > CON, EX
	twelve	4.3	0.8	4.9*	0.8	5.1	1.04	4.6	0.9	EX-rST > CON, EX
MET-hrs	base	23.2	1	23	1	23.1	1.1	23.2	0.8	ns
	three	25*	0.8	24.9*	0.8	23.6*	0.7	22.9	0.6	EX, EX-rST > CON, rST
	six	24.4*	0.8	25.1*	0.8	24.1*	0.7	22.8	0.6	EX-rST > EX, rST, CON; EX > CON
	nine	24.8*	0.8	25.1*	0.8	24.5*	0.7	22.8	0.6	EX-rST > EX, rST > CON
	twelve	24.6*	0.8	25.3*	0.8	24.4*	0.7	22.9	0.6	EX-rST > rST, EX, CON; EX, rST > CON
MVPA (min)	base	32.9	15.5	31.8	20.2	27	19.3	25.8	9	ns
	three	65.8*	14.8	71.3*	15.5	38.5*	12.2	28.2	8.2	EX, EX-rST > CON, rST
	six	59.4*	15	72.1*	15.4	45.1*	12.5	26.2	8.7	EX-rST > rST, EX, CON; EX, rST > CON
	nine	61.9*	15	72.9*	15.7	50.6*	12.6	26.5	8.4	EX-rST > rST, CON; EX, rST > CON
	twelve	61.4*	15	75.8*	15.5	54.2*	12.1	25.2	8.5	EX-rST > rST, EX, CON; EX, rST > CON

Table 7 continued. Total day changes in activity/inactivity measures. * denotes significant change from baseline. EX-rST is exercise and sedentary time reductions, rST is sedentary time reductions, EX is exercise only, CON is control. Total day includes exercise time. SD is standard deviation. Between group differences are significant at $p < 0.05$ after Bonferroni correction.

	Week	EX		EX-rST		rST		CON		Between group differences
		mean	SD	mean	SD	mean	SD	mean	SD	
Percent Sedentary (%)	base	69.2	8.1	71.4	7.4	68.2	8	66.1	7.1	ns
	three	66.1*	5.4	68.4*	5.6	66.2	6.5	71.2*	5.4	rST, EX-rST, EX < CON
	six	69.7	5.2	66.1*	5.8	64.8*	6.5	70.9*	5.7	rST, EX-rST < CON; EX-rST < EX
	nine	67.7	5.4	66.8*	6	61.5*	6.7	73.2*	5.4	rST, EX-rST, EX < CON
	twelve	69.6	5.6	66.4*	6	63.4*	6.2	70.4*	5.4	rST, EX-rST < CON; EX-rST < EX
Percent Standing (%)	base	22	6.6	20.1	6.6	23	5.9	25	5.4	ns
	three	23.9	4.6	21	4.8	23.8	5	20.5*	4.2	EX, EX-rST > CON
	six	21.3	4.5	22.8*	4.6	23.8	5	21.2*	4.4	EX-rST > CON
	nine	23	4.6	22.4*	4.8	26.2*	5.2	18.9*	4.2	rST, EX-rST, EX > CON
	twelve	21.2	4.8	22.8*	4.8	25	4.8	21.4*	4.5	EX, EX-rST > CON
Percent Stepping (%)	base	8.8	2.3	8.4	2.7	8.7	3.1	9	2.3	ns
	three	10.1*	1.5	10.6*	2	10*	2.2	8.3	1.7	EX-rST > CON
	six	9	1.9	11.0*	1.9	11.4*	2.2	7.9	1.9	rST, EX-rST > CON, EX
	nine	9.2	1.9	10.7*	2	12.3*	2.2	8	1.7	rST, EX-rST > CON, EX
	twelve	9.1	1.6	10.9*	2	11.6*	2.1	8.2	1.8	rST, EX-rST > CON, EX
Steps per day	base	6120	1855	5879	2370	5689	2491	5818	1513	ns
	three	6852*	1239	7853*	1420	6955*	1550	5512	1151	EX, EX-rST > CON
	six	5967	1209	8137*	1410	7841*	1586	5381	1217	rST, EX-rST > CON, EX
	nine	6040	1259	7915*	1436	8797*	1594	5405	1182	rST, EX-rST > CON, EX
	twelve	6218	1268	7964*	1428	8855*	1528	5243	1194	rST, EX-rST > CON, EX

Table 8. Changes in total day without exercise training activity/inactivity measures. * denotes significant change from baseline. EX-rST is exercise and sedentary time reductions, rST is sedentary time reductions, EX is exercise only, CON is control. SD is standard deviation. Between group differences are significant at $p < 0.05$ after Bonferroni correction.

Breaks per day	base	43.8	12.4	43.5	14.3	41.8	8.7	44	12.7	ns
	three	44.7	6.6	45	7.2	42.7	7.2	42.9	7.1	ns
	six	38.9*	6.4	47.4*	7	39.4	7.2	43.6	7.6	EX-rST > EX
	nine	39.1*	6.6	48.6*	7.2	43.8	7.1	48.3	7.4	CON, EX-rST>EX
	twelve	39.7*	6.8	45.1	7.2	44.3	6.9	41.2	7.5	ns
Break Rate (breaks·sed.hour⁻¹)	base	4.6	1.5	4.4	1.5	4.6	1.4	4.9	1.7	ns
	three	5.1*	0.8	4.9*	0.8	4.8	1.1	4.5	0.8	EX-rST> CON
	six	4.4	0.7	5*	0.8	4.8	1.1	4.4	0.9	EX-rST>EX, CON
	nine	4.6	0.8	5.2*	0.8	5.3*	1.1	4.8	0.8	EX-rST> rST
	twelve	4.3	0.8	4.9*	0.8	5.1	1	4.6	0.9	ns
MET-hrs	base	23.2	0.9	23	1	23.1	1.1	23.2	0.8	
	three	23.7*	0.6	23.9*	0.6	23.6*	0.7	22.9	0.6	rST, EX-rST>CON
	six	23.3	0.6	23.9*	0.7	24.1*	0.7	22.8	0.6	rST, EX-rST>CON, EX
	nine	23.4	0.6	24*	0.7	24.5*	0.7	22.8	0.6	rST, EX-rST>CON, EX
	twelve	23.3	0.6	24*	0.6	24.4*	0.7	22.9	0.6	rST, EX-rST>CON, EX
MVPA (min)	base	32.7	12.9	31.9	17.9	27	19.3	25.8	9	
	three	38.2*	9.7	47.9*	10.7	38.5*	12.2	28.2	8.2	EX-rST > EX, CON
	six	32.9	9.7	47.8*	10.8	45.1*	12.5	26.2	8.7	rST, EX-rST>CON, EX
	nine	33.7	9.9	47.3*	11	50.6*	12.6	26.5	8.4	rST, EX-rST>CON, EX
	twelve	34.6	9.9	47.4*	10.8	54.2*	12.1	25.2	8.5	rST> EX-rST > CON, EX

Table 8 continued. Changes in total day without exercise training activity/inactivity measures. * denotes significant change from baseline. EX-rST is exercise and sedentary time reductions, rST is sedentary time reductions, EX is exercise only, CON is control. SD is standard deviation. Between group differences are significant at $p < 0.05$ after Bonferroni correction.

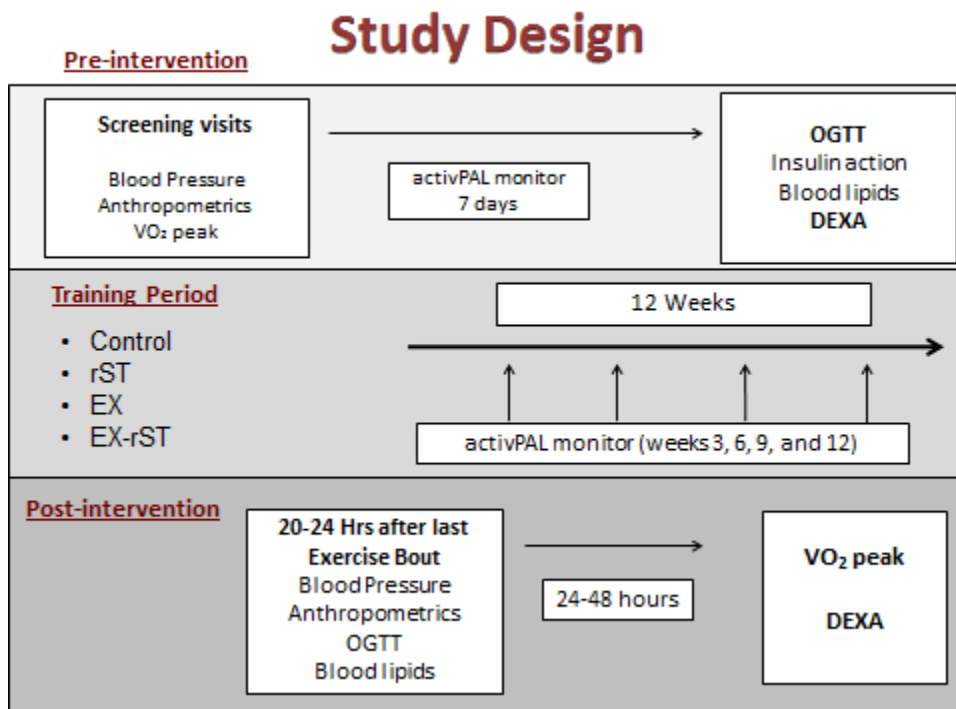


Figure 5. Overview of study design. Anthropometrics includes height, weight, waist circumference. OGTT is measure of insulin action. DEXA is dual X-ray absorptiometry test. rST is sedentary time reductions, EX is exercise only, and EX-rST is exercise and sedentary time reduction.

		EX		EX-rST		rST		CON	
		mean	SD	mean	SD	mean	SD	mean	SD
VO2 peak (ml/kg/min)	pre	26.0	4.6	24.3	5.1	24.6	5.0	23.5	2.3
	post	28.3	5.1	27.2	6.2	24.8	5.4	23.2	3.5
	% change	9.3**†	8.8	11.8**†	8.2	0.7	5.4	-1.5	7.8
VO2 peak (L/min)	pre	2.6	0.6	2.5	0.7	2.5	0.8	2.3	0.4
	post	2.7	0.7	2.6	0.7	2.5	0.8	2.2	0.5
	% change	6.0*†	8.3	7.7**†	8.3	0.6	5.2	-1.4	8.4
BMI	pre	35.2	5.3	35.0	4.2	34.9	4.4	34.8	5.3
	post	34.1	4.7	33.9	4.4	34.8	4.1	34.6	4.8
	% change	-2.96**†	3.9	-3.21**†	2.4	0.0	2.1	-0.4	2.1
Weight (kg)	pre	98.9	17.7	100.1	14.5	101.2	15.2	96.3	14.1
	post	95.7	16.0	96.7	14.3	101.2	14.7	95.9	13.1
	% change	-3.0**†	3.8	-3.4**†	2.3	0.1	2.0	-0.3	2.0
Body Fat (%)	pre	45.4	6.5	44.5	8.3	45.3	5.8	45.9	5.9
	post	44.1	6.0	42.5	8.1	45.1	6.5	46.6	6.2
	% change	-2.7*^	4.1	-4.6**†	4.2	-0.6	4.4	1.6	2.4
Systolic BP mmHg	pre	124.8	10.6	122.6	7.9	127.3	10.4	133.8	7.2
	post	117.4	8.3	116.7	8.3	122.6	11.8	127.9	9.5
	% change	-4.3*	5.5	-4.5	8.6	-3.6*	6.0	-5.4	9.3
Diastolic BP mmHg	pre	77.3	8.9	78.8	6.8	82.9	5.3	80.1	10.0
	post	76.6	8.4	75.3	8.3	78.9	6.9	78.3	6.3
	% change	-0.5	10.3	-1.0	14.9	-4.1*	11.7	-4.7	7.2

Table 9. Pre and Post intervention values for body composition, cardiorespiratory fitness and blood pressure. EX-rST is exercise and sedentary time reductions (n=16) , rST is sedentary time reductions (n=14), EX is exercise only (n=16), CON is control (n=8). Significant pre-to-post intervention change within group is denoted by * (p<0.05), ** (p<0.01). † is significantly different than CON and rST. ^ is significantly different than CON.

		EX		EX-rST		rST		CON	
		mean	SD	mean	SD	mean	SD	mean	SD
CISI	pre	2.4	1.1	2	1.1	2	1	2	1.4
	post	2.8	1.6	2.3	1.1	2.1	0.9	2.1	1
	% change	17.5	35.3	24.2*	37.9	13	42.1	20.8	42.7
FPI μU/mL	pre	18.2	11.3	20.7	11.4	23.8	16.2	19.3	10.4
	post	16.2	9.8	17.5	7.1	20.2	14.8	16.5	12.3
	% change	-8.5	40.6	-5.5	31.4	-11.7	24.8	-4.9	34.6
2-hr Insulin μU/mL	pre	103.8	53.8	140.9	83.7	82‡	47.2	164.9	157.3
	post	65.1	38.6	105.6	98.7	84.8	21.7	151.5	105.2
	% change	-27*†	42.1	-30.4***†	25.2	28.6	58	27.1	85.7
Insulin AUC μU/mL	pre	1299	4468	14988	8288	12682	5443	17080	13275
	post	12212	4828.9	12621	8197	12444	4816	16302	11419
	% change	-6.5	21.1	-15.7**	17.5	3.2	30.5	5.8	41.9
FPG mmol/L	pre	5.3	0.5	5.7	1	5.8	0.6	5.7	0.9
	post	5.4	0.5	5.7	0.7	5.8	0.8	5.5	0.7
	% change	1.8	8	0.8	7.7	0.1	7.1	-2.9	4.6
2-hr glucose mmol/L	pre	6.7	1.4	7.8	2.5	7	1.7	8.3	2.1
	post	6.5	1.1	7	2.3	8	2.5	7.9	1.8
	% change	-0.3	21.3	-7.8	23.9	14.6	17.3	-1.9	20.7
Glucose AUC mmol/L	pre	949	198	1001	259	983	178	1093	169
	post	930	171	969	222	1019	210	1054	171
	% change	-1.1	10	-2	14.8	4	11.9	-3.4	8.9

Table 10. Pre and Post intervention values for insulin action variables. EX-rST is exercise and sedentary time reductions (n=16) , rST is sedentary time reductions (n=14), EX is exercise only (n=16), CON is control (n=8). Significant pre-to-post intervention change within group is denoted by * (p<0.05), ** (p<0.01). † is significantly different than CON and rST. ‡ is significantly different than CON at baseline.

		EX		EX-rST		rST		CON	
		mean	SD	mean	SD	mean	SD	mean	SD
Total cholesterol mmol/L	pre	4.4	1.0	4.6	1.3	5.0	0.8	4.2	0.7
	post	4.5	0.7	4.4	1.0	4.9	0.6	4.5	0.8
	% change	4.8	14.9	-0.6	17.6	-0.5	9.8	7.9	22.9
HDL cholesterol mmol/L	pre	1.6	0.4	1.6	0.5	1.8	0.5	1.6	0.6
	post	1.7	0.4	1.7	0.5	1.7	0.3	1.5	0.6
	% change	9.8	22.0	11.6	37.6	0.4	18.8	1.5	27.1
TG mmol/L	pre	1.8	1.0	2.2	1.3	1.9	1.4	1.8	0.7
	post	1.4	0.8	1.7	0.9	2.1	1.5	1.9	1.3
	% change	-19.5*	31.8	-18.8*	25.7	24.2	46.6	-3.5	48.5

Table 11. Pre and Post intervention values for blood lipids. EX-rST is exercise and sedentary time reductions (n=16) , rST is sedentary time reductions (n=14), EX is exercise only (n=16), CON is control (n=8). Significant pre-to-post intervention change within group is denoted by * (p<0.05), ** (p<0.01). † is significantly different than CON and rST. ^ is significantly different than CON.

CHAPTER VI

SUMMARY AND CONCLUSIONS

Compelling evidence shows that physical activity (PA) is associated with a reduced risk of chronic disease (18). On average, when previously non-exercising individuals participate in an exercise training program they decrease disease risk factors (e.g., insulin action, triglycerides and cholesterol) and improve cardiorespiratory fitness (2). However, there is remarkable individual variability in response to exercise training (2). Some individuals will not increase or even decrease their CRF and show little to no improvement in heart disease risk factors.

Improving population levels of PA is a major public health priority (18); therefore it is critical to identify levels of non-exercise PA and inactivity that contribute to exercise non-response. Exercise training studies often standardize and precisely quantify the volume of purposeful exercise, however the activity and inactivity during the remaining 95% of the day (when the individual is not training) is rarely considered. Among the few studies that have quantified non-exercise activity, there are large individual differences in non-exercise activity (6, 13-14, 16, 23). *Therefore, the overall objective of this dissertation was to apply validated sedentary behavior (SB) and PA measurement techniques during an exercise training study to determine if time spent in SB and PA outside of training influences the physiological response to training.*

The majority of evidence linking SB to health outcomes is based on self-report questionnaires, which may be sufficient for establishing cross-sectional associations but may not be acceptable for prospective or intervention trials (8). The first step in addressing the overall dissertation objective was to validate measurement techniques for measuring SB. It was particularly important to verify that the monitors were sensitive to changes in SB, since these monitors were to be used in an intervention study. In Chapter 3, the first validation of activity monitors for measuring SB compared to a criterion of direct observation was conducted. This new evidence, based on two 6-hour direct observation periods per subject, showed that the

activPAL (AP) is an accurate and precise monitor for measuring SB and is sensitive to reductions in sedentary time. The commonly used ActiGraph (AG) monitor was less accurate, less precise and not sensitive to changes in behavior compared to the AP. These findings were supported in Chapter 4, where the validity of the measurement tools over a 7-day period was examined to determine if existing measurement tools were able to detect changes in free-living sedentary time. The activPAL detected a 5% reduction in sedentary time while AG monitor did not detect a change pre-to post- intervention. While the AG monitor was more accurate than self-report questionnaire estimates of sedentary time, the inability to detect changes in sedentary time hampers its usefulness as a tool to quantify sedentary time in an intervention trial. *Therefore, the results from Chapters 3 and 4 supported the use of the AP monitor as the exposure measure of daily activity and inactivity during an intervention study.*

There is an abundance of evidence suggesting that sedentary time is associated with poor health outcomes. However, the evidence is based on cross-sectional (5, 9-11), prospective surveillance (4, 20), animal models (1, 24), or lab-based studies that use short-term (i.e., 1-day) experimental designs in humans (21). There are no known intervention studies examining the health effects of reducing sedentary time and few studies have addressed the feasibility of reducing sedentary time in a free-living environment. Therefore, prior to implementing the 12-week intervention, the efficacy of a targeted intervention to reduce sedentary time based on tailored messages to replace sedentary time with standing time and light-intensity activity was performed. In Chapter 4, evidence is presented verifying that it is possible to decrease sedentary time among overweight, non-exercising individuals with sedentary occupations. Specifically, participants decreased sedentary time by 5%, which is equivalent to a 48 minute reduction over the course of a 16-hour waking day. The framework for the intervention from Chapter 4 was applied during the 12-week intervention study to examine the effect of reducing sedentary time, both with and without exercise, on disease risk factors.

The overall objective of this dissertation was to determine if participants who reduce sedentary time and increased light-intensity activity during an exercise training study had greater responses to exercise training. As discussed in detail in Chapter 5, Part 2, results from this study suggest that reducing sedentary time and increasing daily activity *in addition to exercise training* may enhance the metabolic benefits of exercise training. Specifically, individuals who exercised and received the sedentary time reduction intervention (EX-rST) improved insulin sensitivity by 24% and decreased insulin AUC by 16%, while the group who trained and did not change non-exercise activity (EX) did not have significant improvements in either measure. However, contrary to our original hypothesis, the EX-rST group did not exhibit greater improvements in body composition, blood lipids, or cardiorespiratory fitness compared to EX alone. Changes in CVD risk factors were also examined among a group of participants who reduced sedentary time and increased light-intensity activity but did not exercise (rST). This was the first study to examine the health effects of reducing sedentary time and we showed that a reduction in SB of ~7% for 12-weeks without exercise is not sufficient to elicit health benefits. Because the rST and EX group had similar levels of total day MVPA, steps, sedentary time, and MET-hrs during the intervention, a single bout of exercise could be compared to a similar activity dose accumulated in a different manner. The EX group had greater improvements than rST in all outcomes except for blood pressure, including a 3% decrease in body weight, a 20% reduction in plasma triglycerides, and a 27% reduction in 2-hr insulin concentrations.

Only a few studies, all published within the last two years, have used activity monitors to quantify non-exercise activity (3, 12, 14, 19, 23). Only one of these measured activity at multiple time-points during the intervention, but that study only estimated TDEE and not time in activity intensity categories (23). Therefore, the results from Chapter 5, Part 1 provide the most comprehensive evaluation of habitual SB and PA during an exercise training trial that is available to date. These data highlight the need for monitoring of non-exercise activity during an exercise training study (see discussion section, Chapter 5: Part 1). This study showed that participants in

an exercise training study do not decrease sedentary time without an additional intervention targeting non-exercise behavior and that there are large individual differences in non-exercise activity during the intervention period. In the EX group, approximately half of the participants increased time spent in SB and decreasing non-exercise steps·day⁻¹ during the training trial. Habitual activity and inactivity performed outside of training is a highly variable and important factor that should be considered in determining factors related to non-response to training.

Future Directions

The results from Chapter 5 suggest that individuals who reduce sedentary time and increase daily PA in addition to exercise may have an added benefits in metabolic response compared to those who exercise and do not increase (or maintain) non-exercise habitual activity. The detailed activity measurements obtained in this study were used to verify that participants were compliant to the study protocol on average (i.e., the EX-rST group had greater non-exercise activity than EX, and the rST group had similar increases in total-day activity as the EX group). However, within each group there were substantial individual differences in activity/inactivity measures. For example, among the EX-rST group, one subject decreased non-exercise steps by 500 steps·day⁻¹ while another increased by ~5000 steps·day⁻¹. Two subjects increased non-exercise sedentary time by 1%, while another decreased by 19%. In the future, the detailed activity/inactivity measures can be used to understand if individual activity/inactivity variables explain the magnitude of changes in individual health outcomes. It will be possible to address simple questions such as “Does the individual who decreases non-exercise sedentary time the most have more beneficial changes in health outcomes compared to the individual who increases non-exercise sedentary time the most?” In addition, there may be potential for more complex analyses by considering the activity/inactivity measures as related to an overall pattern of behavior rather than each as an independent predictor variable. Future research should develop a metric of habitual behavior that considers overall sedentary time, breaks, and activity measures

(steps or MVPA). Among the EX-rST group, the correlation between change in steps and change in sedentary time was low ($r=0.39$), suggesting individuals changed behavior by different methods (i.e., standing vs. stepping). Therefore, it may be valuable to determine both the independent effect of each activity/inactivity measure on health outcomes, as well as to quantify the overall activity behavior of the individual and subsequent associations with health outcomes.

In addition to individual differences in the change in activity behaviors, there were large individual differences in baseline levels of sedentary time (range 47 to 86% of the day). Therefore, examining the overall exposure to sedentary time in addition to changes in the variables may be an important next step. For example, is an individual who maintains a low sedentary time level (e.g., 55%) over the course of the intervention more likely to respond positively to training than an individual who begins with 85% of waking hours in SB and decreases to 75% waking hours in SB during the training time? In addition more research is needed to fully characterize the habitual behavior of participants during an exercise training study. The total daily activity measurements from the 16 participants in the EX group provide insight into temporal adaptations, individual, and average group-level changes in activity/inactivity measures. However, these observations can only be generalized to a population that completes a similar activity dose (5-days per week of moderate intensity activity). More research, with varying doses of exercise (days per week and exercise intensities), is needed to answer questions such as “Are individuals more likely to compensate if they exercise at vigorous intensity compared to moderate intensity?” or “Are individuals more/less likely to compensate if they exercise on fewer days of the week and/or for a longer duration?” Based on the large individual differences observed among the EX participants, it is clear that activity monitoring during the intervention period should be implemented by studies examining the impact of differing doses of exercise training on health outcomes. Although the sample size of this study was sufficient to explore preliminary changes in health risk factors, it may be possible that a larger sample is needed to fully characterize patterns of habitual behavior during an exercise

training study that are associated with health outcomes. Future studies should also consider using a more sensitive and reproducible measure of insulin action in order to determine the site of insulin resistance (hepatic, peripheral, or whole-body) that may be affected by exercise training compared to sedentary time reductions (15).

Lastly, more research is needed to understand the associations between SB and health outcomes. The epidemiological literature consistently shows that sedentary time is associated with reduced risk of mortality and other health outcomes. (For recent reviews in this area, see references 7, 17, 22). However, no previous studies have examined the effect of *changing* SB on health outcomes and such trials are necessary to determine if there is a cause-and-effect relationship between SB and health. The current study showed no benefits of reducing sedentary time on health outcomes during a 3-month period. It is possible that the magnitude of change in sedentary time (~5%) and the relatively short period of time (12-weeks) are not sufficient to elicit health benefits. Future studies should examine the effect of greater reductions in sedentary time that are sustained for longer durations in order to determine if an association between SB and health outcomes exists. In addition, more work is needed in human models to determine mechanisms that could be driving associations between SB and health outcomes. Hamilton and colleagues have suggested that a lack of muscle activation inhibits the lipoprotein lipase activity associated with microvasculature of the most oxidative muscles (1, 24). They suggest that lack of LPL activity induces lower clearance of plasma triglycerides in skeletal muscle and lowers plasma HDL concentrations (1). However, these mechanisms have not been replicated in human trials and are not supported by the results of the current study. More work is needed to support the notion that increased levels of SB cause negative health outcomes (18).

In conclusion, the data presented in this dissertation provide validation of activity monitors for measuring SB and present preliminary evidence that activity outside of exercise training may influence the metabolic response to training. This dissertation shows that what is done outside of exercise training can and should be quantified using objective monitors that

assess daily exposure to activity and inactivity behaviors. These results set a standard for how habitual activity and inactivity behaviors should be measured along with careful quantification of activity/inactivity dose during exercise training studies. These results also pave the way for future studies to use validated measurement techniques to understand the impact of exercise training on non-exercise activity/inactivity and the subsequent effect of total daily activity/inactivity on health outcomes.

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