THE SEPARATE EFFECTS OF EXERCISE AMOUNT AND INTENSITY ON TOTAL AND ABDOMINAL ADIPOSE TISSUE IN MEN AND WOMEN WHO ARE ABDOMINALLY OBESE

By

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Abstract

It is well established that exercise is an efficacious method for the management of abdominal obesity; however, the optimal amount and intensity of exercise that is required to combat obesity remains unclear. The purpose of this study was to determine the separate effects of exercise amount and intensity on abdominal and whole body adipose tissue in adults who are abdominally obese.

One-hundred eight participants who were previously sedentary and had abdominal obesity were randomized into one of 4 groups: Control (n=21 (10 females)), low amount, low intensity (LALI) (180 kcal/session for females and 300 kcal/session for males at 50% VO\textsubscript{2}peak, n= 25 (15 females)) high amount, low intensity (HALI) (360 kcal/session for females and 600 kcal/session for males at 50% VO\textsubscript{2}peak, n=32 (21 females)), or high amount, high intensity (HAHI) (360 kcal/session for females and 600 kcal/session for males at 75% VO\textsubscript{2}peak n=30 (19 females)). Participants performed supervised exercise 5 times/wk for 24 wks. Daily dietary logs were completed throughout the intervention and unstructured physical activity was monitored using accelerometers. Change in total and abdominal adipose tissue (AT) and skeletal muscle mass was measured via magnetic resonance imaging.

Exercise duration in minutes was 32 (SD, 4.8) for LALI, 58 (SD, 6.6) for HALI, and 40 (SD, 6.7) for HAHI. There was no difference in unstructured physical activity change and there was no difference in the adherence to prescribed diets between groups. Reductions in VAT was greater in LALI (-0.5 kg; SE, 0.1; \(p=0.001\)), HALI (-0.5 kg; SE, 0.1; \(p<0.001\)), and in HAHI (-0.5 kg; SE, 0.1; \(p<0.001\)) compared to control but did not differ between the exercise groups \(p>0.139\). Reductions in total AT, SAT, total
abdominal AT, abdominal SAT, weight and waist circumference was also greater in all exercise groups compared to control (p<0.002) but did not differ between groups (p>0.05).

These findings indicate that there is an intensity and amount independent reduction in adipose tissue depots with exercise with a preservation of skeletal muscle mass, which highlights that there are several exercise treatment options for the management of abdominal obesity.
Co-Authorship

Dr. Robert Ross was responsible for the conceptual design of the trial that the document was based upon. Acquisition of the data was a collaborative effort and performed by previous graduate students and staff within the Cardio Metabolic and Lifestyle Management Laboratory from 2009-2013. Theresa E. Cowan was responsible for all MRI data analysis and writing within this document. Paula Stotz and Theresa E. Cowan were responsible for statistical analysis and data management. Dr. Robert Ross provided critical revisions for the manuscript.
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# Table of Contents

Abstract............................................................................................................................................. ii

Co-Authorship........................................................................................................................................ iv

Acknowledgements............................................................................................................................... v

List of Tables .......................................................................................................................................... x

List of Figures ........................................................................................................................................ xi

List of Abbreviations.............................................................................................................................. xii

Chapter 1: General Introduction ........................................................................................................... 1

Chapter 2: Review of the Literature ....................................................................................................... 3

2.1 Measurement of Adipose Tissue Distribution: A Historical Perspective ........................................ 3

2.2 Using Magnetic Resonance to Measure Adipose Tissue Distribution ........................................... 5

2.2.1 Magnetic Resonance Image Acquisition....................................................................................... 5

2.2.2 Magnetic Resonance Image Analysis............................................................................................ 7

2.2.3 Determination of Tissue Volume using Multiple MR Images...................................................... 9

2.2.4 Limitations of MR Analysis ........................................................................................................ 11

2.3 The Comparison of Visceral and Subcutaneous Adipose Tissue and Their Relations to Metabolic Health ...................................................................................................................... 11

2.4 The pathophysiology of adipose tissue and metabolic dysfunction................................................ 13

2.5 Suggested cut-offs for visceral adipose tissue............................................................................... 15

2.6 Exercise amount and intensity......................................................................................................... 17

2.7 The Effects of Exercise on Skeletal Muscle..................................................................................... 19
Appendix B: Letter of Permission to use Figure 1 ............................................................ 72
Appendix C: Letter of Permission to use Figure 3 .......................................................... 76
Appendix D: Protocol for MR Image Acquisition ......................................................... 77
Appendix E: MRI Tag Legend ..................................................................................... 78
Appendix F: Cardiorespiratory Fitness Test (VO2max) .............................................. 79
Appendix G: Exercise Prescription ............................................................................ 81
Appendix H: Accelerometry – Actigraph .................................................................. 84
Appendix I: Nutritional Assessment & Counseling .................................................... 86
Appendix J: Example of Statistical Analysis ............................................................... 89
List of Tables

Chapter 2: Literature Review

Table 1.2 Amount of visceral adipose tissue and associated morbidity and mortality ..........16

Table 2.2 Summary of studies examining the effects of exercise amount and/or intensity on
visceral fat reduction. ........................................................................................................30

Chapter 3: Manuscript

Table 1.3 Participant Characteristics ..............................................................................44

Table 2.3 Exercise Intervention Descriptive Data ..........................................................47

Table 3.3 Change in anthropometric and MRI variables at 24 weeks .........................48

Table 4.3 Absolute and Relative Change in Daily Physical Activity and Sedentary Time at
baseline, 8 and 16 weeks ................................................................................................49

Table 5.3 Analysis of Dietary Intake .............................................................................50
List of Figures

Chapter 2: Literature Review

Figure 1.2 Rudimentary schematic of how magnetic resonance is able to use protons, magnets and radio waves to create images of biological tissue. .......................................................... 6

Figure 2.2 An example of using Morpho to segment tissue for an MR image. ......................... 8

Figure 3.2 An Example of how the Region Growing tool is used to segment tissue in SlicOmatic. ................................................................................................................................. 9

Figure 4.2 The determination of tissue volume from MR analysis.............................................10

Figure 5.2 Example of an axial image obtained from the upper thoracic region. Heart beat causes the distortion seen through the middle of the image.........................................................11

Chapter 3: Manuscript

Figure 1.3 Effects of exercise amount and intensity on absolute adipose tissue and skeletal muscle mass change. ..................................................................................................................45

Figure 2.3 Relative effects of exercise amount and intensity on adipose tissue and skeletal muscle mass. .........................................................................................................................46
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
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<td>ASAT</td>
<td>Abdominal subcutaneous adipose tissue</td>
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<td>AT</td>
<td>Adipose tissue</td>
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<td>BMI</td>
<td>Body mass index</td>
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<td>CRF</td>
<td>Cardiorespiratory fitness</td>
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<td>CRP</td>
<td>C-Reactive protein</td>
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<td>CSEP</td>
<td>Canadian Society for Exercise Physiology</td>
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<td>CT</td>
<td>Computed tomography</td>
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<td>CVD</td>
<td>Cardiovascular disease</td>
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<td>DXA</td>
<td>Dual-energy x-ray absorptiometry</td>
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<td>FFA</td>
<td>Free fatty acids</td>
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<td>HALI</td>
<td>High amount, low intensity</td>
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<td>HAHI</td>
<td>High amount, high intensity</td>
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<td>HDL</td>
<td>High density lipoprotein</td>
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<td>HI</td>
<td>High intensity</td>
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<td>Interleukin 6, interleukin 18</td>
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<td>La</td>
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<td>LA</td>
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<td>Abbreviation</td>
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<tr>
<td>LT</td>
<td>Lean tissue</td>
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<td>MetS</td>
<td>Metabolic syndrome</td>
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<td>METs</td>
<td>Metabolic equivalents</td>
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<td>MI</td>
<td>Moderate intensity</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<td>RCT</td>
<td>Randomized control trial</td>
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<td>SAT</td>
<td>Subcutaneous adipose tissue</td>
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<td>Skeletal muscle</td>
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<td>TAT</td>
<td>Total adipose tissue</td>
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<td>TNFα</td>
<td>Tumor necrosis factor alpha</td>
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<td>VAT</td>
<td>Visceral adipose tissue</td>
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<td>WC</td>
<td>Waist circumference</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WHR</td>
<td>Waist to hip ratio</td>
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Chapter 1: General Introduction

Obesity is one of the foremost health concerns of this era as it is linked with the development of the metabolic syndrome [1], cardiovascular disease [2, 3], some cancers [2], type 2 diabetes [4], and mortality [5]. In particular, abdominal obesity, characterized by excess adipose tissue around the mid-section is a known high-risk phenotype [6]. The greater risk associated with abdominal obesity may be due to elevated ectopic fat deposits such as visceral adipose tissue (VAT) [6]. Currently, exercise and a healthful diet are the primary treatments for reducing abdominal obesity [7]. It is well established in the literature that decreasing energy intake and increasing energy expenditure leads to a negative energy balance, weight loss, and improved metabolic health [8]. However the optimal amount and intensity of exercise needed to reduce VAT as well as total and regional AT depots is currently unknown. In other words, for a given amount of exercise, measured by kcal/session, does increasing the exercise intensity elicit a greater reduction in VAT, and for a given exercise intensity, does increasing the amount of exercise result in a greater reduction in VAT?

The findings of meta-analyses and systematic reviews regarding the effect of exercise amount on adipose tissue reduction are inconsistent. Some reviews support the notion of a dose response, noting that with increased amount of exercise in the absence of a hypocaloric diet there is a corresponding decrease in VAT [9] and subcutaneous adipose tissue (SAT) [10]. In contrast, Vissers et al. [11] suggest that amount is unimportant and regardless of the caloric expenditure there will be a similar decrease and that exercise intensity and not amount had a greater effect on reducing
VAT. However, due to the large variation of exercise amounts and intensities that were employed in the interventions that were included in the preceding reviews, it is difficult to truly separate the effects of exercise amount and intensity.

Currently Keating et al. [12] is the only exercise intervention that has examined the separate effects of exercise amount and intensity on VAT within a single study without the manipulation of diet. Keating et al. [12] followed adults who are sedentary and obese for 8-weeks. Participants were randomized to either 30-45 minutes of exercise at 50% of VO$_2$peak, 30-45 minutes at 60-70%, or 45-60 minutes of exercise at 50% of VO$_2$peak. The authors observed that in the absence of major weight loss (only ~0.4-1.4 kg lost) reductions in visceral AT were independent of exercise amount and intensity. While Keating et al. [12] provides insight into the effects of exercise amount and intensity on abdominal adiposity with minimal weight loss, the authors’ findings are limited by the use of time rather than energy expenditure to form the basis of the exercise prescribed, which makes it challenging to truly separate the individual effects of exercise amount and intensity.

Determining the optimal amount and intensity of exercise for obesity management, would assist health care providers in prescribing the most efficient exercise program for individuals who are in need of an intervention. Accordingly, in this ancillary study we sought to determine the effects of exercise amount and intensity on total and abdominal AT in previously sedentary adults who are abdominally obese. To address our research question, a secondary analysis was performed on data from a recent randomized control trial completed in our laboratory [13], which was used to determine the effects of exercise intensity on insulin sensitivity and waist circumference.
Chapter 2: Review of the Literature

Obesity is a worldwide pandemic and is recognized by the WHO as the 5th leading cause for death [14]. In particular, abdominal obesity is associated with greater risk of morbidity and mortality, which may be due in part to elevated ectopic fat depots such as visceral adipose tissue (VAT) [6]. While there are conflicting definitions of VAT, it generally encompasses the mesenteric and omental fat depots which surrounds the organs within the abdominal cavity [15]. However, due to the difficulty of measuring the mesenteric and omental depots in vivo, our laboratory defines VAT as the AT which extends from 5 cm below the space between the 4th and 5th lumbar spine (L4-L5) to 15 cm above it and encompasses both the intraperitoneal and extraperitoneal AT [16]. Regardless of the specific definition of VAT, AT located within the abdominal cavity is associated with morbidity and mortality [1, 5]. For example, cross sectional data indicates that VAT and not subcutaneous adipose tissue (SAT) is a greater predictor of fasting blood glucose, HDL, and triglycerides above and beyond traditional predictors of health risk such as body mass index (BMI) and waist circumference (WC) [1]. Others have found that VAT and not overall AT is a predictor of diabetes [4]. Additionally, VAT is an independent predictor of all-cause mortality independent of other ectopic fat depots such as liver fat [5]. The following review will cover the historical progression of measuring abdominal obesity, the use of MRI to determine whole body and abdominal AT distribution, the pathophysiology of AT and the effects of exercise on AT.

2.1 Measurement of Adipose Tissue Distribution: A Historical Perspective

Jean Vague, a French physician, was the first to observe that, by comparison to excess deposition of adipose tissue located within the hip and thigh region, excess
adipose tissue located around the abdomen was a phenotype most often associated with chronic diseases such as CVD and diabetes [17]. Vague coined the terms android and gynoid obesity, to describe or discriminate between those with central and peripheral adipose tissue distributions [17]. This remarkable observation first published in 1956 was not revisited until the 1980s when a group of researchers in Sweden used the waist to hip ratio (WHR), which was developed to quantify and put numeric value to Vague’s observations [18], to characterize differences in adipose tissue distribution and, accordingly, health risk. The authors found that both men and women with a greater WHR, or in other words individuals who had abdominal obesity, were more likely to have detrimental metabolic profiles [18]. It was later determined that while WHR is useful in cross sectional studies, its use in weight loss interventions may be limited, as both waist and hip circumference decrease proportionally [19]. In other words, the lack of change in WHR failes to identify important reductions in abdominal adiposity and consequently, health risk [19].

To address the limitations of using WHR researchers began to use WC alone as a predictor of morbidity and to determine the effectiveness of different interventions on the management of abdominal obesity. Indeed, Seidell et al. [20] were among the first to demonstrate that WC alone was associated with markers of cardiovascular disease. More recently, Ardern et al. [21] developed WC cut offs within BMI categories to indicate health risk and to further discriminate between abdominal obesity and lower body obesity. While WHR, WC and BMI measurements give insight to where AT is distributed (eg. lower vs. upper body) these methods fail to determine the amount of SAT and VAT, which have different implications on health risk. For example two individuals with the
same WC can have varying amounts of VAT and corresponding different health risk [22]. The arrival of imaging techniques has allowed researchers to separate the amount of SAT and VAT and determine how these two tissues relate to health.

Computer tomography (CT) was first used to differentiate abdominal SAT and VAT depots in 1983 by Tokunaga et al. [23]. Shortly after this, Fujioka and colleagues [24] in 1987 used CT to examine the relationship between VAT, impaired glucose tolerance, and blood lipids, which revolutionized the study of abdominal obesity. The advent of the use of MRI in determining AT distribution allowed researchers to take multiple images of a body without exposing a person to radiation as is the case with CT [25]. The first whole body MRI study was completed in 1992 by Ross et al. [26] who used this new method to characterize adipose tissue distribution in women. Following the initial study, researchers from the same group used MRI to determine the effects of diet and exercise on changes in abdominal AT during weight loss [27]. Now MRI is established as the criterion method for determining body tissue distribution [28].

2.2 Using Magnetic Resonance to Measure Adipose Tissue Distribution

2.2.1 Magnetic Resonance Image Acquisition

The acquisition of magnetic resonance (MR) images is based on the interaction of protons with a magnetic field and the use of radio waves to obtain cross sectional images from biological tissues [29]. To start, first consider that protons behave like magnets. Under normal circumstances proton’s magnetic fields align in all directions, however when a proton is placed inside of a larger magnet, the proton will align itself with the magnetic field (Figure 1A, 1B) [29].
Figure 1.2 Rudimentary schematic of how magnetic resonance is able to use protons, magnets and radio waves to create images of biological tissue.

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A: Protons aligned normally. B: Protons aligned within a magnet depicted as the gray bard north (N) and south (S) with a radio wave (RW) being sent at the protons; C. Alignment of protons after a radio wave has been absorbed; D. the relaxation of protons and the release of energy as the protons relax; E. Protons aligned in a magnet. Image modified with permission from MRI made easy (…well almost) by H. H. Schild 1990 published by Schering AG, now owned by Bayer Inc.

When a radio wave pulse is applied to protons in a magnet (Figure 1B), the proton absorbs the energy and fall out of line (Figure 1C) with the magnetic field but then relaxes and returns to its original position in line with the magnetic field. As the proton relaxes, it emits energy, which can then be detected within the MRI machine (Figure 1D) [29]. Different body tissues have different densities of protons and different relaxation rates, and therefore different signal intensities in response to the radio pulse.
These signals are used to create a gray level MR image, where different tissues are lighter or darker depending on the tissue signal intensity [29]. With the particular protocol described in the following study (T1 weighted), fat tissue appears brighter, compared to muscle and other lean tissue, which appears darker [26]. These gray level images are then analyzed using specialized computer software to determine the amount of adipose and muscle tissues within a given image [30].

2.2.2 Magnetic Resonance Image Analysis

A commonly used software program that is used to analyze MR images is SliceOmatic (Tomovision 2014). This program was originally developed by Yves Martel in the early 1990s to help with the analysis of MR images [31]. The two tools within the SliceOmatic image analysis software which are commonly used within our laboratory are ‘Morpho’ and ‘Region Growing’.

Morpho works by segmenting a gray level image into homogeneous sections using a watershed algorithm [32]. The algorithm determines and draws on the border sections (water partitioning lines) that have similar signal intensities within the gray level image [33]. As stated above, each tissue emits different signal intensities, thus Morpho creates a mosaic on top of the image segmenting the different tissues (Figure 2) [26, 29, 32, 33]. An advantage to using Morpho is that it creates an objective way to discriminate between different tissues. However, a tissue is not always segmented correctly due to inherent artifacts in the image and therefore a trained individual is required to review the images to correct the tissue borders.
Figure 2.2 An example of using Morpho to segment tissue for an MR image.

Panel A. Example of a cross sectional gray level image of L4L5 from a 50 year old, 5 ft. 3 inch, 75kg female. Panel B shows the same cross sectional image with water partitioning lines shown by the blue lines which are identifying distinct regions with similar signals. Panel C shows a segmented L4-L5 image (143cm$^3$ of visceral adipose tissue and 348 cm$^3$ of subcutaneous adipose tissue).

Region growing is another method within sliceOmatic that assists with the segmentation of tissue. This tool uses a threshold/histogram technique to distinguish between the darker and lighter pixels of a gray level image (Figure 3) [32]. As seen in figure 3, along the y-axis is the number of pixels, and along the x axis is the signal of the intensity with the minimum intensity on the left and the maximum on the right [32]. A threshold can then be manually selected and any tissues within that threshold will be tagged as the appropriate tissue [32]. With the figure below, the threshold is set to segment adipose tissue.
Figure 3.2 An Example of how the Region Growing tool is used to segment tissue in SlicOmatic.

Panel A. Histogram box from sliceOmatic, the green shaded area is a selected threshold set to select adipose tissue; Panel B. Gray level image from the mid thigh with adipose tissue depicted by light gray and lean depicted by the darker gray colour. Panel C. The previous gray level image with adipose tissue segmented as green. The orange in the middle of the image is the femur.

2.2.3 Determination of Tissue Volume using Multiple MR Images

The method for calculating tissue volume used in this study is illustrated in Figure 3, Panel 2. The tissue volume is determined by using the image thickness ($t$), tissue area ($A_1$), the area of the consecutive image ($A_2$), distance between the consecutive image ($h$), and the total number of images ($N$). Tissue volume can be converted to a mass value by multiplying the volume of AT by 0.92g/cm$^3$ and muscle by 1.04g/cm$^3$ [34].
In the first step, tissue area for a given gray level image is determined by subjecting the image to automated techniques such as “region growing” (based on voxel intensity) or “morpho” (grouping homogeneous voxels) methods. In the next step, the tissue area (cm$^2$) in a given image is determined by multiplying the number of voxels by the individual voxel surface area. In the third step, whole body or abdominal volumes are calculated using a three dimensional formula. This formula adds the volumes of truncated cones as defined by pairs of consecutive images where $I$ is the image number, $A$ is the tissue area for a given image, $t$ is the image thickness, $h$ is the distance between consecutive images, and $N$ is the number of images. Skeletal muscle and adipose tissue mass (kg) can be determined by multiplying the volumes (liters) by 1.04 and 0.92, respectively, the assumed constant density for skeletal muscles and adipose tissue. FOV= field of view.

2.2.4 Limitations of MR Analysis

Limitations of MRI include the heterogeneity of the magnetic field, which can result in artifacts in the gray level image [35]. Secondly, there are parts of the images that are challenging to segment due to distortion of the images caused by movement by the participant [36]. For example, a heartbeat can result in image distortion (see figure 3). In order to address these limitations a trained individual is required to examine each image and make a subjective decision as to how the image should be segmented. This subjectivity is an apparent limitation that results in intra- and inter-individual error when segmenting tissue.

Figure 5.2 Example of an axial image obtained from the upper thoracic region. Heartbeat causes the distortion seen through the middle of the image

2.3 The Comparison of Visceral and Subcutaneous Adipose Tissue and Their Relations to Metabolic Health

Interventions that utilize liposuction to surgically remove SAT provide some insight to the effects of SAT and VAT on health; however, the results of these studies are conflicting. Guigliano and colleagues [37] observed improvement in fasting HOMA and reduced inflammation markers (CRP, IL6, IL18 and TNFα) equivalent to 2.7 ± 0.7kg of
SAT loss, following liposuction. Findings from this study suggest that SAT is important to the development of insulin resistance and inflammation, which predicts the development of type 2 diabetes. While this does not support or refute the importance of VAT in the development of metabolic diseases it does emphasize that SAT may also be part of the causal pathway.

In contrast, Klein et al. [38] found no effect of large volume liposuction (9.1±3.7kg of primarily abdominal SAT) on adipose tissue, muscle, or liver insulin sensitivity measured by hyperinsulinemic euglycemic clamp. Additionally, there was no improvement in inflammation markers or lipid profiles. These findings are of great interest as the weight lost via liposuction is equivalent to an ~18% reduction in fat mass. Given that the weight loss achieved in the study by Klein et al. [38] did not lead to improvement in inflammation markers or lipid profiles, this suggests that the removal of SAT alone is not enough for metabolic improvement. Two main ideas from this intervention are: first, the process of weight loss through diet and/or exercise is important for improvement of metabolic health and weight loss though removing AT does not result in metabolic improvements, and second, that VAT and not SAT is likely the primary pathogenic adipose tissue.

The stark differences in the findings of Guigliano et al. [37] and Klein et al. [38] may be due to methodological issues such as measuring insulin resistance via fasting HOMA[37] as opposed to hyperinsulinemic euglycemic clamp[38], the location of liposuction (various locations [37] vs primarily abdominal [38]) and the follow-up duration (6 months [37] vs 2.5 months[38]). With the above conflicting results it is likely that both SAT and VAT play critical rolls in the development of metabolic disease such
as type 2 diabetes. It is also clear that the effects of exercise on both SAT and VAT should be examined as the independent effects of these two AT depots have on metabolic health remains uncertain.

### 2.4 The pathophysiology of adipose tissue and metabolic dysfunction

Currently, there are several central hypotheses how excess adipose tissue, primarily in the abdomen, may cause abnormal metabolic profiles such as insulin resistance: the portal vein hypothesis, the inflammation theory, and the lipid overflow-ectopic fat model.

The portal vein hypothesis was first presented by Bjorntorp in 1990 [39]. Bjorntrop and colleagues showed that the visceral fat of normal weight men and women who are abdominally obese releases free fatty acids (FFA) at a greater rate [40] in response to a stressor, which is then delivered to the liver via the portal vein [41, 42]. The influx of FFA induces hepatic insulin resistance and increased gluconeogenesis, resulting in increased circulating blood insulin and glucose, which are risk factors for type 2 diabetes [39]. Additionally, FFAs promote the production of very low-density lipoproteins (VLDL) from the liver which in turn leads to increased low density lipoproteins (LDL), which is a risk factor for cardiovascular disease (CVD) [39]. The portal hypothesis therefore suggests that the close proximity of VAT to the liver creates a local toxic effect, which then leads to metabolic dysfunction. However, a growing amount of evidence does not support this theory. For example, work by Jensen and colleagues provides evidence to refute this hypothesis [43]. Jensen’s group found a greater contribution of FFA to portal circulation from peripheral AT (90-95% in individuals who are lean and 50-60% in individuals who are obese) [43]. These results suggest that in contrast to
findings from Bjorntrop et al., [39] total AT may be more important than a specific depot such as VAT in terms of FFA delivery to the liver [43].

The inflammation hypothesis [44] relies on the well-established understanding that adipose tissue is an endocrine organ in addition to a metabolic sink. The hypothesis suggests that as AT stores increase there is a suppression of the anti-inflammatory compound adiponectin and an increase of pro-inflammatory compounds such as IL6, TNF $\alpha$, and CRP. These compounds are secreted into the blood stream resulting in systemic inflammation which then leads to whole body insulin resistance and elevated blood glucose [44].

The last theory, which is rapidly gaining popularity, is the lipid overflow ectopic fat model. This theory suggests that abdominal obesity and its downstream metabolic consequences are a marker of dysfunctional SAT [44, 45]. There is a well-established link between AT cell hypertrophy and metabolic disease, where increased AT cell size is associated with insulin resistance [6]. In the presence of a positive energy balance, if SAT is unable to compensate for the influx of energy it undergoes hypertrophy. Excess energy is then accumulated in VAT, and other ectopic energy depots [44, 45]. As VAT increases in size there is an increased secretion of IL6, TNF $\alpha$, CRP and FFA and decreased adiponectin, which then leads to systemic inflammation and insulin resistance as previously stated in the inflammation and portal hypotheses above [44]. Benatti and colleagues [46] provide evidence for this theory; the authors argue that following liposuction, excess energy is no longer able to be stored in SAT due to the sudden decrease in available SAT, which leads to a compensatory increase in VAT.
Additionally, in the Hoorn study, researchers found that body fat in the lower body, primarily in women, is associated with superior glucose control [47]. This suggests that individuals who have the capacity to store greater amounts of fat in the femoral gluteal region have functional SAT which can be used as an effective energy depot, as compared to individuals with less lower body AT.

While the mechanism linking VAT and metabolic dysfunction has not been fully elucidated, it is expected that VAT is part of the pathway. Thus, the above theories strongly suggest that excess VAT is a central component of increased metabolic health risk but also that whole body AT may contribute to both health and disease.

### 2.5 Suggested cut-offs for visceral adipose tissue

There is no consensus in the literature for whole body, visceral or subcutaneous adipose tissue cut-points to establish risk for morbidity or mortality. Suggested cut-off for total body AT are 21-33% and 8-21% for female and male Caucasians, respectively [48]. These cut offs were developed based on a BMI from 18.5-25kg/m² and vary based on ethnicity [48]. A limitation of using percent body fat alone is that it does not indicate where the AT is located as the risk associated with AT depends on the locations; abdominal AT is associated with higher risk that gluteal femoral AT [47].

The suggested cut point for VAT is less clear as there are several methods to determine VAT; single MRI or CT slice compared to multiple slices. Despres et al. [49] found >130cm² of VAT at L4-L5 was associated with decreased HDL, increased LDL and elevated insulin levels in males and females. Whereas our laboratory has published data showing that 200cm² at the same region (L4-L5) was associated with marked
increased risk of all-cause mortality in men [5]. In contrast, the largest prospective study that has examined VAT and risk is the Framingham Heart study. This group used multiple CT images and found that a 1 SD increase in VAT was associated with an odds ratio of 1.9 in women and 2.6 in men for developing metabolic syndrome (MetS). Using the averages and SD for the sample population it can be said that a ~60% increase in VAT in women increases risk for MetS by 90%, and in men a 45% increase in VAT is associated with a 160% increased risk in MetS.

Table 1.2 Amount of visceral adipose tissue and associated morbidity and mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Measurement</th>
<th>Population</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abraham [50] -MetS components</td>
<td>30 contiguous 5mm slices from S1 up</td>
<td>Men and Women from the third generation Framingham cohort</td>
<td>In women a 500cm³ increase, which is equivalent to a 45% increase of VAT in women and 25% in men is associated with a 0.13mmol/L increase in fasting glucose and 0.1mmol/L decrease in HDL and with an OR of 2.58 for MetS.</td>
</tr>
<tr>
<td>Britton [2] -CVD and cancer</td>
<td>25 contiguous 5mm think slices from S1 to the head (125mm)</td>
<td>Men and Women from the third generation Framingham cohort</td>
<td>A 1SD increase in VAT, which is equivalent to a 57% increase was associated with a HR of 1.43 for risk of cancer. If an individual in the 3rd tertile reduced their VAT by 43% to be in the 1st tertile would result in a reduction in CVD from 8% to 2%</td>
</tr>
<tr>
<td>Despres et al. [49] -MetS outcomes</td>
<td>L4-L5 in men and women</td>
<td>Men and women</td>
<td>&gt;130cm² of VAT at L4-L5 was associated with decreased HDL, increased LDL and elevated insulin levels in males and females.</td>
</tr>
<tr>
<td>Fox [1] -MetS</td>
<td>25 contiguous 5mm think slices from S1 to the head (125mm)</td>
<td>Men and Women from the third generation Framingham cohort</td>
<td>OR of 3.0 for metabolic syndrome per 1SD which is equivalent to a 61% increase in VAT in women. In Men a 1SD increase, which is equivalent to a 45% increase in VAT is associated with an OR of 4.0 for MetS.</td>
</tr>
<tr>
<td>Kuk [5] -Mortality</td>
<td>L4-L5 in men</td>
<td>141cm² (61.1)</td>
<td>OR 1.83 per 1SD (61.1) mortality, or in other words a 43% increase in VAT is associated with an 83% risk of death which can be inferred that a 21% increase in VAT is associated with a 42% increase in mortality.</td>
</tr>
<tr>
<td>Neeland [4] -Diabetes</td>
<td>Single image at L2-L3 but used it to calculate abdominal AT (BMI averaging ~35)</td>
<td>No diabetes 2.4kg(IQR of 1.9-3.1) With diabetes 2.9 (IQR of 2.5-3.4)</td>
<td>1.4kg, which is equivalent to a 57% increase of VAT is associated with an OR of 2.4 for diabetes and absolute risk increase of 8.8%</td>
</tr>
<tr>
<td>Nicklas [3] -MI</td>
<td>L4L5 Women 70-79, measuring MI And men</td>
<td>Elderly men and women 70-79 Women ~330cm² and men were 230cm²</td>
<td>HR= 1.67 for every 66.3 cm # in women, no association found in men. For every 66cm at L4L5 there was a 67% increased risk of MI.</td>
</tr>
</tbody>
</table>

1SD= 1 standard deviation; CVD = cardiovascular disease; HDL = high density lipoprotein; HR = hazards ratio; L4-L5= the pace between lumbar vertebra 4 and 5; LDL= low density lipoprotein; OR = odds ratio; VAT= Visceral adipose tissue;
Currently, exercise and a healthful diet are among the few methods for the treatment of obesity [7]. Previous research from our group has observed that a 10% weight loss is associated with an approximate 35% reduction in VAT [51]. It is often recognized that a 5-10% reduction in weight is considered clinically significant; this would then correspond to an 18-35% reduction or a 20-60cm³ at L4-L5 reduction in VAT for an average individual who is abdominally obese. Additionally, Schafer et al. [52], have found through diet and exercise than an 8% decrease in VAT was associated with a 17% increase in insulin sensitivity, which indicates that even a relatively small reduction in VAT is associated with substantive improvements in metabolic health.

Both exercise- and diet-induced weight loss show similar reductions in VAT and SAT [53]. Moreover, exercise without weight loss can lead to reductions in VAT [53, 54]. Thus, it appears that there is a robust mobilization of VAT regardless of the mode of the lifestyle intervention. However, there are additional benefits to using exercise as part of an obesity management strategy such as improvements in CRF and maintenance of lean tissue in addition to reducing VAT [53, 54]. Therefore, obesity treatment and weight reduction should incorporate exercise. However, there currently is no consensus on the optimal amount and intensity of exercise needed to reduce total and abdominal adipose tissue and further research will be required to address this question.

2.6 Exercise amount and intensity

Exercise dose has three components: amount, intensity, and frequency [55]. Exercise amount can be determined as a time, an absolute caloric expenditure, or a relative caloric expenditure (kcal/kg). However, if exercise is prescribed as time rather
than energy expenditure, this can result in different caloric expenditures if the intensities are different. For example, an individual would burn fewer calories exercising for 30min at 50% \( \text{VO}_2\text{peak} \) compared to 30min at 75% of \( \text{VO}_2\text{peak} \), with the resulting differences in energy expenditure representing a confounding variable with respect to the effects of exercise amount. Exercise intensity refers to how hard a person is working during an exercise session and is commonly prescribed as a percent of \( \text{VO}_2\text{peak} \) or max heart rate. With higher intensities individuals expend more energy per unit of time than lower intensities. Intensity can be prescribed as an absolute or relative intensity. For example, if a brisk walk of 3.5mph (absolute intensity) were prescribed to an individual with high fitness compared to an individual with low fitness, the intensity would be classified as a low intensity for the high fit individual and moderate intensity for the low fit individual, as the high fit individual would be utilizing a lower percentage of their \( \text{VO}_2\text{peak} \). Lastly, exercise frequency refers to how often the exercise takes place.

The current Canadian physical activity guidelines, or the recommended dose of exercise, is 150min of moderate to vigorous physical activity per week [56]. Within these guidelines it is implied that the intensity of the physical activity is unimportant as long as an individual reaches the prescribed amount of physical activity in minutes. However, there is a paucity of interventions, in particular randomized control trials (RCTs), which have addressed the question of exercise amount and intensity. In order to isolate the effects of exercise intensity and amount on total and abdominal adipose tissue, two components of the exercise dose equation need to be held constant while the other is manipulated.
2.7 The Effects of Exercise on Skeletal Muscle

When examining the effects of exercise, or a negative energy balance in general, it is important to also consider the changes in skeletal muscle (SM) mass in addition to AT that may occur. This is because AT has a higher energy density than SM (9400kcal/kg vs 1800kcal/kg for AT and lean tissue respectively) and therefore can provide insight into the effects on weight change as a result of lifestyle interventions [57]. For example, if two people were prescribed the same negative energy balance but one person lost more AT and the other lost more SM, which is less energy dense than AT, theoretically the person who lost more muscle mass would have also lost more weight. By examining both AT and SM it provides a clearer picture of the individuals energy balance.

Previous research from our lab has shown that SM mass is maintained with exercise induced weight loss [16, 53, 54]. Prior investigations have demonstrated that lower relative muscle mass (eg. ratio of muscle mass to fat mass) has been associated with the development of the metabolic syndrome (MetS); however, absolute muscle mass is positively associated with MetS [58]. This paradox may be explained by observations that individuals who are obese typically have a greater amount of total absolute muscle compared to an individual who is lean, indicating that muscle mass per se may not be directly in the causal pathway for the development of metabolic syndrome [59]. Regardless, decreased muscle mass is associated with increased mortality and the maintenance of muscle mass during weight loss is of importance [60].

To the author’s knowledge no studies have examined the effects of aerobic exercise amount and intensity on SM during exercise induced weight loss and only two studies
have examined the effects of aerobic exercise intensity on SM during weight loss. Irving et al. [61] observed maintenance of mid-thigh muscle in women with metabolic syndrome who performed either low or high intensity exercise (below lactate threshold vs half way between lactate threshold and VO$_{2peak}$) matched for exercise amount (16wks). In contrast, Jung and colleagues [62] examined the effects of exercise intensity on skeletal muscle in women who were overweight and had type 2 diabetes. Participants either exercised for 12 weeks at a moderate intensity (3.5-5.6 METs) or high intensity (> 5.6 METs) at a fixed amount of 500kcal/day, 5days/wk or were in the control group. A novel finding from this study was that those in the high intensity group had increased cross sectional area at the midway point between the superior border of the patella and top of the greater trochanter compared to control, while the moderate intensity group maintained muscle area. This may indicate that a higher intensity is needed to induce muscle hypertrophy. However, these findings were observed in the absence of major weight loss (<3%, p=0.32). Thus, more research is needed to examine the effects of exercise intensity on whole body SM during weight loss.

2.8 The Effects of Exercise Amount and Intensity on Adipose Tissue

In 2001, Janssen and Ross [10] were the first to summarize observations on the effect of exercise amount on AT reduction. Reviewed studies shared the following Inclusion criteria: a caloric deficit induced by exercise alone, participants characterized by overweight or obesity, the use of imaging (MRI, CT, or X-ray) to measure/analyze AT, and an identified caloric expenditure for the prescribed exercise. The authors concluded that there is an inverse relationship between exercise and SAT reduction, in that with
increased energy expended per week there is a greater reduction in SAT. However, there was insufficient evidence to make a similar conclusion regarding the effects of exercise dose on VAT reduction [51]. Absent from this review is consideration of the effect of exercise intensity on AT reduction; more recent reviews have addressed this gap.

Ohkawara et al. [9] performed a systematic review in 2007, incorporating findings from more recent trials. To be included in the review, the authors considered trials wherein the negative energy balance was induced by exercise alone, minimizing the effect of diet. The researchers included nine RCTs and seven non-RCTs. From these studies, the authors established that there was sufficient evidence to conclude that there is an inverse relationship between exercise and VAT reduction in individuals without metabolic disorders [9]. In other words, as the amount of exercise increases, there is a proportional reduction in VAT ($r=\cdot.75$). The review also indicated that a minimum of 10 MET-h/wk is necessary to decrease VAT, which is equivalent to a 70kg and a 90kg person expending 700kCal/wk and 900kCal/wk, respectively. Similar to that of Ross et al. (2001), this review did not examine the effects of exercise intensity on AT reduction.

More recently, Vissers et al. [11] conducted a meta-analysis and systematic review which examined both exercise intensity and amount in relation to VAT reduction. The authors found a significant effect of exercise intensity and no effect of exercise amount on VAT reduction. In this paper there were 15 articles that met the inclusion criteria, which consisted of: adult participants, the use of imaging techniques to quantify VAT, and no dietary component to the intervention, and either aerobic or resistance exercise.
Using the cut offs of <45%, 45-55%, and >55% of VO$_2$peak to define light, moderate and vigorous intensity exercise, respectively, the authors determined that only moderate and high intensity exercise reduced VAT.

None of the previous reviews examined the effect of exercise intensity on AT for a fixed exercise amount and conversely, the effect of exercise amount on AT while holding intensity constant. For example, in the meta-analysis conducted by Ohkawara et al. [9] the optimal intensity by which an individual should exercise at to expend 10METhr/wk (ie. 700kcal/wk for a 70-kg person) is unclear. Considering findings from Ohkawara et al. [9] in combination with observations from Vissers et al. [11], it would suggest an intensity of >55% of VO$_2$peak would be needed to see the greatest reduction in VAT. However, there are currently only two studies that have examined both exercise amount and intensity on AT reduction within a single study and the findings of these studies are conflicting [12, 63]. If the aforementioned reviews were used to develop exercise guidelines, it would be implied that exercise intensities of 55% VO$_2$peak or >75% VO$_2$peak would elicit the same reductions in AT, which has not been fully elucidated. While these reviews begin to clarify effects of exercise amount and intensity on adipose tissue reduction, the disparities between studies make it difficult to make comparisons and corresponding recommendations for exercise guidelines.

2.9 Systematic Review of the Separate Effects of Exercise Amount and Intensity on Abdominal Adipose Tissue

To clarify the difference in observations in the above reviews and to consider the effects of exercise amount and intensity on AT, a systematic review was performed. A
Medline search was done using the terms “exercise” and “amount” or “dose” or “intensity” and “obesity” or “adipose tissue” or “visceral adipose tissue”. The reference sections of the identified studies were searched to identify additional relevant studies that could be included in the review.

To be included, studies were required to meet the following criteria:

1. A minimum of two exercise interventions that had either two distinct exercise amounts while attempting to control for exercise intensity or that had two distinct exercise intensities while attempting to control for exercise amount
2. A measurement of visceral adiposity either through MRI, CT, or DXA
3. Participants had to be adults >18 years old

A total of seven studies were included, which incorporated 16 different exercise interventions. All seven of the interventions examined the effects of exercise intensity on abdominal AT reduction and two of the interventions examined the effects of exercise amount on changes in abdominal AT.

2.9.1 Exercise Amount and Adipose Tissue Reduction

In a seminal study by Slentz et al. [63] the authors examined the effects of both exercise amount and intensity on VAT and its relation to metabolic outcomes. The exercise intervention is summarized in Table 2 and the effects of exercise intensity will be discussed in a section below. The results indicated that a high amount of exercise (23kcal/kg/wk) was necessary to reduce VAT from baseline, whereas a low amount (14kcal/kg/wk), regardless of the intensity resulted only in VAT maintenance compared
to baseline [63]. Nevertheless, all of the exercise treatments were superior to control, which increased VAT over the 24wk study. Additionally, only the high amount group experienced reductions in abdominal SAT compared to all other groups [63]. However, a major limitation of this study is that participants were instructed to maintain baseline weight throughout the intervention [64]. This was done because the authors speculated that improvements in their primary outcome, insulin sensitivity, would be driven by changes in the muscle and not by AT, therefore to control for AT weight was maintained [64]. While this highlights the effects of exercise alone without weight loss on VAT and abdominal SAT maintenance and reduction depending on exercise amount, it limits the ability to examine the effects of exercise-induced weight loss on AT. Previous research from our lab has shown that while exercise without weight loss can reduce AT there are greater reductions in AT with exercise-induced weight loss; therefore the effects of exercise amount, independent of dietary manipulation, should be examined [53, 54].

A trial by Keating et al. [12] is the only other study, to the author’s knowledge, that has examined both the effect of exercise amount and intensity within a single study. In contrast to Slentz et al., [63] the authors found reductions in AT to be independent of exercise amount [12]. Participants exercised for 30-45min/day or 45-60min/day at 50% VO$_2$peak and both exercise groups had similar reductions in VAT and abdominal SAT compared to control. Compared with Slentz et al., [63] participants were instructed to maintain their baseline diet in an attempt to create a negative energy balance through exercise alone [12]. Keating et al. [12] also used several abdominal MRI images to determine abdominal AT changes, while Slentz et al. [63] used a single CT slice. An important finding from Keating et al. [12] is that despite the low amount low intensity
group exercising for ~2hr less each week than the high amount low intensity group, these participants experienced similar reductions in abdominal AT. This aids physicians and patients by providing varying treatment options that are equally effective. For example, if time is a barrier to exercise for an individual, a physician can prescribe a physical activity program to accommodate for this.

2.9.2 Exercise Intensity and Adipose Tissue Reduction

Presently, there are few intervention studies that have specifically examined the effects of two different exercise intensities on AT change in adults within the same trial (Table 2). In the pivotal study by Slentz et al. [63] described above, the authors also examined the effect of intensity for the same exercise amount of 14kcal/kg/wk. The authors found that regardless of the intensity for the given amount of exercise, participants were able to maintain VAT compared to baseline but this was superior compared to the control group, which experienced an increase in VAT. There was also no difference in the change in abdominal SAT compared to control. From this, the authors concluded that exercise intensity does not affect abdominal AT reduction for a given amount of exercise.

Likewise, Keating et al. [12] found reductions in abdominal AT to be independent of exercise intensity. When comparing intensities of 50% vs 60-70% of VO\textsubscript{2}peak for participants who exercised 30-45min/day 3 days/wk for eight weeks in adults who are sedentary and obese, the two groups experienced similar reductions in VAT and abdominal SAT [12]. However, an inherent limitation of the Keating et al. [12] study, which used time rather than energy expenditure to prescribe exercise amount, is that for
a given time a higher intensity will have a greater energy expenditure (calories per session) because of a higher rate of energy expenditure compared to a lower intensity. Interestingly, despite the fact that the participants in the high intensity group expended more calories per session they still experienced similar reductions in abdominal AT compared to the low intensity group, which further supports their finding that reductions in VAT and ASAT are amount independent.

In another study, Nicklas et al. [65] found no effect of exercise intensity on VAT or abdominal SAT reduction. Participants were prescribed exercise at 8 kcal/kg/wk at a low intensity (45-50% of VO₂peak) or moderate intensity (70-75% of VO₂peak) while also manipulating diet to obtain a total negative energy balance of 2800kcal/wk. The strength of this intervention was that the authors were able to stringently control energy deficit and weight loss between groups to examine the effects of exercise intensity on VAT and abdominal SAT reduction. However, a limitation is that the percent of total energy deficit caused by exercise varied between participants. For example, a 100kg person would expend 800kcal/wk or ~30% of their total caloric deficit via exercise whereas a 70kg individual would expend 560kcal/wk or 20%/wk of deficit via exercise. As previously demonstrated in our lab there are greater health benefits from weight loss due to exercise alone than to diet alone when the absolute energy deficit is the same [53, 54].

The three other studies that have examined effect of exercise intensity on VAT reduction in adults prescribed exercise based on absolute caloric expenditure (kcal/wk rather than kcal/kg/wk) (Table 2). Irving et al. [61] found that exercise prescription of 2000kcal/wk at a low or high intensity was not enough to induce a reduction in abdominal AT compared to control in either exercise group. However, the high intensity
group did experience reductions in total abdominal AT, abdominal SAT and VAT compared to baseline, and greater reductions in total abdominal AT and abdominal SAT compared to the low intensity groups despite no difference in VAT reduction between the two exercise groups. A limitation of the study is that exercise intensity was prescribed based on ratings of perceived exertion rather than a percentage of VO$_{2\text{peak}}$ making it difficult to isolate the effects of exercise intensity. Likewise, Coker et al. [66] found that with 1000kcal/wk of exercise-induced energy expenditure, only the high intensity (75% of VO$_{2\text{peak}}$) and not the moderate intensity (50% of VO$_{2\text{peak}}$) exercise groups decreased VAT compared to baseline with no difference in abdominal SAT compared to baseline for either exercise group.

In contrast to Irving et al. [61] and Coker et al. [62], Jung et al. [62] found that moderate intensity (3.5-5.2METS for 2500kcal/week) in type 2 diabetics reduced total abdominal AT and VAT compared to control but there was no difference in the high intensity group (>5.2METS for 2500kcal/week) compared to control. However, only the high intensity group had reductions in abdominal SAT compared to control. The results of Jung and colleges may differ because it has been previously shown that type 2 diabetics are resistant to reductions in VAT compared to non type 2 diabetics [67].

### 2.9.3 The effects of Exercise Intensity on lower body adipose tissue

Irving et al. [61] found only the high intensity group had reductions in lower body AT, measured using a single CT slice of the thigh compared to baseline but this did not differ from the other groups. In contrast, Coker et al. [66] found no change in lower body AT also measured with a single CT slice in any of the groups compared to baseline or
control but that the high intensity group was experiencing a trend for reductions compared to baseline. Likewise Jung et al. [62] found that none of the exercise groups experienced reductions in lower body AT compared to control or baseline. This lack of differences could be due to the small sample size as there were 7-11 participants per group [61], 6 participant per groups [66], and 8-12 participants per group [62].

2.9.4 Summary of the effects of exercise intensity on abdominal adipose tissue distribution

To summarize the studies above, four of the seven studies measured total abdominal AT and of these, only one study found that increasing exercise intensity resulted in greater reductions in total abdominal AT compared to baseline [61], one found that moderate exercise resulted in greater reductions in total abdominal AT compared to control whereas the high intensity exercise group did not [62], and the two other studies found reductions in total abdominal AT to be independent of exercise intensity [63, 68]. All seven studies had measures of abdominal SAT and of these, three studies found that increasing the exercise intensity resulted in a greater reduction of abdominal SAT [61, 62, 68] while the others did not [12, 63, 65, 66]. Two studies found that with an increased intensity there is a greater reduction in VAT [61, 66] one study found moderate intensity exercise reduced VAT but high intensity did not [62], another study found that neither exercise group had reductions in VAT [68], and three studies found reductions in VAT to be independent of exercise intensity [12, 63, 65].

Inspection of Table 2 indicates that there are conflicting observations in the current literature regarding the effect of exercise amount and intensity on abdominal AT reduction. Differences in methodologies and limitations in study design have largely
contributed to the inability to provide clear evidence in support of or against the effect of exercise intensity on VAT reduction. Currently, no recommendation can be made in terms of the best exercise to elicit the greatest reduction in AT and more research is needed to answer this question. Additionally the majority of the studies had small sample sizes (five of the seven interventions included in the review had n ≤ 12/group) [12, 61, 62, 66, 68]. Additionally these studies were relatively short in duration (≤12 weeks). The two studies with larger sample sizes (>40/group) and longer duration [65] [63], manipulated diet by advising participants to change their caloric intake to compensate for their energy expended in exercise, which confounds the results of the effects of exercise alone on AT reduction.

2.10 Summary

From the above literature review it is evident that little can be decisively concluded regarding the effects of exercise amount and intensity on total and abdominal AT reduction. Thus, there is a clear gap in the literature that needs to be addressed. The following thesis aims to address some of these gaps by utilizing the data from a stringently controlled RCT with 3 different exercise conditions, varying in both amount and intensity of exercise prescription, and employing criterion methods to measure whole body and abdominal AT and muscle mass.
Table 2.2 Summary of studies examining the effects of exercise amount and/or intensity on visceral fat reduction.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Group, N</th>
<th>Sex</th>
<th>Age</th>
<th>Population</th>
<th>Duration</th>
<th>Intervention</th>
<th>Method</th>
<th>Δ TAT</th>
<th>Δ ASAT</th>
<th>Δ VAT (cm³)</th>
<th>ΔVAT (%)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coker et al. [66]</td>
<td>Control N=6</td>
<td>M+F</td>
<td>67</td>
<td>Ow/ob</td>
<td>12 wk</td>
<td>1000kcal/wk @ 50% VO₂peak</td>
<td>CT L4L5</td>
<td>+10 ± 6</td>
<td></td>
<td></td>
<td>0</td>
<td>Intensity dependent; Reduction of VAT compared to baseline with HI but not with MI</td>
</tr>
<tr>
<td></td>
<td>MI N=6</td>
<td>M+F</td>
<td>70</td>
<td></td>
<td>12 wk</td>
<td>1000kcal/wk @ 75% VO₂peak</td>
<td></td>
<td>-13 ± 4</td>
<td></td>
<td>-39 ± 11†</td>
<td>~ -20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HI N=6</td>
<td>M+F</td>
<td>73</td>
<td></td>
<td>12 wk</td>
<td></td>
<td></td>
<td>-12 ± 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irving et al. [61]</td>
<td>Con N=7</td>
<td>F</td>
<td>51</td>
<td>Ob</td>
<td>16 wk</td>
<td>2000kcal/wk below lactate threshold</td>
<td>CT L4L5</td>
<td>-28cm²</td>
<td>-16</td>
<td>-2</td>
<td>0</td>
<td>Intensity Dependent; Reduction of VAT compared to baseline with HI but not with MI</td>
</tr>
<tr>
<td></td>
<td>MI N=11</td>
<td>F</td>
<td>51</td>
<td></td>
<td></td>
<td>2000kcal/wk 3 session half way between L₄ threshold and VO₂peak</td>
<td></td>
<td>-11cm²</td>
<td>-11</td>
<td>-7</td>
<td>-5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HI N=9</td>
<td>F</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-58cm²†</td>
<td>-46†</td>
<td>-25†a</td>
<td>-17†</td>
<td></td>
</tr>
<tr>
<td>Jung et al. 2012 [62]</td>
<td>Control N=12</td>
<td>F</td>
<td>56</td>
<td>T2D</td>
<td>12wk</td>
<td>2500kcal/wk, 5 sessions/wk for 60min (5.5-5.2MET’s)</td>
<td>CT L4L5</td>
<td>0.5 ± 6.0</td>
<td>2.3 ± 6.3</td>
<td>-1.5 ± 7.8</td>
<td>-8.0 ± 12.8</td>
<td>Intensity dependent; Reduction of TAT and VAT with MI compared to control but not with HI</td>
</tr>
<tr>
<td></td>
<td>MI N=8</td>
<td>F</td>
<td>57</td>
<td></td>
<td></td>
<td>2500kcal/wk, 5 sessions/wk for 30min (&gt;5.3MET’s)</td>
<td></td>
<td>-9.0 ± 8.6%</td>
<td>-4.6 ± 10.1</td>
<td>14.7 ± 9.8*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HI N=8</td>
<td>F</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-7.6 ± 12.2%</td>
<td>-7.2 ± 12.4*</td>
<td>-8.0 ± 12.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keating et al. 2015 [12]</td>
<td>Control N=12</td>
<td></td>
<td></td>
<td>Sedentary Ow/Ob</td>
<td>8 wk</td>
<td>MRI Diaphragm to pelvis</td>
<td></td>
<td>+320 ± 156 (+2.6%)</td>
<td>+93 ± 84</td>
<td>3.4</td>
<td>Intensity independent; Amount independent; All groups had similar magnitude of ASAT and VAT compared to control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LA, HI Low N=12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30-45min/day 2days a week with 1 home based brisk walk @ 60-70% VO₂peak on a bike</td>
<td></td>
<td>-568 ± 139 (-5%)*</td>
<td>-258 ± 88*</td>
<td>-7.2*</td>
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<tr>
<td></td>
<td>HA, MI N=12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45-60min/day 3days/wk with 1 home brisk walk @ 50% VO₂peak</td>
<td></td>
<td>-597 ± 202 (-5%)*</td>
<td>-387 ± 120*</td>
<td>-11.0*</td>
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<tr>
<td></td>
<td>LA, MI N=12</td>
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<td></td>
<td></td>
<td></td>
<td>30-45min 2days/wk with 1 home based brisk walk @50% VO₂peak</td>
<td></td>
<td>-166 ± 141 (-1.6%)*</td>
<td>-213 ± 106*</td>
<td>-7.1*</td>
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<tr>
<td>Lee et al. 2012 [68]</td>
<td>Control N=7</td>
<td>F</td>
<td>38</td>
<td>OW/ob</td>
<td></td>
<td>Wk1-4 14.2kcal/kg/wk for 3d/wk Wk 5-9 18.9kcal/kg/wk for 4 d/wk Wk 10-14 23.6kcal/kg/wk 5d/wk 50% VO₂peak</td>
<td>CT L4L5</td>
<td>No Δ</td>
<td>No Δ</td>
<td>No Δ</td>
<td>Reduction of TAT and VAT is intensity independent but reduction in ASAT was intensity dependent Reduction of VAT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HI N=7</td>
<td>F 42</td>
<td>Wk1-4 14.2 kcal/kg/wk for 3d/wk</td>
<td>Wk 5-9 18.9 kcal/kg/wk for 4 d/wk</td>
<td>Wk 10-14 23.6 kcal/kg/wk for 5 d/wk</td>
<td>70% VO₂peak</td>
<td>-40 †</td>
<td>-40 †</td>
<td>No Δ</td>
<td>compared to baseline with HI but not with MI</td>
<td></td>
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<tr>
<td>Nicklas et al. [65]</td>
<td>MI +diet N=40</td>
<td>F 57</td>
<td>OW/Obe 20 wk 8 kcal/kg/wk ~700 kcal/wk (net 2800 kcal/wk with diet) @ 45-50% HHR</td>
<td>CT L4L5 &amp; DXA -14/26 ± 764 cm³ †</td>
<td>-591 ± 340 †</td>
<td>-35 †</td>
<td>Intensity independent; All group had similar magnitude of ASAT and VAT compared to control</td>
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<tr>
<td></td>
<td>HI +diet N=38</td>
<td>F 59</td>
<td>20 wk 8 kcal/kg/wk or ~700 kcal/wk (net 2800 kcal/wk with diet) @ 70-75% HHR</td>
<td>-1007 ± 1136 cm³ †</td>
<td>-630 ± 298 †</td>
<td>-34 †</td>
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<tr>
<td>Slentz et al. [63]</td>
<td>Control N=47</td>
<td>M+F</td>
<td>Sedentary Ow/obese 24 wk 14 kcal/kg/wk @ 40-55% VO₂peak</td>
<td>CT single L4L5 3.9 ± 10.4 †</td>
<td>1.1 ± 11.9</td>
<td>+8.6 ± 17.2 †</td>
<td>Intensity independent reduction in SAT and VAT; Amount dependent reduction in TAT, VAT and ASAT</td>
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<tr>
<td></td>
<td>LA, MI N=40</td>
<td>M+F</td>
<td>24 wk 14 kcal/kg/wk @ 40-55% VO₂peak</td>
<td>0.2 ± 10.6 † b</td>
<td>-1.2 ± 11.8 % b</td>
<td>-1.7 ± 19.7 *</td>
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<tr>
<td></td>
<td>LA, HI N=46</td>
<td>M+F</td>
<td>24 wk 14 kcal/kg/wk @ 65-80% VO₂peak</td>
<td>2.0 ± 15.5 † b</td>
<td>3.1 ± 18.7 % b</td>
<td>-2.5 ± 21.3 *</td>
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</tr>
<tr>
<td></td>
<td>HA, HI N=42</td>
<td>M+F</td>
<td>24 wk 23 kcal/kg/wk @ 65-80% VO₂peak</td>
<td>-6.8 ± 12.0 † *</td>
<td>-6.8 ± 12.0 † *</td>
<td>-6.9 ± 20.8 † *</td>
<td></td>
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</tbody>
</table>

ASAT = abdominal subcutaneous adipose tissue; CT= computed tomography; F = females; HA = high amount of exercise; HI = high intensity exercise ; LA = low amount of exercise; La = lactate M= males; METs = metabolic equivalents MI= moderate intensity exercise; MRI = magnetic resonance imaging; Ob = obese; Ow = overweight; Sed = sedentary; TAT = total adipose tissue; wk = weeks; VAT = visceral adipose tissue; No Δ indicates there was no change compared to baseline when values could not be estimated from figures. *p<0.05 compared to control; † p<0.05 compared to baseline; a p<0.05 compared to Moderate intensity (Irving et al. [61]); b p<0.05 compared to high amount vigorous intensity (Slentz et al. [63]).
Chapter 3: The Separate Effects of Exercise Amount and Intensity on Total and Abdominal Adipose Tissue in Men and Women Who Are Abdominally Obese
3.1 Abstract

**Background:** Although exercise is an established strategy for reducing obesity, the separate effects of exercise differing in amount and intensity on total and abdominal adipose tissue continues to be the source of uncertainty and debate.

**Objective:** The purpose of this study was to determine the separate effects of exercise amount (kcal/session) and intensity (% of VO\textsubscript{2peak}) on total and abdominal adipose tissue (AT) in adults who are obese.

**Methods:** Participants were 108 (60% female) sedentary, middle-aged (mean (SD) 52.7 (7.6) years), adults with abdominal obesity who completed a 24 week intervention. Participants were randomly assigned to: Control (n=21), low amount, low intensity exercise (LALI) (180 and 300 kcal/session for women and men, respectively, at 50% of VO\textsubscript{2peak}, N=25), high amount, low intensity exercise (HALI) (360 and 600 kcal/session for women and men respectively at 50% VO\textsubscript{2peak}, N=32); high amount, high intensity exercise (HAHI) (360 and 600 kcal/session for women and men, respectively, at 75% of VO\textsubscript{2peak}, N=30). Participants were asked to perform supervised exercise 5 times/week. MRI was used to measure whole body and abdominal adipose tissue and skeletal muscle mass. Unstructured physical activity performed outside of the prescribed exercise was monitored using accelerometers.

**Results:** Exercise duration in minutes was 32 (4.8) for LALI, 58 (6.6) for HALI, and 40 (6.7) for HAHI. There was no change in unstructured physical activity or caloric intake between exercise groups. Reduction in total AT, subcutaneous AT, total abdominal AT, abdominal SAT, lower body AT, weight and waist circumference were greater in all
exercise groups compared to control at 24 weeks (p<0.002), but did not differ between each other (p>0.05). Reduction in VAT was greater in LALI (-0.5 kg; SE, 0.1; p=0.001), HALI (-0.5 kg; SE, 0.1; p<0.001), and in HAHI (-0.5 kg; SE, 0.1; p<0.001) compared to control, but did not differ between the exercise groups p>0.14. Skeletal muscle did not change at 24 weeks within any exercise group compared to control (p>0.32)

**Conclusion:** Substantial reduction in total and abdominal AT with a preservation of skeletal muscle mass was observed independent of exercise amount and intensity.

**Keywords:** Abdominal obesity, exercise amount, exercise intensity, visceral adipose tissue
3.2 Introduction

It is now firmly established that habitual exercise is associated with marked reduction in total and abdominal adipose tissue (AT) independent of age, gender and ethnicity [11, 53, 54, 69]. Systematic reviews have provided support for a dose response; with increased amount of exercise in the absence of caloric restriction, there is a corresponding decrease in subcutaneous adipose tissue (SAT) [10] and VAT [9], though this is not agreed on by all [11]. The discrepancies in these reviews may be due to the difficulty in comparing exercise amount at a fixed intensity and conversely exercise intensity at a fixed amount between different studies. Consequently, at present the optimal amount and intensity of exercise required to elicit the greatest reduction in total and abdominal obesity remains unclear. Keating et al. [12] report that following an 8-week intervention in adults who are sedentary and obese who were prescribed exercise of either 30-45 minutes at 50% of VO$_{2\text{peak}}$ 3d/wk, 30-45 minutes at 60-70% VO$_{2\text{peak}}$ 3d/wk, or 45-60 minutes of exercise at 50% of VO$_{2\text{peak}}$ 4d/wk, and that reductions in VAT and abdominal SAT were observed independent of exercise amount and intensity [12]. While these findings provide insight, it is difficult to truly separate the effects of exercise amount and intensity because the authors used time rather than caloric expenditure to fix exercise amount, resulting in different energy expenditure in each of the group. Additionally, because there is disagreement between Keating et al. and systematic reviews, with respect to the effects of exercise amount, additional research is needed to untangle the relationship between adipose tissue reduction and amount of exercise.
Despite disagreement, there is a growing body of literature that suggests with an increased amount of exercise there is a greater reduction of weight and AT [9, 10, 70]. Therefore we hypothesized that for a fixed intensity of exercise that increasing the amount will result in greater reduction of total and abdominal adipose tissue. In terms of exercise intensity there is more conflicting results, where some reviews and studies have found with increased exercise intensity there is a greater reduction in abdominal AT [11, 61, 66] while others have not [12]. In terms of regional adipose tissue mobilization, VAT is more lipolytic and sensitive to catecholamines compared to other AT depots [71]. With higher intensity exercise there is a greater release of catecholamines which would initially imply that there may be a greater mobilization of VAT with a higher intensity, however, the rate of whole body lipolysis remains constant with increasing intensities [72]. Additionally, it has been suggested that VAT unlikely contributes to fat oxidation during exercise [72], we therefore hypothesized that there will be no difference in total and abdominal AT reduction when the amount of exercise is held constant and the intensity is manipulated.

Determining the separate effects of exercise amount and intensity on total and abdominal obesity may provide treatment options for practitioners seeking to optimize individual treatment strategies for adults who are obese. Accordingly, in this ancillary study we sought to determine the separate effects of exercise amount and intensity on total and abdominal adipose tissue in previously sedentary adults who are abdominally obese.
3.3 Methods

Setting and Participants: Details of the trial design and methods are published [13] as are the findings from the primary analysis [73]. Briefly, we conducted a 24-week, single center, randomized controlled trial with a parallel group design between September 2009 and May 2013. The primary objective of the original investigation was to determine the separate effects of exercise intensity and amount on waist circumference and glucose tolerance among 300 sedentary adults who are abdominally obese. Potential participants were excluded if they reported a history of heart disease, stroke or any condition that would prevent them from engaging in exercise, if they were already engaging in two or more planned exercise sessions per week and if they were diabetic. All participants provided informed consent prior to participation. The original study and this ancillary analysis were approved by the Queen’s University Health Sciences Research Ethics Board.

Of the three hundred participants recruited into the primary trial, 129 of those who completed the study (n=217) had whole body MRI data pre- and post- intervention. Of these 129 participants, 21 participants were excluded due to poor image quality (2 participants) or inaccurate positioning within the magnet post-treatment (19 participants). In total 108 participants were included in this analysis. Of the participants included, 21 were in the control group (10 Female, 11 Male), 25 were in the low amount, low intensity group (LALI; 15 Females, 10 Males), 32 were in the high amount, low intensity group (HALI; 21 Females, 11 Males) and 30 were in the low amount, high intensity group (LAHI; 19 Females, 11 Males).

Exercise intervention
Participants were randomized into one of 4 groups: 1) no-exercise control, 2) low amount, low intensity exercise (LALI; 180 and 300 kcal/session for women and men, respectively, at 50% of maximum oxygen consumption [VO_2peak]), 3) high amount, low intensity exercise (HALI; 360 and 600 kcal/session for women and men, respectively, at 50% of VO_2peak), and 4) high amount, high intensity exercise (HAHI; 360 and 600 kcal/session for women and men, respectively, at 75% of VO_2peak). Participants were asked to exercise 5 days per week for 6 months at the prescribed exercise intensity.

Participants were asked to walk and/or jog on a treadmill until they reached the time required to achieve the desired energy expenditure (kilocalories per session) five times per week for 24 weeks. Heart rate and VO_2peak data obtained from the baseline maximal exercise test was used to calculate the target heart associated with a VO_2peak of approximately 50% (LALI and HALI) and approximately 75% (HAHI) for each participant. At these exercise intensities, the energy expenditure targets (exercise amount) for women and men, respectively, were 180 and 300 kcal for the LALI group and 360 and 600 kcal for the HALI and HAHI groups. Maximal exercise tests were repeated at weeks 4, 8, and 16 to adjust the prescribed exercise heart rate. This was done to verify the relationship between heart rate and VO_2 because cardiorespiratory fitness typically increases with exercise, which would then alter the time required to achieve the prescribed exercise amount (eg. energy expenditure).

All exercise sessions were supervised, and all exercise participants were asked not to engage in any structured exercise outside of the supervised sessions. Heart rate was monitored every 5 minutes for all exercise participants at every session to help
ensure adherence to the prescribed exercise intensity. Participants in the control group were asked to maintain baseline physical activity levels.

**Assessment of Body Composition**

Whole body adipose and skeletal muscle tissue was measured by magnetic resonance imaging (MRI) at baseline and 24 weeks using a 1.5 Tesla magnet at the Kingston General Hospital using a protocol previously described [30]. Briefly, participants entered the magnet in a prone position, feet first, L4-L5 was landmarked using a sagittal scout image. Once the L4-L5 intervertebral space was identified, 10mm thick images, 40mm apart were taken from L4-L5 to the lower extremity (feet). The participants were then required to exit the magnet and re-enter head first with their arms extended. The L4-L5 inter-vertebral space was relocated, and 10mm thick images, 40mm apart were taken from L4-L5 to the upper extremity (hands) (please see Appendix D for details). As previously described [30, 74] specialized image analysis software (sliceOmatic version 5.0, TomoVision, Montreal, QC) was used to quantify the various tissues. One of the author’s, TC, analyzed all MRI data and was blind to group assignment. Total adipose and skeletal muscle tissue was derived using all images (~41 images per participant). Abdominal AT was determined using 5 consecutive images beginning 1 below L4-L5, L4-L5 and three images above; lower body AT was measured from the head of the femur to the lower extremities. The procedure used for tissue identification is shown in Appendix E. The algorithm used to derive various tissue volumes and convert volume to mass values is shown in section 2.2.3 of this document.

**Accelerometry**
Physical activity performed outside of the supervised exercise sessions (unstructured physical activity) was monitored using ActiGraph GT3X accelerometers for a 1-week period at baseline, 8, and 16 wks. To be included in the analysis participants had to have worn the accelerometer for a minimum of 10hr/day for at least 4 days each period with one weekend day. Established accelerometer cut points of <100cpm, 100 to <1951 and ≥1951 were used to classify sedentary time, light physical activity (LPA), and moderate to vigorous physical activity (MVPA) [75]. In order to determine unstructured PA at 8 and 16 weeks, structured exercise that was performed in the laboratory was removed from TPA using an in house program that removed bouted PA >20min. To be classified as bouted PA at least 80% of the bout had to have reached the MVPA cutoffs; for example a 20min bout of PA had to have at east 16min of MVPA.

**Dietary Regimen**

During a one week baseline period, participants were instructed to maintain baseline body weight through maintenance of calorie intake while recording self-reported daily consumption of self-selected foods. During the intervention participants were instructed to maintain the calorie intake targets determined during baseline. All participants were prescribed a balanced diet and were asked to submit daily self-reported diet intake records for the duration of the intervention.

**Cardiorespiratory fitness**

Cardiorespiratory fitness (VO$_2$ peak) was assessed using standard open-circuit spirometry techniques (SensorMedics, Yorba Linda, CA) during a graded exercise test
in which participants walked on a treadmill at a self-selected speed at zero elevation for three minutes, after which the incline was increased by 5% for two minutes, then by 2% every subsequent two minutes until volitional fatigue [13].

**Statistical analysis**

Participant characteristics are presented as means ± standard deviations (SD). To determine the effects of treatment on total and regional AT distribution, skeletal muscle, unstructured PA, and sedentary time, a mixed model was performed using SAS version 9.2 (SAS Institute). The model included terms for group (control, LALI, HALI, and HAHI), time (baseline and 24wks), and gender (male and female) as well as a group by time, and gender by time interaction terms. An extended mixed model, which included gender by group and a gender by group by time interaction terms, was also performed to verify that the effect of treatment did not vary by gender. An unstructured covariance matrix was used on the models. A p value of 0.05 was used to determine statistical significance with no correction for multiple comparisons. An ANOVA was used to determine whether differences existed between group adherence to prescribed diet, the model included terms for group and adherence (actual caloric intake minus prescribed caloric intake). Descriptive statistics and univariate analysis were performed using SPSS (IBM SPSS).

**3.4 Results**

Baseline characteristics are shown in Table 1. Participants were middle-aged (52.7 ± 7.6 years), with abdominal obesity (WC: 109.4 ± 10.8 cm) and more than half were females (60.2%). Across groups, participants had normal blood pressure, blood lipid profiles, and fasting glucose at baseline (Table 1)
Table 2 summarizes the participants’ adherence to the exercise program. Those in the LALI, HALI and HAHI attended 88.4%, 94.9%, and 92.8% of the 120 prescribed exercise sessions respectively. The average exercise time was 31.9 ± 4.8 min, 57.8 ± 6.6 min, 40.2 ± 6.7 min for the LALI, HALI and HAHI groups respectively. The improvement in VO$_2$peak at 24 weeks was greater in LALI (adjusted mean difference ± SE, 0.2 ± 0.1 L/min, p=0.006), HALI (0.5 ± 0.1 L/min, p<0.001), and HAHI (0.6 ± 0.1 L/min, p<0.001) compared to control.

Table 3 presents the change in total and abdominal AT and skeletal muscle mass. Because there was no gender by group by time interaction, gender was collapsed across groups. There was a group by time interaction for all tissues (p<0.05) except skeletal muscle. Post hoc analysis revealed that total adipose tissue, whole body SAT, abdominal AT, ASAT, and lower body AT were reduced in all exercise groups compared to control (p<0.05) but did not differ from each other (Table 3, p>0.05). The reduction in VAT at 24 wks was greater in LALI (adjusted mean difference ± SE, -0.5 kg ± 0.1 kg, p=0.001), HALI (-0.5 kg ± 0.1 kg, p<0.001), and HAHI (-0.5 kg ± 0.1 kg, p<0.001) compared to control, but there were no differences between the exercise groups (Figure 1). There was no change in skeletal muscle mass compared to control in any exercise group (p>0.05). Body weight and waist circumference were reduced in all exercise groups compared to control (p<0.05), but did not differ between exercise groups (p>0.05).

Table 4 presents within group changes in total daily physical activity and sedentary time. The change in total unstructured physical activity was not different between groups at 8 (p > 0.06) and 16 wks (p>0.18). Sedentary time did not change in
any of the groups. No differences were observed among the exercise groups for total caloric intake or dietary fat intake (p>0.5, Table 5).
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control Baseline</th>
<th>Control 24 wks</th>
<th>LALI Baseline</th>
<th>LALI 24 wks</th>
<th>HALI Baseline</th>
<th>HALI 24 wks</th>
<th>HAHI Baseline</th>
<th>HAHI 24 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>54.7 ± 6.6</td>
<td>52.1 ± 8.1</td>
<td>51.8 ± 8.1</td>
<td>52.8 ± 7.4</td>
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<tr>
<td>Gender F:M</td>
<td>10:11</td>
<td>15:10</td>
<td>21:11</td>
<td>19:11</td>
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<tr>
<td>Weight, kg</td>
<td>90.0±17.2</td>
<td>89.3±17.5</td>
<td>94.1±14.6</td>
<td>93.4±14.9</td>
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<tr>
<td>WC, cm</td>
<td>107.1±10.9</td>
<td>106.0±11.4</td>
<td>111.3±11.0</td>
<td>109.4±9.8</td>
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<td>109.4±11.8</td>
<td>103.2±10.5</td>
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<tr>
<td>BMI, kg/m²</td>
<td>30.7±3.6</td>
<td>30.6±3.7</td>
<td>33.0±4.2</td>
<td>31.5±4.5</td>
<td>33.0±4.4</td>
<td>30.8±4.6</td>
<td>32.5±3.7</td>
<td>30.4±3.2</td>
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<tr>
<td><strong>MRI</strong></td>
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<tr>
<td>Total AT, kg</td>
<td>36.8±8.1</td>
<td>37.3±8.9</td>
<td>43.2±8.7</td>
<td>39.4±9.6</td>
<td>42.0±8.6</td>
<td>38.0±10.0</td>
<td>42.9±8.3</td>
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<td>Total SAT, kg</td>
<td>27.9±7.0</td>
<td>28.5±7.7</td>
<td>34.4±8.2</td>
<td>31.7±9.0</td>
<td>33.3±8.4</td>
<td>30.4±9.4</td>
<td>33.7±7.3</td>
<td>30.0±6.8</td>
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<tr>
<td>Total abdominal AT, kg</td>
<td>8.7±2.2</td>
<td>8.8±2.4</td>
<td>9.8±2.0</td>
<td>8.8±2.2</td>
<td>9.5±2.1</td>
<td>8.4±2.3</td>
<td>9.7±2.7</td>
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<tr>
<td>VAT, kg</td>
<td>3.4±1.5</td>
<td>3.2±1.4</td>
<td>3.2±1.3</td>
<td>2.6±1.0</td>
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<td>2.5±1.2</td>
<td>3.2±1.5</td>
<td>2.6±1.2</td>
</tr>
<tr>
<td>ASAT, kg</td>
<td>5.0±1.5</td>
<td>5.2±1.7</td>
<td>6.4±1.5</td>
<td>5.9±1.7</td>
<td>6.1±1.7</td>
<td>5.5±1.9</td>
<td>6.1±1.6</td>
<td>5.3±1.4</td>
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<tr>
<td>Lower body AT, kg</td>
<td>10.5±2.7</td>
<td>10.6±2.8</td>
<td>13.4±4.3</td>
<td>12.2±4.3</td>
<td>12.8±3.6</td>
<td>11.4±3.8</td>
<td>13.0±3.0</td>
<td>11.6±2.7</td>
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<tr>
<td>Total SM, kg</td>
<td>26.1±7.7</td>
<td>25.3±7.7</td>
<td>24.7±5.1</td>
<td>23.9±4.9</td>
<td>24.7±6.3</td>
<td>24.1±6.2</td>
<td>25.6±6.3</td>
<td>24.6±5.9</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
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<tr>
<td>Systolic Blood Pressure, mmHg</td>
<td>122.8 ± 14.8</td>
<td>119.3 ± 10.3</td>
<td>121.1 ± 12.6</td>
<td>122.2 ± 15.3</td>
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</tr>
<tr>
<td>Diastolic Blood Pressure, mmHg</td>
<td>79.4 ± 7.2</td>
<td>78.3 ± 7.7</td>
<td>79.2 ± 9.0</td>
<td>80.6 ± 8.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol, mmol/l</td>
<td>4.9 ± 1.0</td>
<td>5.2 ± 0.9</td>
<td>5.3 ± 0.8</td>
<td>5.2 ± 0.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>1.7 ± 1.0</td>
<td>1.5 ± 0.8</td>
<td>1.5 ± 0.6</td>
<td>1.4 ± 0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td>1.2 ± 0.3</td>
<td>1.2 ± 0.3</td>
<td>1.3 ± 0.4</td>
<td>1.3 ± 0.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>3.0 ± 1.0</td>
<td>3.3 ± 0.7</td>
<td>3.4 ± 0.7</td>
<td>3.3 ± 0.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Glucose, mmol/l</td>
<td>5.5 ± 0.6</td>
<td>5.3 ± 0.4</td>
<td>5.4 ± 0.5</td>
<td>5.5 ± 0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data is presented as the mean ± standard deviation. LALI = low amount, low intensity; HALI = high amount, low intensity; HAHI = high amount, high intensity; WC = waist circumference; BMI = body mass index; MRI = magnetic resonance imaging; AT = adipose tissue; SAT = subcutaneous adipose tissue; VAT = visceral adipose tissue; ASAT = abdominal subcutaneous adipose tissue; TG = triglycerides. HDL = high density lipoprotein; LDL = low density lipoprotein.
Figure 1.3 Effects of exercise amount and intensity on absolute adipose tissue and skeletal muscle mass change.

AT= adipose tissue; LALI = Low amount, low intensity; HALI = high amount, low intensity; HAHI = high amount, high intensity. * p<0.05 compared to control.
Figure 2.3 Relative effects of exercise amount and intensity on adipose tissue and skeletal muscle mass.

AT = adipose tissue; LALI = Low amount, low intensity; HALI = high amount, low intensity; HAHI = high amount, high intensity. * p<0.05 compared to control.
Table 2.3 Exercise Intervention Descriptive Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>LALI</th>
<th>HALI</th>
<th>HAHI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adherence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of sessions prescribed, <em>n</em></td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Mean sessions attended, <em>n</em></td>
<td>106.1 ± 21.0</td>
<td>113.9 ± 6.0</td>
<td>110.7 ± 8.8</td>
</tr>
<tr>
<td>Mean attendance, %</td>
<td>88.4 ± 17.5</td>
<td>94.9 ± 5.0</td>
<td>92.8 ± 7.3</td>
</tr>
<tr>
<td><strong>Adherence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescribed energy expenditure, <em>kcal/session</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>300</td>
<td>600</td>
<td>600</td>
</tr>
<tr>
<td>Women</td>
<td>180</td>
<td>360</td>
<td>360</td>
</tr>
<tr>
<td>Mean actual energy expenditure, <em>kcal/session</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>303.0 ± 6.5</td>
<td>610.1 ± 8.4</td>
<td>601.0 ± 28.5</td>
</tr>
<tr>
<td>Women</td>
<td>182.9 ± 3.9</td>
<td>365.1 ± 5.7</td>
<td>364.0 ± 16.6</td>
</tr>
<tr>
<td>Prescribed exercise intensity, % <em>VO₂peak</em></td>
<td>50</td>
<td>50</td>
<td>75</td>
</tr>
<tr>
<td>Mean actual intensity, % of <em>VO₂peak</em></td>
<td>50.7 ± 0.7</td>
<td>52.0 ± 2.8</td>
<td>74.7 ± 0.4</td>
</tr>
<tr>
<td>Mean exercise duration, <em>min/session</em></td>
<td>31.9 ± 4.8</td>
<td>57.8 ± 6.6</td>
<td>40.2 ± 6.7</td>
</tr>
</tbody>
</table>

Data presented as mean ± standard deviation. LALI = Low amount, low intensity; HALI = high amount, low intensity; HAHI = high amount, high intensity.
Table 3.3 Change in anthropometric and MRI variables at 24 weeks.

<table>
<thead>
<tr>
<th>Variable</th>
<th>LALI vs. Control</th>
<th>HALI vs. Control</th>
<th>HAHI vs. Control</th>
<th>HALI vs LALI</th>
<th>HAHI vs LALI</th>
<th>HAHI vs HALI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthropometric</strong></td>
<td>Value</td>
<td>P Value</td>
<td>Value</td>
<td>P Value</td>
<td>Value</td>
<td>P Value</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>-4.0 ± 1.1</td>
<td>&lt;0.001</td>
<td>-5.7 ± 1.1</td>
<td>&lt;0.001</td>
<td>-5.8 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WC, cm</td>
<td>-4.1 ± 1.2</td>
<td>&lt;0.001</td>
<td>-5.5 ± 1.1</td>
<td>&lt;0.001</td>
<td>-5.3 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td>Value</td>
<td>P Value</td>
<td>Value</td>
<td>P Value</td>
<td>Value</td>
<td>P Value</td>
</tr>
<tr>
<td>Total AT, kg</td>
<td>-4.4 ± 1.0</td>
<td>&lt;0.001</td>
<td>-4.6 ± 1.0</td>
<td>&lt;0.001</td>
<td>-5.6 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total SAT, kg</td>
<td>-3.2 ± 0.9</td>
<td>&lt;0.001</td>
<td>-3.5 ± 0.8</td>
<td>&lt;0.001</td>
<td>-4.3 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Abdominal AT, kg</td>
<td>-1.1 ± 0.3</td>
<td>&lt;0.001</td>
<td>-1.2 ± 0.3</td>
<td>&lt;0.001</td>
<td>-1.5 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAT, kg</td>
<td>-0.5 ± 0.1</td>
<td>0.001</td>
<td>-0.5 ± 0.1</td>
<td>0.001</td>
<td>-0.5 ± 0.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Abdominal SAT, kg</td>
<td>-0.6 ± 0.2</td>
<td>0.002</td>
<td>-0.7 ± 0.2</td>
<td>&lt;0.001</td>
<td>-1.0 ± 0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lower body AT, kg</td>
<td>-1.4 ± 0.4</td>
<td>0.001</td>
<td>-1.6 ± 0.4</td>
<td>&lt;0.001</td>
<td>-1.6 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total SM, kg</td>
<td>-0.1 ± 0.4</td>
<td>0.869</td>
<td>0.1 ± 0.4</td>
<td>0.768</td>
<td>-0.2 ± 0.4</td>
<td>0.549</td>
</tr>
</tbody>
</table>

Data presented as mean ± standard error. LALI = Low amount, low intensity; HALI = high amount, low intensity; HAHI = high amount, high intensity; WC = waist circumference; MRI = magnetic resonance imaging; AT = adipose tissue; SAT = subcutaneous adipose tissue; VAT = visceral adipose tissue; ASAT = abdominal subcutaneous adipose tissue; SM = skeletal muscle.
Table 4.3 Absolute and Relative Change in Daily Physical Activity and Sedentary Time at baseline, 8 and 16 weeks.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>LALI</th>
<th>HALI</th>
<th>HAHI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Unstructured physical activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wear time, min</td>
<td>949.9 ± 77.5</td>
<td>942.1 ± 73.1</td>
<td>928.7 ± 83.0</td>
<td>884.7 ± 78.3</td>
</tr>
<tr>
<td>TPA, min/d</td>
<td>311.8 ± 80.6</td>
<td>307.6 ± 87.6</td>
<td>298.2 ± 83.4</td>
<td>257.6 ± 70.3</td>
</tr>
<tr>
<td><strong>8 Wk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wear time, min</td>
<td>912.5 ± 67.7</td>
<td>888.6 ± 69.4</td>
<td>898.5 ± 71.6</td>
<td>845.7 ± 53.7</td>
</tr>
<tr>
<td>TPA change, min/d</td>
<td>-1.9 ± 17.4</td>
<td>-32.9 ± 14.9*</td>
<td>-7.1 ± 13.1</td>
<td>-4.4 ± 15.0</td>
</tr>
<tr>
<td><strong>16 Wk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wear time, min</td>
<td>925.0 ± 71.1</td>
<td>899.5 ± 65.5</td>
<td>858.7 ± 69.5</td>
<td>888.5 ± 91.3</td>
</tr>
<tr>
<td>TPA change, min/d</td>
<td>15.1 ± 20.4</td>
<td>-24.8 ± 17.2</td>
<td>-31.8 ± 14.4*</td>
<td>-2.5 ± 15.5</td>
</tr>
<tr>
<td><strong>Sedentary activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED, min/d</td>
<td>630.6 ± 86.6</td>
<td>630.0 ± 103.6</td>
<td>625.9 ± 93.3</td>
<td>623.2 ± 69.9</td>
</tr>
<tr>
<td><strong>8 wk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED change, min/d</td>
<td>-29.6 ± 21.2</td>
<td>-27.5 ± 18.2</td>
<td>-43.6 ± 15.9*</td>
<td>-56.3 ± 18.3*</td>
</tr>
<tr>
<td><strong>16 wk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SED change, min/d</td>
<td>-4.2 ± 22.7</td>
<td>-26.5 ± 19.1</td>
<td>-36.6 ± 16.1*</td>
<td>8.8 ± 17.3</td>
</tr>
</tbody>
</table>

Baseline min/day and wear time is presented as mean ± standard deviation, change at 8 and 16 is presented as mean ± standard error. LALI = Low amount, low intensity; HALI = high amount, low intensity; HAHI = high amount, high intensity; PA = physical activity. Sample size was 14, 19, 26, and 21 at baseline; 14, 29, 26, and 19 at 8 wks; and 12, 17, 25, and 21 at 16 wks for control, LALI, HALI, and HAHI respectively.

*p<0.05 vs Baseline; No between group differences were observed for TPA or sedentary time at 8 and 16wks.
Table 5.3 Analysis of Dietary Intake

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>LALI</th>
<th>HALI</th>
<th>HAHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caloric target, kcal</td>
<td>1761.9 ± 869.3</td>
<td>2042.0 ± 311.5</td>
<td>2048.4 ± 546.3</td>
<td>2035.0 ± 460.9</td>
</tr>
<tr>
<td>Adherence, kcal</td>
<td>-221.0 ± 193.7</td>
<td>-127.3 ± 216.1</td>
<td>-78.4 ± 217.5</td>
<td>-91.2 ± 215.3</td>
</tr>
<tr>
<td>Dietary fat target, %</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Adherence, %</td>
<td>-6.3 ± 13.9</td>
<td>-7.3 ± 9.7</td>
<td>-3.0 ± 12.7</td>
<td>-4.0 ± 11.1</td>
</tr>
</tbody>
</table>

Caloric and dietary fat targets are presented as mean ± standard deviation; adherence is presented as mean ± standard error. Control (n=18); LALI = Low amount, low intensity (n=25); HALI = high amount, low intensity (n=32); HAHI = high amount, high intensity (n=30).
3.5 Discussion

The primary finding of this study was that exercise induced a substantial reduction in total and abdominal AT independent of exercise amount or intensity. This result is encouraging and provides health practitioners with lifestyle-based treatment options for managing obesity and in particular abdominal obesity and visceral AT. Specifically, our findings suggest that the reduction in total and abdominal adiposity in response to exercise consistent with consensus guidelines worldwide of ~150 minutes of moderate PA per week [56] is as efficacious as moderate exercise performed for ~300 minutes per week.

Our primary observations are consistent with those of Keating et al. [12] who observed reductions in VAT and abdominal SAT independent of exercise amount and intensity in response to three different exercise prescriptions varying in amount and intensity in a population which was sedentary and obese. Limitations of this study include the use of time rather than caloric expenditure to fix exercise amount, which resulted in a different weekly caloric expenditure in the three exercise groups, two of which were intended to be matched for exercise amount, and also the use of unsupervised exercise for one day a week in each exercise group. We addressed these limitations with a more rigorously controlled study design that isolates exercise amount through caloric expenditure rather than time. Additionally, we provide evidence that reductions in total AT and leg AT are independent of exercise amount and intensity, and also occur in the absence of between group differences in the changes of whole body SM, sedentary behavior, and diet.
Previous research from our group has shown that exercise induced weight loss maintains skeletal muscle mass compared to diet induced weight loss [51, 53, 54]. Our findings extend this, as it is the first study to demonstrate that there is an apparent preservation of whole body SM regardless of both exercise amount and intensity with exercise induced weight loss. These findings are consistent with Irving et al. [61] who observed maintenance of mid-thigh muscle in women with metabolic syndrome who performed either low or high intensity exercise (below lactate threshold vs half way between lactate threshold ad VO_{2peak}^) matched for caloric expenditure for 16wks. Prior investigations have demonstrated that lower relative muscle mass (eg. ratio of muscle mass to fat mass) has been associated with the development of the metabolic syndrome (MetS); however, absolute muscle mass is positively associated with MetS [58]. This paradox may be explained by observations that individuals who are obese typically have a greater amount of total absolute muscle compared to an individual who is lean, indicating that muscle mass per se may not be directly in the causal pathway for the development of the metabolic syndrome [59]. Regardless, decreased muscle mass is associated with increased mortality and the maintenance of muscle mass during weight loss is of importance [60]. Taken together with our primary findings, this indicates that there is a robust mobilization of abdominal and whole body AT in combination with a preservation of whole body muscle mass with a variety of exercise prescriptions, which further supports the utility of exercise as a strategy to manage obesity.

Contrary to our expectations we did not observe an effect of exercise amount on the reduction on total or abdominal AT. Based on the energy expenditure of the exercise interventions and the crude estimate of 3500kcal of energy expenditure is equivalent to
one pound of weight loss [76], both the HALI and HAHI groups attained the expected weight loss whereas the LALI group had a greater weight reduction than expected. Previous studies have also found discrepancies between expected and observed weight loss, where as a lower amount of exercise has resulted in a greater than expected weight loss [70, 77, 78]. Interestingly, Rosenkilde et al. [78] observed that participants who were sedentary and overweight who exercise for 30 min/day or 60min/day experienced weight and adipose tissue reductions of a similar magnitude. Similar to our findings, Resenkilde et al. [78] observed reduction in AT, independent of amount, in the absence of differences in diet or unstructured PA, monitored via accelerometers, between exercise groups. In our study, an explanation for the LALI group having a greater than expected weight loss may be explained by a contamination of the LALI group. This would have occurred through exercising with the two HA groups, where the participants in LALI group observing the weight loss of the other exercise groups, may have inadvertently changed their behavior, which may have resulted in a selective over-reporting of caloric consumption in the LALI group [79]. It is well-established that there are inaccuracies in the self-report of caloric intake [79] with an error of >35% in individuals who are obese [80]. In addition social networks have been associated with obesity and weight loss intensions [81, 82], which provides support for a contamination of the LALI group. However, an over-reported dietary intake counters the well-established observation that individuals tend to under-report their caloric consumption [83], and therefore it remains unclear why there was no difference in adipose tissue reductions with an increased amount of exercise.
When the amount of exercise is fixed/matched, it has been shown that there is no difference in total fat oxidation in response to exercise of low or high intensity [84]. Our findings extend these observations by suggesting that for a fixed amount of exercise, manipulating the exercise intensity does not influence the mobilization of total or abdominal adiposity over a 6 month duration. However, our findings differ from Coker et al. [66] and Irving et al. [61] who both observed that a higher intensity of exercise results in a greater mobilization of VAT in individuals who are obese. However, both of these studies were small in size (n= 6-11/grp) and in addition Irving et al. [61] prescribed exercise intensity based on rating of perceived exertion (RPE) rather than as a percent of VO$_{2\text{peak}}$ making it difficult to quantify exercise intensity. Although intensity was not associated with differences in reductions in adipose tissue, it is important to note that our lab and others have found that a higher exercise intensity is associated with greater improvements in CRF and insulin sensitivity [73, 85].

We observed a ~17.5% reduction in VAT independent of exercise amount and intensity. These results are consistent with other exercise trials that have observed a exercise induced reduction of VAT with a range from 10-35% [86] in response to a comparable negative energy balance (900-4000kcal/week) [86, 87]. This is relevant as a VAT reduction of ~17% is associated with significant improvements in blood lipid profiles (15-20% reduced TG, LDL) and improved fasting insulin levels (12-20% reduction in fasting insulin) in obese adults [54, 88, 89].

The primary strength of this trial was the strict control over the exercise prescriptions. Additionally, accelerometers were used to monitor unstructured PA to ensure that the changes in AT were due to the exercise prescription and not additional energy.
expenditure. Limitations include the limited number of participants per group, which may indicate that this ancillary study was not powered to make comparisons between exercise groups. However, given the small difference in VAT between groups (~0.1kg), it is unclear that even if there was a statistical difference between exercise groups that this would hold any clinical relevance. Another limitation is the potential contamination of the LALI group by the HALI and HAHI groups, potentially resulting in the LALI group inadvertently changing their behavior.

3.6 Conclusion

In summary, we observed reductions in total and abdominal AT independent of exercise amount and intensity with the prescribed exercise within this trial. However, we are cautious to suggest that exercise amount in unimportant in the reduction of AT as our findings counter those of systematic reviews that suggest a dose relationship between exercise amount and AT reductions, and we cannot provide a certain explanation for why we found no differences with increased exercise amount. However, our results are encouraging as it offers healthcare providers with several efficacious exercise prescriptions that can be used to manage abdominal obesity. Finally, our findings contribute to the large body of evidence [90] that provides support for the use of exercise as a strategy to treat abdominal obesity.
Chapter 4: General Discussion

4.1 Summary of Key Findings

Two principal findings arose from this study; 1) there is a substantial reduction in total and abdominal AT depots with the exercise that was prescribed in this trial, independent of both exercise amount and intensity; and 2) contrary to expectations, when the amount of exercise is doubled there is no additional reduction in whole body and abdominal AT. While some other studies have examined the effects of exercise intensity and/or amount on abdominal AT, this study is novel because it is the first to rigorously control exercise amount and intensity in addition to utilizing whole body MRI to determine the separate effects of exercise amount and intensity on AT and SM distribution. These findings extend the current literature because it provides three exercise prescriptions that induce similar reductions in total and abdominal AT.

4.2 Key strengths and Limitations

To date this is the largest RCT that has utilized whole body imaging techniques to examine the effect of exercise amount or intensity on AT distribution independent of diet. The primary strength is the strict control over the exercise prescriptions. This was done by performing multiple measures of cardiorespiratory fitness throughout the intervention in order to alter exercise prescription to match caloric expenditure targets as participants increased their fitness, and by recording heart rate every 5 min during exercise sessions. Additionally accelerometers were used to monitor unstructured PA to ensure that the changes in AT were due to the exercise prescription and not additional energy expenditure from unstructured activity. Accelerometers were also used to
monitor sedentary time, an emerging behavior that is associated with abdominal obesity [91]. Lastly, participants filled out daily dietary logs which were also used to ensure that the changes in AT were due to our intervention and not due to changes in caloric intake.

Despite the careful design and implementation of the exercise intervention, there are several limitations of this study. The primary limitation is decreased generalizability of these findings to a free-living adult due to the high internal validity of the intervention. In addition, because this was an ancillary study it is unclear weather or not the sample size was large enough to make comparisons between the exercise groups. However it is unclear weather the 0.1kg difference of VAT we observed between exercise groups, even if there was a statistical difference, would provide any clinical relevance.

4.3 Directions and Future Research

The results of this study lead to further important research questions. Three unique areas of interest include: 1) the development of behavioral strategies to encourage individuals to maintain an exercise program; 2) the analysis of AT quality changes in response to varying amounts and intensities of exercise; and 3) the individual variation in response to exercise.

Our findings that exercise in combination with a healthful diet results in decreased adiposity supports a large body of literature that exercise is an efficacious method for obesity management [90]. It also provides evidence that the current Canadian physical activity guideline of 150 minutes of moderate-vigorous PA is an appropriate dose of exercise for the treatment of abdominal obesity. However, there are a growing number of scientific reviews and popularized lay articles that suggest that
exercise does not help with weight loss or obesity management [92, 93] and even go so far to say that it causes weight gain [94]. These articles are misleading in that an exercise-induced negative energy balance will cause weight loss due to the laws of thermodynamics. Nonetheless, the aforementioned reviews that paint exercise as ineffective do address the important issue of the effectiveness of exercise, or the ability for individuals to adopt and maintain physical activity changes, which is a major issue for any lifestyle intervention. With merely 15% of Canadians achieving guideline physical activity [95], which is equivalent to the exercise prescribed in the LALI group, it is clear that the larger problem may not be the efficacy of exercise but rather the ability of individuals to sustain a physically active lifestyle. While studies like the present one can be used to provide recommendations for the amount and intensity of exercise, evidently more research is needed to develop strategies for individuals to adopt and more importantly maintain a physically active lifestyle.

One of the assumptions that is made while doing MRI analysis is that there is uniform quality of AT. In other words, with MRI analysis we are only able to distinguish the amount of AT and not whether or not it is healthy or unhealthy AT. In contrast, recent research has shown that x-ray computed tomography (CT) can be used to not only determine the amount of AT but also the quality of the AT (eg. how much lipid is present in the AT). Indeed, the Framingham study has demonstrated that AT quality measured via CT is a predictor of insulin resistance [96]. However, since AT quality is a recent scientific development, no interventions using this outcome have been performed. First, it would need to be established whether there is a change in AT quality as a result of exercise or lifestyle interventions. After the effect of exercise on AT quality is
determined it would allow researchers to address a plethora of research questions addressing the separate effects of exercise amount and intensity on AT quality. Answering these questions would extend the findings of the present study by determining whether potential changes in AT quality mirror the exercise amount- and intensity-independent reductions in AT, or, whether the generally recognized dose relationship between exercise and health is mediated by the quality of the AT.

There was a remarkable inter-individual variation in the response to exercise in each of the exercise groups, despite the homogeneous sample and the tightly control energy expenditure and intensity. The range of VAT change was +0.5 kg to -2.2kg and SAT loss from +4.2 kg to -15kg. Additionally, while at a group level, all exercise groups achieved the same VAT reduction, some individuals in each group did not respond to the exercise intervention, with minimal reduction of VAT. The notion of a non-responder is not novel, but it invokes a new question of whether the same person who was a non-responder in the LALI group would still be a non-responder in the HAHI group. Future research is needed in this area in order to identify people who will and will not benefit from exercise interventions specifically target to reduce AT, which will assist with the prescription of the ideal exercise intervention on the individual level [97].

4.4 Contribution to the Field of Study

Our study adds to the limited evidence on the separate effects of exercise amount and intensity on obesity management. Additionally, our results of an exercise intensity-independent reduction in whole body and abdominal AT support the Canadian physical activity guidelines of 150min of MVPA per week, which imply that intensity is unimportant as long as the amount of exercise is achieved. We also contributed to the
emergent body of evidence that has found that with an increased amount of exercise there is no further reduction in weight, and we extend this by observing this phenomenon for VAT and whole body AT as well.

4. 5 Summary and Conclusion

In summary we found that exercise induced reductions in total and regional AT were independent of both exercise amount and intensity for the given exercise prescriptions within this trial. While the independent effect of exercise amount on total and abdominal AT distribution was unexpected and the mechanism of these findings remains unclear, future research will enhance our understanding of the biological processes (AT mobilization) taking place in response to exercise varying in amount. Finally, these findings provide prescription options for physicians who use exercise as a treatment strategy for obesity management.
References


31. About us- Overview


69. Hunter GR, Brock DW, Byrne NM, Chandler-Laney PC, Del Corral P, Gower BA: *Exercise training prevents regain of visceral fat for 1 year following weight loss*. *Obesity (Silver Spring)* 2010, **18**:690-695.


82. Leahey TM, Gokee LaRose J, Fava JL, Wing RR: Social influences are associated with BMI and weight loss intentions in young adults. *Obesity (Silver Spring)* 2011, **19**:1157-1162.


Appendix A: Ethics Approval Form

QUEEN’S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS
RESEARCH ETHICS BOARD (HSREB)

HSREB Initial Ethics Clearance
September 10, 2015

Ms. Theresa Cowan
School of Kinesiology & Health Studies
Queen’s University

ROMEO/TRAQ: #6016330
Department Code: PHE-153-15
Study Title: The separate effects of exercise amount and intensity on whole body and regional adipose tissue in abdominally obese men and women
Co-Investigators: Dr. R. Ross
Review Type: Delegated
Date Ethics Clearance Issued: September 10, 2015
Ethics Clearance Expiry Date: September 10, 2016

Dear Ms. Cowan,

The Queen’s University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board (HSREB) has reviewed the application and granted ethics clearance for the documents listed below. Ethics clearance is granted until the expiration date noted above.

- Protocol

Documents Acknowledged:

- CORE Certificate – T. Cowan

Amendments: No deviations from, or changes to the protocol should be initiated without prior written clearance of an appropriate amendment from the HSREB, except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

Renewals: Prior to the expiration of your ethics clearance you will be reminded to submit your renewal report through ROMEO. Any lapses in ethical clearance will be documented on the renewal form.

Completion/Termination: The HSREB must be notified of the completion or termination of this study through the completion of a renewal report in ROMEO.
**Reporting of Serious Adverse Events:** Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information.

**Reporting of Complaints:** Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete.

Yours sincerely,

Albert J. Clark

Chair, Health Sciences Research Ethics Board

The HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations, Canadian General Standards Board, and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is qualified through the CTO REB Qualification Program and is registered with the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protection (OHRP). Federalwide Assurance Number: FWA#:00004184, IRB#:00001173

HSREB members involved in the research project do not participate in the review, discussion or decision.
Appendix B: Letter of Permission to use Figure 1

Hi Theresa,

It was a pleasure speaking with you yesterday.

Please accept this email as Bayer’s confirmation that it does not object to the proposed use of the image you created for your Master’s thesis.

I wish you all the best with your thesis.

Regards / Cordialement,

Marc A. Fust

Senior Counsel / Avocat-conseil principal

Bayer Inc.
Law, Patents & Compliance / Service du contentieux et de la conformité
Toronto (Mississauga)
Phone: +1 905-282-5504
E-mail: marc.fust@bayer.com
Web: www.bayer.ca

From: Theresa Cowan [mailto:telcowan@gmail.com]
Sent: Wednesday, September 09, 2015 7:42 PM
To: Marc Fust
Subject: Re: Permission Request

Hi Marc,

Here is the PDF of the book MRI made easy, I derived my image from pages 7, 19, 21, 23, and 40-43, and I also attached the figure as a PDF and an example of a letter of permission for another figure I used in my literature review.

Regards,

Theresa

On 2015-09-09, 4:08 PM, Marc Fust wrote:
Hi Theresa,

I am now available for the rest of the afternoon. If you are available, please call me at your convenience at 416 489 3615. This is my home number, so please use it if you are calling at 6:30 as well.

Regards,

Marc A. Fust

From: Theresa Cowan [mailto:telcowan@gmail.com]
Sent: Wednesday, September 09, 2015 09:29 PM W. Europe Standard Time
To: Marc Fust
Subject: Re: Permission Request

Hello Marcus,

I can call you this evening at 6:30pm, should I call the number 1-905-282-5504? If that doesn't work I will call you tomorrow at 4.

Regards,

Theresa

On 2015-09-09, 2:33 PM, Marc Fust wrote:

Hi Theresa,

I may be available later this afternoon, but I cannot guarantee a time. Happy to discuss this evening if that works for you. I can also offer up tomorrow afternoon at 4:00 p.m. Let me know if anything works best for you.

Regards,

Marc A. Fust

From: Theresa Cowan [mailto:telcowan@gmail.com]
Sent: Wednesday, September 09, 2015 07:51 PM W. Europe Standard Time
To: Marc Fust
Subject: Re: Permission Request

Hello Marc,

Thank you for your reply, what time would it be best for me to phone you? I attached the image that I would like to use in my review of literature section for my Master's Thesis, I created a simplified version from several of the images in MRI made easy (...well almost) by Dr. Hans H. Schild.

Regards,

Theresa Cowan

MSc Candidate
Queen's University
School of Kinesiology and Health Studies
28 Division St. Kingston ON

On 2015-09-09, 10:08 AM, Marc Fust wrote:
Hi Theresa,

I have been advised that you are looking to obtain permission to modify and use an image from a Schering AG publication. Can you please call me to discuss? I need better understand exactly what you are proposing to do. If you could also send me a copy of the image in question, that would be helpful.

Regards / Cordialement,
Marc A. Fust
Senior Counsel / Avocat-conseil principal

Bayer Inc.
Law, Patents & Compliance / Service du contentieux et de la conformité
Toronto (Mississauga)
Phone: +1 905-282-5504
E-mail: marc.fust@bayer.com
Web: www.bayer.ca


The information contained in this e-mail is for the exclusive use of the intended recipient(s) and may be confidential, proprietary, and/or legally privileged. Inadvertent disclosure of this message does not constitute a waiver of any privilege. If you receive this message in error, please do not directly or indirectly use, print, copy, forward, or disclose any part of this message. Please also delete this e-mail and all copies and notify the sender. If you would like to withdraw your consent to or unsubscribe from commercial electronic messages, please email optoutallbayerinc@bayer.com. We may still send messages for which we do not require consent. Thank you.

Si vous souhaitez retirer votre consentement ou ne plus recevoir nos messages commerciaux électroniques, envoyez un courriel à optoutallbayerinc@bayer.com. Nous pourrions continuer à vous envoyer des messages qui ne requièrent pas votre consentement. Merci.
Appendix C: Letter of Permission to use Figure 3

July 30, 2015

Theresa Cowan
School of Kinesiology and Health Studies
Queen’s University
28 Division St.
Kingston, ON K7L 3N6
Canada


Dear Ms. Cowan:

Thank you for your interest in material published by Human Kinetics.

We are pleased to approve your permission request for this one-time use of figure 7.2 on page 91 of Human Body Composition, Second Edition, in your Master’s thesis. This is your confirmation that we are granting nonexclusive print and electronic rights in the English language, for distribution throughout the world, contingent upon your use of the following credit line adjacent to the reprinted material.

CREDIT LINE:


FEE: WAIVED

In the future, should you wish to formally publish this material, please request permission again.

Sincerely,

Martha Gullo
Rights Manager
Ph: 217-351-5076 ext. 2223
Email: marthag@hkusa.com
Appendix D: Protocol for MR Image Acquisition

Protocol
T1-weighted, spin-echo pulse sequence
Each image = 10 mm thickness, 40 mm spaces
TR = 210 ms; TE = 17 ms; 1/2 NEX
FOV = 48 cm X 36 cm (Rectangular)
Matrix = 256 X 256 (may be different for some images)
Each acquisition = 7 images
Time = 26 seconds (breath hold on first group from L4-5 down and first two groups from L4-5 up)

Sequence of Series to Acquire Images
- Sagittal, coronal and axial scouts to locate L4-L5
- L4-L5 down (3-4 groups depending on height of participant, breath hold for first group in pelvis)
- Scout(s) to locate L4-L5
- L4-L5 up (3-4 groups depending on height, breath hold for two groups in abdomen and chest)

* For each group of 7 images, data is acquired over 310 mm
Appendix E: MRI Tag Legend

SERENA MRI TAG LEGEND

<table>
<thead>
<tr>
<th>Tag #</th>
<th>Colour</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Red</td>
<td>Muscle</td>
</tr>
<tr>
<td>2</td>
<td>Light Green</td>
<td>Subcutaneous Adipose Tissue (SAT)</td>
</tr>
<tr>
<td>3</td>
<td>Dark Blue</td>
<td>Intrapelvic Adipose Tissue (images –10 and –15 below L4-L5)</td>
</tr>
<tr>
<td>4</td>
<td>Purple</td>
<td>Liver</td>
</tr>
<tr>
<td>5</td>
<td>Yellow</td>
<td>Arm Bone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(humeral head to hand)</td>
</tr>
<tr>
<td>6</td>
<td>Orange</td>
<td>Leg Bone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(femoral head to foot)</td>
</tr>
<tr>
<td>7</td>
<td>Light Blue</td>
<td>Intraperitoneal Adipose Tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(images –5, L4-L5, +5, +10, +15)</td>
</tr>
<tr>
<td>8</td>
<td>Magenta</td>
<td>Head Lean Tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(all images where head is visible)</td>
</tr>
<tr>
<td>9</td>
<td>Blue</td>
<td>Intrathoracic Adipose Tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(image +20cm to top of lung)</td>
</tr>
<tr>
<td>10</td>
<td>White</td>
<td>Bone other than arm or leg bone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ie. Vertebrae, pelvic, clavicle)</td>
</tr>
<tr>
<td>11</td>
<td>Dark Green</td>
<td>Lean tissue other than bone or muscle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ie. Organ, etc.)</td>
</tr>
<tr>
<td>12</td>
<td>Aqua</td>
<td>Head Adipose Tissue</td>
</tr>
<tr>
<td>13</td>
<td>Pink</td>
<td>Interstitial Adipose Tissue</td>
</tr>
<tr>
<td>14</td>
<td>Dark Purple</td>
<td>N/A for SERENA</td>
</tr>
<tr>
<td>15</td>
<td>Dark Yellow</td>
<td>Lung</td>
</tr>
<tr>
<td>16</td>
<td>Dark Pink</td>
<td>N/A for SERENA</td>
</tr>
</tbody>
</table>

- Tag 14 was used to identify foreign objects in the body, ex. hip replacements, breast implants, etc…
Appendix F: Cardiorespiratory Fitness Test (VO2max)

Personnel

- Research Assistants

Training Program:

Prior to performing a VO2max test on SERENA participants, under the supervision of a Graduate Student or trained Research Assistant, all Research Assistants will be required to:

1. Undergo the test themselves
2. Show competence in performing all steps of the test (set-up, participant preparation, calibration, data entry and transfer, etc.)

List of Measured Variables

Maximal oxygen consumption (L/min)

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

Measurement Devices

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

Measurement Procedures

Cardiorespiratory fitness tests will be performed at Hotel Dieu Hospital. The VMax system must be turned on 30 minutes in advance of attempting system calibration. Calibration will take 30 minutes on average. Thus, the first scheduled test for that day should be at least 1 hour after the Research Assistant arrives. We will schedule 45 minutes per participant. The participants will change into an athletic shirt and shorts, and wear a pair of comfortable shoes suitable for brisk walking or jogging (they should be reminded to bring all items on the day of the test). We give them a Polar heart rate monitor to wear so we can record heart rates every 20 seconds throughout the test. Ideally the test should last between 8-12 minutes, beginning with a relatively brisk pace at level grade, increasing grade to 5% at the 3rd minute, and then further increasing the grade by 2% every 2 minutes thereafter. If after 2 minutes at the maximal incline of 15% the subject has not reached exhaustion, the speed must increase (generally by 0.2 mph). Heart rates are observed and recorded on the VO2 Data Collection Sheet by a Research Assistant, who will hold a receiver watch while standing close to the
participant. Breath-by-breath analysis of respiratory gases is also recorded throughout the test.

**Criteria for a successful VO$_2$max test**

There are a number of popular criteria in the literature which are to be used to assess whether the participant being tested has actually achieved VO$_2$max.

- Plateau in VO$_2$ (oxygen uptake) with increasing work rate (increasing treadmill incline, speed or both). For our purposes we will define plateau in VO$_2$ as $\Delta$VO$_2$ <0.05 L/min at VO$_2$max and the data point 40 seconds above or below, with increases in external work
  - **Note:** This criteria is often criticized as it has been shown that approximately 50% of individuals undergoing VO$_2$max testing never reach a true plateau.
- RQ > 1.10: This suggests non-metabolic production of CO$_2$ and reliance on anaerobic metabolism.
- Heart rate (beats per minute or bpm) exceeding age predicted max HR (220-age) minus 12bpm. For example, for a 20 year old, the HR to be exceeded = 188 bpm (220-20 -12)
Appendix G: Exercise Prescription

Regardless of exercise group, all men and women will be asked to perform walk/jog type exercise on a motorized treadmill to expend the desired energy (kcal/session) according to group assignment. Individuals will exercise 5 times per week at the required intensity (relative to VO$_2$) for the duration of the 6-month treatment period. Due to the pragmatic issues associated with using our target population the treatment period may be extended for some participants by up to two weeks, for a total of 26 weeks. Using the heart rate and oxygen consumption data obtained from the baseline cardio respiratory fitness test, the heart rate associated with a VO$_2$ of ~ 50\% (Group LVLI and HVLI) and ~75\% (LVHI) will be determined and prescribed for each participant. Follow up exercise tests will be performed on all participants at weeks 4, 8, 16, and 24 to verify the relationship between heart rate and oxygen consumption. Thus we will continually adjust the heart rate-oxygen consumption relationship for each individual thereby adjusting for improvement in cardio respiratory fitness which will alter the duration of exercise required to achieve the prescribed exercise dose (e.g., energy expenditure in kilocalories). Heart rate will be monitored and recorded every 5 minutes during each exercise session using a Polar heart rate monitor (see below).

Calculating Exercise Prescription:

i. Determine Quality of VO$_2$ Results

To calculate exercise prescription, the exercise monitors must receive a baseline VO$_2$ result for a participant. The results should be reviewed to ensure that the test is a valid indicator of aerobic fitness for the individual. To determine this, first 3 of the 4 criteria to indicate a “good” test need to be met and indicated by the RA who completed the test. Second, the exercise monitor should look at the values (absolute VO$_2$, Relative VO$_2$, HR, VE, RQ) and determine that they are reasonable based on expected values for the target demographic. If they are not reasonable an explanation should be determined (physiological or mechanical) and a repeated test should be considered after a consultation with the principal investigator and the RAs.

iii. Calculating Exercise Prescription

1) With the file still open, select the “Time Calculator” worksheet at the bottom of the page.

2) Enter the caloric target based on the gender and group of the participant into cell “B2” under Baseline in the Expected Kcal row. It should automatically fill in across all future tests as well. If not you may have to do this manually.

3) From the participants VO$_2$ results, take the heart rate corresponding to the proper intensity (50 or 75\%) and enter it into the “Ave HR” row under the correct visit.

4) Next, from the VO$_2$ Data, copy the slope and intercept from under the Kcal/HR heading (L24/L25) and paste this into the “Time Calculator” in rows 3 & 4. You must also remove the negative sign from the intercept value as it is already built into the calculation.
5) This will provide you with the exercise prescription of a target heart rate (bpm) and duration of exercise (minutes) to achieve the caloric target for the participant. These values should be copied and pasted into the proper cells of the PA Sheet within the file (duration should be rounded to the nearest minute that will achieve the caloric target).

The formula that is used to calculate the time is the same formula used to calculate daily caloric expenditure but re-arranged to isolate the variable we seek, which is in this case time. The formula for time is as follows:

\[
\text{Time} = \frac{\text{Caloric Expenditure}}{(\text{Slope} \times \text{Ave HR})} - \text{Intercept}
\]

6) Now, you must enter the participant’s correct values into the formula for calculating daily caloric expenditure on the PA sheet. Copy the slope and intercept from the Time calculator worksheet and paste them into the Kcal column on the PA sheet (cell “Y6 & Y7”).

7) These values need to be entered into the caloric expenditure formula in the Kcal column, which is as follows:

\[
\text{Caloric Expenditure} = \left( \text{Slope} \times \text{Ave HR} \right) - \text{Intercept} \times \text{Time}
\]

For each aerobic exercise session, we obtain a starting heart rate and then obtain the exercise heart rate every 5 minutes thereafter. Participants will be instructed to wear a Polar heart rate monitor each time they arrive for an exercise session. These monitors consist of a T31 coded transmitter, which is strapped to their chests, and a wrist unit, which is strapped to their wrists like a watch or attached to the machine directly in front of the participant. The participants will weigh in (without their shoes) and their weight will be recorded prior to the start of each session in order to track progress with both diet and exercise components.

After telling the exercise monitor the starting heart rate, participants will step onto one of seven treadmills and begin their 5 minutes warm up. The five-minute walking warm up is designed to elevate heart rate from a non-exercise rate to the target exercise range. It is not included as part of the prescribed daily exercise, therefore not counting towards the daily number of calories expended. Target exercise heart rate ranges are specific to each participant, calculated from the most recent \( \text{VO}_{2\text{max}} \) test, and written on the weekly exercise session record. Participants are encouraged to choose a speed and grade after the 5 minute warm up that will elevate their heart rates into the exercise range. Once within the range ( +/- 3bpm), participants can maintain or adjust walking/jogging speed and treadmill grade as desired every five minutes after telling the monitor the “steady state” heart rate for that exercise interval. All exercise heart rates, treadmill speed and grade associated with those heart rates are recorded by the Exercise Monitor(s) onto the weekly Exercise Record as well as into the electronic file.

There may be some variance in perceived difficulty of the moderate exercise. Some exercisers will need more encouragement than others to “pick up the pace” to elevate their heart rates sufficiently. Others need to be reminded to not get too intense as their
competitive natures may drive them on to “improve” the calories burned each day or move on to a greater treadmill speed or grade.

A five minute walking cool down at the end of each session is also performed, designed to return the exercise heart rate back to near-starting levels. Participants are encouraged, but not required to stretch upon completion of exercise. Participants wash and rinse the transmitter and chest straps at the sink in the exercise room and hang them to dry in preparation for the next group of participants.

1.10.2.1 Making up Missed Sessions:

Participants are encouraged to attend 5 sessions/week as prescribed by the treatment, but due to other commitments cannot always do so. In order to make up for missed sessions participants are allowed to complete extra sessions during a week (i.e. 6 or 7 visits) in order to catch up on those missed. This is not meant to be a regular occurrence but may be needed in cases where time is missed such as vacation, illness or injury. Additionally, if participants are unable to attend extra whole sessions they can make up for missed calories expended by completing extra time during their regular sessions to burn the equivalent calories to those lost during missed sessions (i.e. Divide a missed sessions time by 5 and add that amount of time on to each session that week).

In the event of individuals who are going on extended vacations but would like to continue do complete exercise we are willing to provide them with our Polar Heart Rate monitors. Participants can self-report sessions by recording their Heart Rate every 5 minutes for the duration of their exercise. We strongly discourage individuals from taking these types of vacations during the duration of the study and we do not provide them with this option unless there are warranted circumstances.

In cases where there is no other option participants may be allowed to complete 2 sessions in one day. However, this is on a individual basis and all factors must be considered (Intensity, length of workout, physical harm, possible injury, belief of being capable) and should only be done for those who are behind a great deal and/or nearing the end of the program. If participants are going to come in once and complete 2 sessions at once, have them stop once they have reached their caloric target and have them start a second session from the beginning. A second warm up is not necessary. When recording this on the their physical activity record use the same weight as the first session and leave the resting heart rate blank unless they would like to do another 5 minute warm-up. This will give them the frequency they are trying to achieve as well as the caloric expenditure.
Appendix H: Accelerometry – Actigraph

The Actigraph GT3X is a triaxial accelerometer designed to collect motion data (counts or acceleration, steps and body position) in three axes. The GT3X is most commonly worn at the waist and provides time sensitive information pertaining to physical activity intensity, frequency, and duration. Equations, such as the Freedson equation (MSSE 30(5): 777-781) are available to convert the raw count data into physiologically meaningful data such as energy expenditure or physical activity intensity levels (light, moderate, vigorous).

Each participant will wear the accelerometer for a one-week period at weeks 0, 8, 16 and 25. Accelerometers will be given out by the RAs at the anthropometric appointments. For control participants at 8 weeks, an accelerometer will be prepared by an RA and given to the nutritionist to hand out (the nutritionist will let the RAs know when the controls are coming in for their 8 week appointment).

List of Measured Variables

- Minutes per day of sedentary behaviour (<100 cpm), light physical activity (100-1951 cpm) moderate physical activity (1952-5724 cpm), vigorous physical activity (≥5725 cpm), and total or incidental physical activity (>100 cpm).
- Counts per minute over the entire wear day, of sedentary behaviour, light physical activity, moderate physical activity, vigorous physical activity, and total or incidental physical activity.
- Sleep duration
- Minutes per day of bouted (≥10 consecutive minutes) and unbouted (<10 consecutive minutes) activity

Important Points to Mention During the Initial Meeting with the Participant

1. We are putting an activity monitor on which will give us an indication of how much physical activity you do. It records how often you move around and how quickly you move around.
2. The activity monitor does not interfere with any medical devices and is not harmful.
3. The activity monitor should be worn on the elastic band around your waist, preferably right next to the skin but it can go over a tight-fitting shirt if it is itchy, or can be looped through belt holes on pants and should be situated directly above the right hip. Please ensure that the elastic is not loose and the activity monitor is not flopping around because it will not collect good data.
4. The activity monitor should be worn at all times for the next 7 days and nights except it should be removed for all water-based activities such as swimming, showering, or bathing because it is not waterproof. If you are uncomfortable
wearing the accelerometer to sleep or if you try it and it keeps you awake, do not feel obligated to wear it at night. It is most important that you are wearing it during your waking hours. So, if you are not wearing it to sleep, please put it on as soon as you wake up in the morning and remove it immediately prior to climbing into bed at night.

5. If the monitor is removed, please record on this log sheet what time(s) and why the activity monitor was removed. Also, please record the times you wake up in the morning and fall asleep at night. Finally, if you experience any problems or have any comments or suggestions please write that in on the bottom of the sheet. Alternatively, if you have any immediate concerns while wearing the device please contact (???) at (???)

6. Although the activity monitor is very durable, please be careful and gentle with it as it is very expensive.

7. Have you made an appointment to come back next week? Please remember to wear the activity monitor back and bring the log sheet to that appointment. If you do not have an appointment than we can arrange a time when I can meet you at the front doors of the SKHS building to pick it up from you. You will receive a call the day before it is to come back to remind you and make arrangements if necessary.

Example of Accelerometer Graph
Appendix I: Nutritional Assessment & Counseling

In the SERENA Study, we prescribe exercise to participants but we do not prescribe caloric restriction. It is expected that the participant will follow a healthful diet (recommended by the Canada Food Guide) with the guidance of the study Nutritionist and stay within their suggested caloric range. This is an important characteristic of the proposed study as it will allow us to isolate the effects of exercise dose and intensity on the primary outcomes. We will know that the negative energy balance induced is a consequence of the increase in energy expenditure respective to the individual exercise treatment.

**Personnel**
- Consultant Dietician (to ensure key messages are correct)
- Nutritionist

**Measurement/Assessment Equipment**
- Ring binder to hold materials
- Blank Dietary Records
- Food models
- Canada’s Food Guide (Health Canada)
- Nutrition Facts leaflet (Health Canada)
- T-Factor booklet
- Handouts for nutrition sessions
- Instruction sheet summarizing the steps required to fill out the food records
- Form for the participant to record their frequently used foods

**Assessment Procedures**
In the SERENA Study, each participant will meet with the study Nutritionist and participate in a series of educational seminars designed to teach proper food selection and preparation as designed by the study Nutritionist. For all participants (i.e., including control group) the diet composition will provide energy as follows: approximately 50 to 55% carbohydrate, 15-20% protein and 30% fat. Participants will be asked to submit daily diet records for the duration of the program. Although time-consuming, submission of daily food records is a critical step in the design of individual success strategies for compliance to the dietary (caloric and composition) requirements of the study.

*During the first session with the nutritionist the following will take place:*

1. The participant will meet with the study Nutritionist to discuss the expectations of the nutrition component of the study. This participant will be made aware of the following points:
   a. This is a physical activity intervention. They will be expected to follow a healthful diet but the primary focus of the study is NOT weight loss.
b. Participants must not make any changes to their current way of eating unless advised by the study Nutritionist

c. Participants are expected to maintain weight during the baseline period and follow the prescribed caloric intake throughout the course of the study.

The Nutritionist will introduce the concept of self-monitoring and instruct the participant on the proper way to fill out the food records provided (The participant is required to hand in daily food records throughout the entire intervention period). The participant will be given a nutrition binder and taught basic tools for portion size estimation. The participant will be instructed not to change anything in terms of diet composition for the first week that they fill out the food records. They will hand in their first set of food records 6 days after the first session. A second meeting will be set up within 24-48 hours of them handing in their food records. At this time they will be given their target calorie and fat intake that they are to maintain for the duration of the study. These values are determined by taking the average calorie and fat intake reported over the 6 days.

**Food Record Instructions:** (give instruction handout to participant)

a. Each day you are required to fill out this form and write down everything you have eaten (this includes butters, spreads, dressings and the little bites of food you may eat while cooking)

b. Time - You must fill out the time you’ve eaten. This is pretty self-explanatory. It is helpful to write down your food just before or after eating to ensure accurate recording (so that you don’t forget anything you have eaten).

c. Amount/Portion – It is important to estimate the portion sizes carefully. (We will go over these in a minute)

d. Food – Fill out exactly what you have eaten. Be as descriptive as possible. Include brand names and the cooking method so that we can look up some of the material if we need to. (e.g. Equality mild cheddar cheese, PC raspberry vinaigrette dressing, Parmalat skim milk, broiled vs. roasted chicken from butcher, etc.)

e. Calories & Fat - Record the calories as well as the total fat (found on the label, in the booklet given or Internet sources). Approximately 30% of your calories should come from fat.

f. Source – Write down where you found the info for calories and fat (ie T-factor book, H-Book, website, label etc)

g. 7) Add up calories – How close are you to your recommended target? (If you are over or under, what adjustments can you make?)

Subsequently, the nutritionist checks in regularly with exercising participants and collects a packet of completed dietary records from each participant on a weekly basis. Those in the control group will drop in once every 2 weeks to weigh in and drop off the previous week’s dietary records for review. Exercisers and controls alike are expected to maintain their target calorie intake throughout the study. Should waist circumference and/or weight change dramatically to an extent unexplained by the prescribed exercise...
treatment, the nutritionist will investigate the issue, determine whether excessive or insufficient calorie intake is driving the changes, and provide counsel accordingly.

**Ongoing Nutritional Counselling (group sessions usually – individual sessions if necessary)**

Along with regular monitoring of weight and checking accuracy of diet records, the nutritionist will meet with all exercising participants for follow-ups at 4, 8, 14 and 22 weeks to review food records, assess progress and address any concerns. At the 14 week appointment, the participant will be given a checklist to review prior to their 16 week OGTT. It is to simply act as a reminder to them regarding food composition and healthy eating, things that they have already learned in the study. At the 22 week appointment, the participant will be given back their 3 days of food records that were recorded prior to their 16 week OGTT and instructed to consume the same composition of food 3 days prior to their 24 week OGTT. The reason for this is to try to obtain an OGTT result that is accurate and representative of the usual habits of the participant. In addition, the nutritionist provides all participants with a series of educational sessions on the fundamentals of maintaining a healthy diet according to Canada’s Food Guide. A total of eight nutritional packages are delivered during the course of the study. It is important to remind participants that although we encourage a healthful diet, total caloric intake must remain constant throughout the study. A summary of the goals for each nutritional session is provided below:
## Appendix J: Example of Statistical Analysis

### Model Information

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