EXPLORATION OF INTERINDIVIDUAL VARIABILITY FOR CHANGE IN WAIST CIRCUMFERENCE AND BODY WEIGHT IN RESPONSE TO STANDARDIZED EXERCISE

by

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Abstract

**BACKGROUND:** Substantial interindividual variability in response to a standard dose of exercise exists independent of the trait under investigation. Whether interindividual variability attributed to exercise exists after accounting for random variability is unknown.

**OBJECTIVE:** To determine the magnitude of the interindividual variability in response to exercise for waist circumference (WC) and body weight (BW) after accounting for random variability and, the extent to which the variability is explained by lifestyle behaviors.

**METHODS:** Participants were 181 (61% female) sedentary, abdominally obese adults (mean, (SD); 53, (7.5) years) who completed a 24-week intervention. Participants were randomly assigned to: control (n=44) or 5 weekly sessions of low amount, low intensity (LALI) (180 and 300kcal/session for women and men respectively at 50% V0\(_2\)peak, n=46); high amount, low intensity (HALI) (360 and 600kcal/session for women and men respectively at 50% V0\(_2\)peak, n=53); or high amount, high intensity (HAHI) (360 and 600kcal/session for women and men respectively at 75% V0\(_2\)peak, n=38). Adherence was ≥ 80% in all exercise groups. Physical activity (PA) performed outside of the prescribed exercise was measured by accelerometer. Daily self-report diet records were used to derive energy intake (kcal) and diet quality (Canadian-Healthy Eating Index-2010, Mediterranean Score). The variability in response to exercise (SD\(_R\)) was determined by separating the random variability from the intervention variability by comparing standard deviations (SD) from both the control and intervention groups.

**RESULTS:** WC and BW were substantially reduced at 24 weeks in all exercise groups compared to control (P<0.01). The variability due to exercise (SD\(_R\)) for change in WC was 3.1, -0.3 and 3.1 cm for LALI, HALI and HAHI groups respectively. Corresponding values for BW were 3.8, 2.0 and 3.5 kg for LALI, HALI and HAHI respectively. No dietary or PA variable was
identified as a determinant of the interindividual variability in response to exercise for WC or BW (p>0.05).

**CONCLUSION:** A substantial interindividual variability in response to exercise was observed for change in WC and BW after accounting for the random variability. The determinants of the heterogeneity in response to exercise remain to be determined.
Co-Authorship

Dr. Robert Ross was responsible for the conceptual design of the primary trial for which this investigation was based. Acquisition of the data described in this thesis was a collaborative effort carried out by previous graduate students and staff within the Cardiometabolic and Lifestyle Research Unit from 2009-2013. Brittany Hammond and Andrea Brennan were responsible for the entry of all dietary record data into the dietary analysis platform. Access to the dietary analysis platform and guidance on dietary concepts was provided by Dr. Benoit Lamarche. Brittany Hammond was responsible for statistical analysis and data management with help from Mr. Andrew Day and Mrs. Paula Stotz. Brittany Hammond was responsible for the writing of the manuscript contained in this document with all critical revisions provided by Dr. Robert Ross.
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to be as calm, cool and collected as you. You have been an amazing friend. I know you will all go on to do great things.

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<th>Description</th>
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<tbody>
<tr>
<td>AMPM</td>
<td>Automated multiple pass method</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BW</td>
<td>Body weight</td>
</tr>
<tr>
<td>C-HEI</td>
<td>Canadian-healthy eating index</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>CRF</td>
<td>Cardiorespiratory fitness (V0_2max, V0_2peak)</td>
</tr>
<tr>
<td>HEI</td>
<td>Healthy eating index</td>
</tr>
<tr>
<td>DASH</td>
<td>Dietary approaches to stop hypertension</td>
</tr>
<tr>
<td>ED</td>
<td>Energy density</td>
</tr>
<tr>
<td>EI</td>
<td>Energy intake</td>
</tr>
<tr>
<td>FFQ</td>
<td>Food frequency questionnaire</td>
</tr>
<tr>
<td>HAHI</td>
<td>High amount, high intensity</td>
</tr>
<tr>
<td>HALI</td>
<td>High amount, low intensity</td>
</tr>
<tr>
<td>HR</td>
<td>Hazard ratio</td>
</tr>
<tr>
<td>LALI</td>
<td>Low amount, low intensity</td>
</tr>
<tr>
<td>MCID</td>
<td>Minimal clinically important difference</td>
</tr>
<tr>
<td>MDS</td>
<td>Mediterranean diet score</td>
</tr>
<tr>
<td>MedScore</td>
<td>Mediterranean score</td>
</tr>
<tr>
<td>PA</td>
<td>Physical activity</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td>R24W</td>
<td>Web-based automated 24-hour recall</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic blood pressure</td>
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</table>
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD&lt;sub&gt;C&lt;/sub&gt;</td>
<td>Standard deviation of control group</td>
</tr>
<tr>
<td>SD&lt;sub&gt;I&lt;/sub&gt;</td>
<td>Standard deviation of intervention group</td>
</tr>
<tr>
<td>SD&lt;sub&gt;R&lt;/sub&gt;</td>
<td>Standard deviation of the ‘true’ interindividual variation in response due to treatment</td>
</tr>
<tr>
<td>TPA</td>
<td>Total physical activity performed outside of the exercise regimen</td>
</tr>
<tr>
<td>USDA</td>
<td>United States department of agriculture</td>
</tr>
<tr>
<td>WC</td>
<td>Waist circumference</td>
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</table>
Chapter 1. General Introduction

Numerous lifestyle-based interventions have been designed to target reductions in obesity [1-6]. The primary observation from systematic reviews confirm that a negative energy balance induced by exercise is associated with a substantial reduction of anthropometric including waist circumference (WC) and body weight (BW) [7]. The findings of these randomized controlled trials (RCT) were derived from the mean response of exercise groups compared to control. As such, the premise in which practitioners prescribe a standard exercise regimen for an individual is based upon the average group response to an exercise treatment. However, the average response of a group does not necessarily mean that all in that group will experience a similar degree of benefit. With the concept of personalized medicine emerging within clinical practice [8], it has become apparent that this “one size fits all” approach may be effective for some individuals, but not for all.

Indeed, it is well established that individuals exhibit a wide range of response to standardized exercise regardless of the trait examined [9]. In the early 1980’s, Bouchard and colleagues were among the first to demonstrate this notion of interindividual variability in response to exercise [10]. For a given dose of exercise, they observed considerable variability in the magnitude of response for cardiorespiratory fitness (CRF), wherein some individuals appeared to experience substantial improvements in a trait, while others did not improve at all. Since these initial observations, several studies have reported considerable heterogeneity in response to exercise for an array of traits. To date, research has focused on the variability of CRF response to exercise [9, 11-13], while measures of body composition such as WC and BW have received less attention. In fact, to our knowledge no study has examined individual variability for WC response to exercise in adults, and few have investigated the response for change in BW [14-
Given that both WC and BW are positively associated with the development of numerous co-morbidities [17-20], the exploration of these simple anthropometric measures in the context of individual response represent an opportune area of research that is of clinical interest.

However, despite a growing body of evidence, in recent years the veracity of the approach to measuring interindividual variability in response to exercise has been questioned [21-24]. Prior investigations have incorrectly assumed that the variability in response for a given trait is solely a consequence of exercise thereby ignoring the individual variability derived from numerous sources including the random variability from both day-to-day biological fluctuations and measurement error. Critics assert that consideration of the control group variability is necessary to adequately quantify interindividual variability in response to exercise [21-23]. Without exception, prior trials investigating individual response have ignored the variability observed within the control group, and consequently have not accounted for the contribution of random variability over time for the given trait under study. Thus, whether interindividual variability attributed to exercise exists after accounting for random variability is unknown.

Correspondingly, assuming ‘true’ variability due to exercise exists, the exploration of determinants could help elucidate why some individuals respond to a greater or lesser extent compared to another. It is possible that changes in behaviour outside of the intervention, including dietary consumption or incidental physical activity (PA), may explain some of the variability for the change in anthropometric measures of obesity in response to exercise. In fact, the relationship between diet quality and anthropometry was highlighted in a systematic review [25]. Thus, differences in diet quality and not just diet quantity, could offer a novel explanation for some of the observed variability. Presently, no study has examined the role of diet quality as measured by index scores in explaining variability in response to exercise. An understanding of the variability in individual response for body composition measures, and what may explain it, is important for the development of a more personalized approach for the management of obesity when using lifestyle-based strategies.
Accordingly, the objective of this study was twofold. First, to determine the existence of interindividual variability for change in WC and BW in response to standardized exercise and second, to identify potential determinants of interindividual variability for change in WC and weight in response to standardized exercise. Our findings will provide clarification into the existence of interindividual variability in response to exercise, and will provide insight into potential determinants of the variability for WC and BW response to exercise.
Chapter 2. Literature Review

2.1 Interindividual variability in response to exercise

Interindividual variability in response to exercise was first recognized in a series of seminal studies conducted in the 1980s [10]. The investigations aimed to determine the genetic influence of individual variability of various cardiovascular adaptations (cardiorespiratory fitness (CRF), ventilatory aerobic and anaerobic threshold) in response to 20 weeks of standard exercise among ten pairs of monozygotic twins [10]. The authors reported high individual variability for cardiovascular adaptations to exercise and attributed the variability to, in large measure, genotype dependency.

Subsequent to these initial observations, a series of reports from the HERITAGE Family Study examined interindividual variability for various other outcomes in response to exercise [9, 26]. In agreement with the twin studies cited above, substantial variability in response to exercise was observed among individuals, regardless of the trait investigated (e.g., \( V_{O2\max} \), BW, body fat, HDL-cholesterol, systolic blood pressure (SBP) and heart rate at 50 watts) [9, 26, 27]. In fact, for a given dose of exercise, not only did the magnitude of response appear to vary, but in some cases, the direction of response as well, where some individuals appeared to respond adversely. For instance, Bouchard et al. reported that while the average change in \( V_{O2\max} \) in response to exercise was a 25% improvement from baseline, individual response ranged from unchanged to doubling of \( V_{O2\max} \) [26]. More recently, others have continued the investigation into individual response to exercise and have begun to explore potential determinants of the observed variability [12, 28-30]. For example, using data from the Dose-Response to Exercise in Postmenopausal Women (DREW) Study, Sisson et al. reported that baseline measures including age and training volume were key determinants of individual variability of \( V_{O2\max} \) with responses ranging from -33.2 to 76.0% change from baseline [12]. To date, the majority of research on individual variability in response to exercise has primarily focused on CRF and corresponding
cardiovascular adaptations [13, 31, 32], which has been recently reviewed [24]. In the past few years, however, several others have examined cardiometabolic risk factors [33] including insulin and glucose [11], BW [14, 15].

2.1.1 Does individual variability in response to exercise truly exist?

Although decades of observations regarding individual variability appear convincing, the conclusions of the previously mentioned studies assume that the variability in response for a trait is solely a consequence of exercise. In fact, the individual variability often attributed to the intervention group (treatment), can include numerous sources of variability such as random (biological and measurement) variability, between-subject variability (if unadjusted for baseline), subject-by-treatment interaction and within-subject variability.

A summary of the potential sources of variability are given in Table 1. The subject-by-treatment interaction, commonly known as the interindividual variability in response to treatment, represents the variability in differences of training response between individuals. However, to adequately quantify the variability for the subject-by-treatment interaction, confounding sources of variability (mentioned above) should be considered.

For these reasons, the early studies describing individual response to exercise have been criticized by those who suggest that limitations in study design and analytical approach confound interpretation [21-23]. Of primary concern, from a design perspective, is that these early studies did not include a control group [9], and consequently could not account for the random variability over time for the trait under study. Furthermore, despite inclusion of a control group in the study design, some authors did not consider incorporating the control group data in their analysis [11, 12, 15, 34], and thus the variability in the subject-by-treatment interaction is not truly isolated.
### Table 1. Sources of variability for an exercise intervention

<table>
<thead>
<tr>
<th>Source of variability</th>
<th>Description</th>
<th>How to account for the variability?</th>
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| **Random variability** | Influences both pre- and post- outcome values for an intervention  
- Comprised of:  
  o *Measurement error*: the difference between the measured value and the ‘true’ value. Different outcome measures are associated with differing amounts of error  
  (ie. error for skin folds > MRI adipose tissue imaging measures)  
  o *Biological variability*: random biological and behaviour fluctuations of an individual independent from the intervention. Different outcomes are associated with different extents of fluctuation  
  (ie. variability of blood pressure > V0₂max measures) | - Relying on the mean of multiple pre- and post-measures reduces measurement error  
- Use $SD_R = \sqrt{SD_I^2 - SD_C^2}$ to separate the contribution of random variability from the subject-by-treatment interaction variability |
| **Between-subject** | The true difference between individuals for a certain value (not change values)  
- (ie. true WC values at baseline vary between individuals) | - Include baseline values as a covariate |
| **Subject-by-treatment interaction** | ‘True’ interindividual variability in response due to treatment  
- The true differences in training response between individuals  
- (ie. In response to standardized exercise, V0₂max truly improved to a greater extent for one individual compared to another) | - Use $SD_R = \sqrt{SD_I^2 - SD_C^2}$ to separate this variability from random variability  
- Within-subject variability still remains (unless accounted for by methods described below) |
| **Within-subject** | Represents the reproducibility of training effects  
- The magnitude of change score differences if the same individual repeated the same intervention  
- Magnitude of this variability is currently unknown  
- (ie. After a washout period, an individual repeats the same intervention and improves their V0₂max to the same degree as the initial intervention) | - Only way to discern this variability from others is to have an individual repeat the same intervention  
- Repeat measures throughout the trial could act as a surrogate for a repeat intervention |
2.1.2 Consideration of random variability

Atkinson and Batterham have addressed the analytical limitations of prior trials by proposing a standard statistical approach that separates the random variability from the intervention variability by using standard deviations (SD) from both the control and intervention groups [23].

To quantify individual response, the variation due to random error (present in both control and intervention groups) is separated from the variation due to the intervention alone (subject-by-training interaction) by using the equation (see below) described by Atkinson and Batterham. In this equation, SD<sub>R</sub> represents the standard deviation (SD) of the ‘true’ interindividual variation in response due to treatment after adjustment for random error and is derived by the square root of the difference between the squares of the standard deviations of the change in the intervention (SD<sub>I</sub>) and the control (SD<sub>C</sub>) group.

\[ SD_R = \sqrt{SD_I^2 - SD_C^2} \]

2.1.3 Consideration of within-subject variability

Although the equation above accounts for random variability, the within-subject variability remains. It is important to note that the implicit assumption for exercise interventions examining individual response is that the training effects among individuals are highly reproducible. It is possible that the observed individual variability is, in fact, due to variable responsiveness to treatment for each individual. This begs the question - would an individual respond similarly if they were to repeat the same intervention? This remains unknown.

To assess within-subject variability, participants would have to repeat the intervention after an appropriate washout period to determine whether individuals would respond in a similar manner. Thus, the separation of subject interaction from within-subject variability can only be achieved through repeat administrations of the intervention to the same individuals. Furthermore,
a large scale multi-period crossover intervention design is, in fact, the only study design that can adequately identify all forms of variability discussed above with the addition of treatment variability as well (variability of the differences between each treatment phase). However, this type of intervention design is not practical or may not even be feasible to carry out due to high participant burden, cost and uncertainty regarding washout periods for training adaptions that may or may not become permanent. As it stands, it remains difficult to delineate potential within-subject variability from subject-by-treatment variability with current RCT designs.

As an alternative solution, Hecksteden A. et al. suggests that repeat testing of outcome measures throughout the duration of the intervention can help account for within-subject variability by comparing segmental slopes of change scores for shorter durations across the treatment period [22]. However, this approach is limited as well. First, the close temporal proximity of the measures may lead to high amounts of autocorrelation (measure of randomness) and a violation of the assumption of random errors. Additionally, training adaptions may not necessarily be linear over the course of the intervention and repeat measures may be expensive and impractical for some interventions. For now, this approach remains a plausible alternative to conducting a repeated cross-over design intervention or conducting a separate reliability intervention trial.

2.1.4 Consideration of clinical relevance

 Taken together, consideration of the approaches suggested by Atkinson and Batterham and Hecksteden A. et al. can help quantify true interindividual variability due to treatment. Once the variability of individual response to treatment has been quantified, it should be determined whether this variability is clinically relevant. Some authors suggest that only true and clinically relevant differences in interindividual response warrant further exploration of potential determinants that may explain individual response [21, 23]. Ultimately, identification of potential
determinants of individual variability could be helpful in elucidating behaviours or traits responsible for differences in response to exercise.

2.1.5 Studies considering SD_{R}

In response to the recent criticism of the inappropriate evaluation of interindividual variability, one study has since reported SD_{R} values as suggested by Atkinson and Batterham. Stock and colleagues were the first to report SD_{R} values for muscular adaptions to short-term resistance training in a group of young-adult women (n=47) [35]. Interestingly, they noted that the SD_{R} value for the majority of their outcomes (ie. change in vastus lateralis muscle thickness, leg extensor peak torque, biceps femoris coactivation) was <0 suggesting that variability in the control group was greater than treatment groups. Thus, the authors conceded that true interindividual variability, as defined by Atkinson and Batterham (2015), did not exist for most variables beyond that of random variability due to biological fluctuations and measurement error. These findings contrast the implicit assumptions of Atkinson and Batterham (2015), which suggest that the variability in the treatment groups would be greater than the control group variability, albeit this may or may not represent a clinically meaningful difference.

2.1.6 Summary

Prior investigations have failed to consider confounding sources of random variability when assessing individual differences in response to aerobic exercise for all traits [35]. Consequently, interindividual variability in response to aerobic exercise has yet to be adequately quantified. Moreover, in contrast to the plethora of research on CRF, other important predictors of obesity-related morbidity and mortality have been left unexploited. For instance, no study has accounted for random variability when examining individual response to exercise for change in BW. Moreover, little is known about the individual variability for WC change in response to
exercise. Thus, interindividual variability in WC and BW in response to standardized exercise represents an opportune area for research that is of clinical interest.

2.2 WC, mortality and morbidity

With few exceptions [36, 37], numerous prospective epidemiological studies have established WC as a significant predictor of morbidity and mortality independent of age, sex and body mass index (BMI) [19, 38-41]. A recent analysis of 650,000 participants from 11 different prospective cohorts, the largest sample size to date, revealed a positive linear association between WC and mortality risk across an extensive range of BMI categories (15-50 kg/m²) for white men and women [40]. With five times more deaths than any individual study, the authors reported that each 5 cm increment in WC was associated with a 7% and 9% increased risk of mortality for white men and women respectively, after adjustment for age, study, BMI, smoking status, alcohol consumption and physical activity (PA) [40]. Upon comparison of those in the highest versus the lowest WC groups, the life expectancy losses at age 40 were approximately 3 and 5 years for men and women respectively.

Other large prospective cohorts that were not included in this pooled analysis are in agreement with these findings as well. For instance, the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort reported a 5 cm increment in WC was associated with a 17% and 13% increased risk of mortality for men and women respectively over a 9.7 year follow-up [42]. Additionally, prospective studies have demonstrated a positive association between WC and risk of developing diabetes [17, 43] and cardiovascular disease (CVD) [19]. For example, in a systematic review and meta-regression analysis of prospective cohort studies that examined the relationship between WC and CVD, it was found that for every 1 cm increment in WC was associated with a 2% increase in CVD incidence in both men and women, after adjustment for age [44]. Thus, based on the strength of evidence mentioned above, one would predict that
reductions in WC would likely result in subsequent improvements in morbidity and mortality risk.

To date, few prospective cohort studies have examined the association between change in WC and morbidity or mortality. Among the few, Berentzen and colleagues reported that a change of 5 cm over 5.8 years was associated with a 9% reduction in risk of mortality after adjustment for change in BMI [45]. Koh-Banerjee et al. observed a positive relationship between WC change and diabetes risk, although this was only true for the highest quintile of WC gain (>14.6 cm) after adjustment for change in BW [46]. Evidence from the Danish Diet, Cancer and Health study found that every 5 cm change in WC was associated with a 9% increased risk for developing diabetes after adjustment for age, chronic disease and change in BMI, although no association was observed among men [17]. Additionally, it has been reported that an increase of 1 cm is associated with a 10% increased risk of Metabolic syndrome incident over a 6.6 years follow-up period among middle eastern men and women [20].

Taken together, this evidence strongly supports the notion that WC should be incorporated in routine clinical practice as a standard assessment (in combination with BMI) for a more accurate appraisal of health risk.

### 2.3 BW, mortality and morbidity

Several meta-analyses have reported a paradoxical association between mortality and excess BW, wherein those who have a higher BMI appear to have a reduced risk of mortality compared to normal BW, rather than the opposite [47, 48]. This relationship has been coined the “obesity paradox” [49-51].

For example, a large meta-analysis recently investigated the association between all-cause mortality and overweight and obesity [52]. Consistent with prior meta-analyses, the authors reported that overweight (BMI of 25 to <30) was associated with a 6% lower mortality
risk compared to normal weight (BMI of 20 to <25), while obesity (BMI>30) was associated with a 18% higher risk of mortality compared to normal weight. Others have found obesity to be associated with increased risk of mortality in addition to overweight [53]. The underlying mechanisms of such a relationship remain poorly understood, though several possible explanations have been proposed [54-56]. For instance, it is well-recognized that the major limitation of using BMI as a measure of obesity is that it does not differentiate differences in body fat distribution, hence the importance of using WC in addition to BMI, as discussed above.

Thus, differences in body fat distribution could influence the relationship between obesity and mortality. For example, several reviews have reported that, contrary to the findings derived by way of BMI, the use of anthropometric measures reveal a linear relationship between abdominal obesity and mortality [40, 57]. Additionally, others have suggested that differences in fitness in large measure, absolve the obesity paradox [56, 58, 59].

Despite the paradoxical relationship between BMI and mortality, several meta-analyses have established that overweight and obesity are strongly associated with numerous co-morbidities[18]. For example, Guh and colleagues recently performed a meta-analysis on the incidence of co-morbidities related to obesity and overweight [18]. The authors identified 18 co-morbidities associated with overweight and obesity including type 2 diabetes, hypertension, stroke and coronary artery disease. Specifically, they noted the strongest association between overweight and Type 2 Diabetes in women (Relative risk (CI); 3.92 (3.10–4.97))

Similar to the findings noted above, evidence for the association between change in BW and morbidity and mortality is mixed, and at times paradoxical [60, 61]. For instance, in a meta-analysis, Harrington and colleagues reported that intentional weight loss provided some benefit for individuals who were classified as unhealthy and obese, however weight loss conferred no benefit for those who were obese and healthy [62]. Furthermore, intentional BW loss for those who were of normal BW was associated with increased risk of mortality. However, as mentioned above, this study is limited by using BMI as there was no consideration of differences in body
composition or fitness. Despite these findings, intentional reductions in BW has been reported to result in several improvements in cardiovascular risk factors [63]. In fact, numerous large RCTs have demonstrated significant improvements in cardiometabolic risk factors with minimal to no BW reduction [2, 3]. For example, findings from the Look AHEAD (Action for Health in Diabetes) study support the notion that minimal BW loss is associated with improvements in cardiovascular disease, wherein those who sustained a 2 to <5% reduction in BW experienced increased odds of improving SBP (Hazard Ratio (HR), 1.24), glucose (HR, 1.75), Hemoglobin A1c (HR, 1.80) and triglycerides (HR, 1.46), compared to those who maintained BW [64]. 

Taken together, although it is evident that a reduction in BW is not required per se to induce improvements in mortality and risk factors, it appears that intentional change in BW is associated with health benefit.

2.4 Exercise and change in WC and BW

Numerous lifestyle-based interventions have been designed to target reductions in anthropometric measures of obesity. The primary observation from systematic reviews confirm that a negative energy balance induced by exercise is associated with a substantial reduction in WC and BW [7]. Of clinical relevance, exercise consistent with consensus guidelines (150 min/week) is an effective means of reducing BW (>2kg) and WC (>2 cm) [1, 4, 65]. Thus, exercise is currently considered a viable treatment option for the management of abdominal obesity, although, some aspects regarding the nature of the relationship between exercise and both WC and BW change require further research, such as individual response to exercise. To ultimately understand differences in individual response to exercise for anthropometric measures, one should first consider the average or group change in WC and BW in response to exercise.
2.4.1 Exercise and change in WC and BW for the group

Previous systematic reviews report that, upon comparison of numerous groups across studies lasting <26 weeks, a positive dose–response relationship existed between exercise-induced energy expenditure (amount, kcal) and both WC and BW among healthy and diabetic overweight adults [5, 6]. While observations based on a comparison across studies are useful, these findings are interpreted with caution. Differences in study design, participant characteristics and methodology across studies are sources for potential confounding variables. For instance, it is possible that variations in exercise intensity across studies could confound the relationship between exercise amount and reduction in WC and BW.

To account for the limitations of this approach, large RCTs designed to examine the effects of variations in exercise dose on anthropometric measures within a study are required. In fact, the Dose-Response to Exercise in postmenopausal Women (DREW) study is the only RCT that has examined the dose-response relationship between exercise energy expenditure (amount) and WC and BW to date. Church et al. investigated the effect of varying doses (50%, 100%, and 150%) of consensus physical activity recommendations on change in CRF among 464 hypertensive postmenopausal women [65]. Participants were randomized to either a non-exercise control group or to an exercise group that expended 4, 8 or 12 kcal/kg of BW per week. Following 6 months of exercise prescription, significant reductions in WC were observed in all exercise groups compared to control, despite an absence of BW reduction. However, contrary to the findings of the prior reviews [5, 6], there were no between-group differences observed for WC reduction despite a tripling of energy expenditure (-1.9, - 2.9, and -1.4 cm for the 4, 8, and 12 kcal/kg per week, respectively).
2.4.1.1 Separate effects of exercise amount and intensity on change in WC and BW

The results of the DREW study are consistent with two other large RCTs which have examined differences in exercise amount and intensity on WC and BW reduction [1, 4]. Briefly, Ross et al. conducted a large RCT over 24 weeks wherein abdominally obese adults (n=300) were randomly assigned to one of four groups: control; low amount/low intensity (180 and 300 kcal/session for women and men, respectively, at 50% of VO$_{2}$peak); high amount/low intensity (360 and 600 kcal/session for women and men, respectively, at 50% of VO$_{2}$peak); and high amount/ high intensity (360 and 600 kcal/session for women and men, respectively, at 75% of VO$_{2}$peak) [4]. Substantial reductions in WC (~5 cm) and BW (~4.5 kg) was observed in all exercise groups compared to control (Figure 1); a finding consistent with other large lifestyle-based interventions [1, 65]. However, careful inspection of Figure 1 reveals no between-group differences despite the doubling of energy expenditure in the high amount compared to the low amount group (Male: 600 vs 300kcal; Female: 360 vs 180kcal). This occurred despite careful control of energy expenditure and monitoring of other potentially confounding variables that could have altered the prescribed negative energy balance (ie. dietary intake, change in PA outside of the exercise prescribed). Although the average reduction in WC among the groups did not differ, it is evident by the size of the confidence intervals that there is a large range of individual exercise response in WC change for a given exercise dose.
Figure 1: Change in WC during 24 weeks of exercise

LALI (low amount/low intensity, 180 and 300 kcal/session for women and men, respectively, at 50% of VO\textsubscript{2}peak; HALI (high amount/low intensity, 360 and 600 kcal/session for women and men, respectively, at 50% of VO\textsubscript{2}peak); HAHI (high amount/high intensity, 360 and 600 kcal/session for women and men, respectively, at 75% of VO\textsubscript{2}peak).

Taken from Ross et al. (2015)[4] (Permission found in Appendix A).

2.4.2 Interindividual variability for change in WC in response to exercise

To my knowledge no study has quantified interindividual variability in response to exercise for WC change. Given the fact that WC can occur in the absence of weight loss, it is important to examine the variability for change in WC in response to exercise separately. Several studies have noted exercise-induced changes in WC independent of change in BW [2, 3, 15]. For example, King et al. noted that those who lose less BW than predicted still experienced a reduction in WC of ~3 cm. Though no study has examined individual exercise response for WC
per se, several studies have examined the heterogeneity of response for change in BW which may provide a clue as to what we would expect to observe for the variability in WC response.

2.4.3 Interindividual variability for change in BW in response to exercise

Numerous studies have noted great heterogeneity in response to exercise for BW change over recent decades. In 1990, Bouchard and colleagues were among the first to note substantial variability in BW change among 5 men [66]. Despite rigorous control of energy intake (EI) and living conditions, after 100 days of supervised exercise at 55% V02max twice a day for 6 days a week (~1000kcal per day), participants induced reductions in BW ranging from 3-12 kg. Though the experimental conditions were tightly controlled, the small sample size and lack of control group make it difficult to account for other sources of variability as discussed above. Since then, numerous studies have been performed to examine potential compensatory mechanisms to explain variability for BW change in response to exercise [14, 28, 29, 67].

For example, King and colleagues sought to investigate the interindividual variability of exercise-induced BW loss and potential compensatory mechanisms following 12 weeks of supervised exercise among 35 men and women [14]. The exercise regime was designed to induce a negative energy balance approximating 500 kcal per session at 70% heart rate maximum for 5 days a week. Despite a mean reduction in BW of 3.7 kg, a substantial heterogeneity in response to exercise was observed ranging from a reduction of 14 kg to a gain of 2 kg. A major limitation of this study is the absence of a control group. Consequently, we cannot be certain whether interindividual variability exists beyond that of other random variability.

Subsequently, Church and colleagues have extended the findings of King et al. by examining whether differing doses of exercise (50%, 100%, and 150% of consensus physical activity recommendations) influenced changes in BW, WC and compensatory responses among sedentary, overweight postmenopausal women [15]. Consistent with the primary investigation
[65], all exercise groups induced significant reductions in BW and WC, although there were no between group differences. Furthermore, they reported that the amount of BW compensation (whether an individual lost less BW than predicted) increases with exercise dose. This observation could suggest that the extent of interindividual variability in BW change in response to exercise is influenced by the amount of exercise performed, though they did not actually quantify this.

Accordingly, Figure 2, shows the variability in BW change among individuals for each group in the aforementioned study. At first glance, one can easily appreciate the wide range of individual response for change in BW. However, it is just as evident that the heterogeneity of response appears to be fairly similar across all groups. In fact, it appears the control group could potentially have greater variability in BW change in comparison to the exercise groups, suggesting that the SDr values would, perhaps, be less than 0. Recall, as described above, the SDr value represents the standard deviation of the ‘true’ interindividual variation in response due to treatment after adjustment for random error and is derived by the square root of the difference between the squares of the standard deviations of the change in the intervention (SDI) and the control (SDC) group. This approach separates the random variability from the variability due to exercise. Unfortunately, as with King et al., the authors did not include the control group in the analysis and, consequently, did not account for random variability. This represents a major limitation when trying to parse the random error from the ‘true’ treatment response (Table 1). Thus, it remains unknown as to whether the heterogeneity in individual response to exercise for BW change really exists beyond that of random variability.
Figure 2. Individual response for change in BW among groups varying in exercise dose

4KKW = 4 kcal/kg of BW per week (50% of consensus physical activity recommendations)

8KKW = 8 kcal/kg of BW per week (100% of consensus physical activity recommendations)

12KKW = 12 kcal/kg of BW per week (150% of consensus physical activity recommendations)

Taken from Church et al. (2009) [15] (Permission found in Appendix A).

Minimal clinically relevant difference for change in WC and BW

As discussed in Section 2.1.5., once the ‘true’ variability of individual response to exercise has been quantified, it should be determined whether this variability represents a clinically meaningful difference. Some authors suggest that only clinically relevant differences in interindividual response deserve further exploration of potential determinants that may help explain individual response, as it is not worthwhile to identify variables that would not infer
meaningful benefit to an individual’s health. Thus, for the purposes of this thesis, a difference of 2 cm and 2 kg for change in WC and BW respectively will be used to represent a MCID, based on the literature reviewed above (Section 2.2 and Section 2.3). If the magnitude of interindividual variability in response to exercise does not meet this MCID, then further investigation of determinants should cease. Ultimately, if meaningful variability exists, identification of potential determinants of individual variability in response to exercise could be helpful in elucidating behaviours or traits responsible for differences in response to exercise.

2.4.4 Summary
It is evident that further research is needed to adequately quantify interindividual variability for both change in WC and BW. If such variability is present and represents a clinically meaningful difference, the identification of different inherent traits or acquired behaviours that influence one’s response to exercise would be of great value for the development of personalized exercise programs in clinical practice.

2.5 Determinants of change in WC and BW in response to exercise
That substantial variability of individual response (assuming this variability were true) was observed despite rigorously controlled and supervised exercise prescription in prior studies suggests that individual differences in other factors that could influence energy balance must be at play. Indeed, differences in both acquired or inherent characteristics could potentially explain some of the variability in response to exercise. For example, differences in sex or initial baseline WC or BW could influence the extent of WC or BW change. Moreover, it is possible that changes in behaviour outside of the intervention, including dietary consumption or incidental PA, may explain some of the variability in the change of anthropometric measures in response to exercise. In fact, with the relationship of diet quality and anthropometry recently highlighted in a
systematic review, it is possible that diet quality, and not just diet quantity, may offer a novel explanation as to why some individuals experienced WC or BW reduction to a greater or lesser extent compared to another. Indeed, whether differences in life-style based behaviours contribute to individual response is of particular clinical interest, as these behaviours could be adjusted accordingly to optimize their response to exercise in the future.

2.5.1 Sex and baseline values

It is possible that differences in sex and initial baseline measurements could influence the magnitude of WC and BW change in response to exercise for each individual.

It is well-known that men are generally taller and have a larger body mass compared to women. In addition, it is established that men and women differ with respect to adipose tissue distribution [68]. Men generally have greater central distribution of fat in contrast to premenopausal women, who generally have greater amounts of peripheral adipose tissue distribution compared to abdominal. Thus, for a given BMI, men typically have a higher BW and WC compared to females [69].

In accordance with regression to the mean[70], it is reasonable to assume that differences in initial baseline values could explain some of the individual variability in response to exercise. If this were true, we would expect that individuals who began the intervention with the highest baseline BW and WC would be among those who experienced the greatest reductions in BW and WC and vice versa. Correspondingly, under the assumption that men are typically larger than women, men would likely reduce their WC and BW to a greater extent than women due to the mere fact that they began the intervention with a higher baseline value.

Conversely, it remains unclear as to whether men and women respond differently to the same exercise stimulus beyond differences in baseline body mass and adipose tissue distribution. Many studies have purported the notion that women reduce their BW to a lesser extent than men
in response to exercise [16, 71, 72], while others have failed to observe any difference between sex [1, 2, 73]. It is possible that differences in exercise prescription may explain the discrepant findings. For instance, Donges et al. recently reported that men experienced greater absolute and relative reductions in abdominal and total adiposity compared to women in response to the same exercise prescription [71]. However, in this study, the prescribed exercise amount was based on number of minutes. Consequently, these results are likely confounded by differences in energy expenditure between men and women. For a given duration and intensity of exercise, energy expenditure can vary significantly between men and women due to differences in body mass [74]. In contrast, rigorously controlled exercise interventions which have prescribed exercise amount based on energy expenditure (kcal) have demonstrated that women are capable of inducing substantial reductions in BW in response to exercise [2] wherein they experience similar relative reductions in total and abdominal adiposity to that of men [3].

Taken together, in accordance with regression to the mean, it is possible that differences in baseline measurements could contribute to the heterogeneity of response for change in WC and BW among individuals. Similarly, differences in sex could also offer a potential explanation for variability in response to exercise, though this would likely be due to underlying differences in body fat distribution and baseline values and not necessarily due to inherent differences in response.

2.5.2 Physical activity

PA is defined as any bodily movement produced by skeletal muscles that results in energy expenditure [75] and includes activity that occurs during sleep, work and leisure [75]. It is possible that alterations in an individual’s amount of PA performed outside of the standardized exercise regimen could influence an individual’s overall amount of WC or BW change. For instance, an increase in the amount of PA (leisure) performed compared to their usual habits at
baseline could contribute to an increase in WC and BW reduction and vise versa. At present, the evidence appears to be inconsistent [28] in regards to whether an increase in exercise could potentially promote increased PA habits [76, 77] or decreased PA habits (increased sedentary time)[78] outside of the exercise regimen. Though several studies examining individual response for change in BW noted that there was no change in the average amount PA performed outside of the exercise regimen at the group level [14, 15], it is possible that individual differences in PA behaviour could account for some of the observed heterogeneity in response for change in anthropometric measures.

2.5.2.1 Accelerometry

To determine whether PA is a potential determinant of interindividual variability in response to exercise requires the accurate assessment of PA performed outside of the exercise regimen. Several devices such as pedometers and accelerometers have been used to obtain objective measures of PA patterns [79]. Specifically, accelerometers are non-invasive movement counters that measure acceleration forces in gravitational units. The device is typically worn on the hip [80] and provides data on the frequency, amount (duration; min) and intensity of PA over a given time frame. As the accelerometer detects the magnitude of an acceleration, it converts the data into “counts”, with higher counts representing a quicker acceleration force. The counts are averaged over a predetermined time frame referred to as an “epoch”. A typical epoch is 1 minute, but can be adjusted depending on the outcome that is being studied. A computer software program converts the raw data into counts per minute. Using established cut-offs [81], the data can be classified into sedentary (<100 counts per minute), light (100-1951 counts per minute), moderate (1952-5724 counts per minute) and vigorous (>5724 counts per minute) activity.

With advancements in technology, a multitude of accelerometer models have been developed. For instance, uniaxial accelerometers measure acceleration in a single plane (vertical), while triaxial accelerometers collect motion data on 3 planes. The triaxial device has
the advantage of capturing activity performed in all directions, compared to a uniaxial model. Modern accelerometers detect acceleration through changes in capacitance [82]. Within the accelerometer, a small polysilicon central plate is suspended between two other fixed plates creating two back-to-back capacitors. Thus, this upgraded technology allows accelerometers such as the Actigraph GT1M and GT3X to detect static (gravity) and dynamic acceleration (movement), compared to former versions.

At present, accelerometers are considered to be practical objective measurement instruments of PA. However, these devices have notable limitations. Accelerometers are unable to assess static or non-ambulatory components of exercise such as carrying weights, are costly for large-scale studies, and require algorithms to derive energy expenditure from raw data output [79, 83, 84].

In summary, the accelerometer device provides objective measures of PA which can be used to investigate whether differences in PA performed outside of the standardized exercise regimen could help explain some of the individual variability for change in WC and BW in response to exercise.

2.5.3 Energy intake

While it is possible that individual variability in response to exercise exists, it is also plausible that a large range of variability in dietary consumption exists among individuals as well. In fact, individual differences in dietary consumption – quantity and quality – may well explain, in small or large measure, the variability for change in WC or BW that is attributed to exercise. Intuitively, an alteration in one’s dietary intake could subsequently influence WC or BW change, wherein a reduction in EI would result in an increased negative energy balance and vise versa.
Although no study has examined the interindividual variability of WC and BW response to a standardized dietary regimen per se, several studies have examined dietary compensation behaviour and individual variability for change in BW in response to exercise. Consistent findings from acute exercise studies reveal no compensatory adjustments in EI in response to an acute bout of exercise [85-87], though Stubbs and colleagues have reported partial compensation (~30%) in EI in response to standardized exercise over 2 weeks [78].

In contrast, the relationship between chronic exercise and EI alterations has been left largely unexplored. Of the few studies that have considered this, findings appear inconsistent [14-16, 88]. For example, a recent study reported that the amount of EI change (kcal) for a given dose of exercise (2500 kcal/week) among obese men and women (n=35) varied substantially over a 12 week exercise intervention [14]. Although there was no significant change in mean EI over the duration of the trial, inspection at the individual level revealed that those who lost less BW than predicted had an increased EI compared to those who lost their predicted amount of BW and whose EI remained unchanged. It is important to note that this study is limited by the absence of a control group and thus, the findings should be interpreted with caution.

In contrast, Church et al. failed to observe differences in EI between compensators and noncompensators among exercise groups varying in exercise dose (50%, 100%, and 150% of consensus physical activity recommendations) [15]. In this context, compensation referred to the difference between predicted and actual weight loss. An individual who lost less BW than expected were classified as compensators, while those who lost the predicted amount of BW were classified as noncompensators. Differences in dietary assessment could explain the discrepant findings. For instance, King et al. measured twenty-four hour energy and macronutrient intake from test meals at baseline and week 12, while Church et al. assessed diet with a food frequency questionnaire, a tool that is not intended to derive EI.
Thus, further research is needed to clarify the contribution of EI on individual response for WC and BW change in response to exercise. Accordingly, it remains possible that individual differences in change in EI could explain some of the variability for WC or BW change over a long-duration exercise intervention despite the average EI remaining unchanged at the group level.

2.5.3.1 Assessment of EI

To clarify whether change in EI is a determinant of variability in WC and BW response to exercise requires the precise assessment of diet. Accurately assessing diet has proved to be a challenge for nutritional research [89]. To date, dietary assessment has relied primarily on self-report measures, which are associated with varying degrees of both random and systematic error [90, 91]. Random error such as the day-to-day variability in an individual’s diet can be mitigated with repeat measures [91]. Thus, examining 3-day diet records at multiple time points throughout an intervention will reflect an individual’s usual food consumption more accurately compared to a 3-day diet record at one time point. Systematic error, such a consistent underreporting of certain food items, is more difficult to correct and requires reference to another measurement instrument (ie. biomarkers)[91].

Several dietary assessment instruments have been designed to capture an individual’s usual dietary intake including diet records and 24-hour recalls (described below). In addition, food frequency questionnaires (FFQs) are another commonly used instrument for assessing dietary intake. These questionnaires ask respondents about the frequency of food and beverage consumption from a list of foods for a specific period. FFQs are primarily implemented in large prospective epidemiological studies due to the large number of participants and ease of administration.
2.5.3.2 Diet record

For the purpose of this thesis, we derived EI from self-report diet records collected from a previously completed trial [4]. A diet record is a common self-report tool used to assess dietary intake. An individual is asked to record amounts and descriptions of all food and beverages consumed throughout the day. A diet record is intended to be completed as food consumption occurs. While diet records are inexpensive and simple to administer, several issues with self-report measures have been extensively reviewed [90]. Major concerns include reactivity bias, social desirability bias, and participant burden which can ultimately lead to underreporting. For example, the mere act of recording one’s dietary consumption as it occurs can lead to reactive behaviour where an individual modifies their consumption behaviour [92]. Additionally, social desirability can lead to further reactivity and underreporting as well [93]. Furthermore, the quality of diet record data has been shown to decrease with increasing amounts of records due to the burden of completing the records [94]. Indeed, the combination of these factors can lead to systematic errors in measurements often resulting in underreporting across all diet records [90, 95]. Specifically, diet records have been shown to underestimate EI and other macronutrients such as protein as much as 4-37% when compared to recovery biomarker studies [96-98]. Despite these limitations, diet records are inexpensive measures that can provide a plethora of general information regarding specific meals of the day. Furthermore, the reactivity associated with self-report can be used as a tool to increase awareness and self-monitoring of lifestyle behaviours [99]. Table 2 summarizes the strengths and limitations of self-repot diet records.

In summary, the current limitations of self-report dietary assessment are widely acknowledged in nutritional science. In fact, many agree that due to these limitations diet records should not solely be used to derive EI [89, 90]. Nevertheless, self-report dietary assessment tools continue to provide valuable dietary data that current biomarkers cannot identify and thus, data from diet records in clinical research should not be dismissed [90]. Furthermore, the use of self-report has ultimately lead to the recognition of numerous diet-related disease in the past [100].
Therefore, as we await the day of an inexpensive and non-invasive objective measure of diet, self-report measures continue to be a practical source of collecting dietary information among individuals.
### Table 2. Strengths and limitations of a self-report diet record

<table>
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<tr>
<th>Instrument</th>
<th>Administration</th>
<th>Description</th>
<th>Strengths</th>
<th>Limitations</th>
<th>Error</th>
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<tbody>
<tr>
<td>Diet record</td>
<td>Log/diary (paper or electronic)</td>
<td>Respondent records descriptions and quantities for all foods and beverages consumed (intended to be completed at the time of consumption)</td>
<td>Meal specific details</td>
<td>Potential for reactivity bias (the mere act of recording consumption can induce a change in their consumption behaviour)</td>
<td>Underestimation of EI and protein ranges from 4-37% compared to DLW [96, 97]</td>
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<td></td>
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<td>No reliance of memory (if completed at the time of consumption)</td>
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<td>Largest biomarker study to date (n=450) [98] reported an underestimation of 20% and 4% for EI and protein respectively</td>
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<td></td>
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<td>Minimal participant training</td>
<td>High participant burden (time consuming, requires considerable cognitive effort)</td>
<td>Reporting error increases with increased recording periods</td>
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<td>Reactivity can be used as a tool for behaviour change/awareness</td>
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<td>Potential for social desirability bias</td>
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<td>If used as a 24-hour recall, there can be reliance on memory</td>
<td>Underreporting more common for overweight/obese population and women</td>
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<td>High burden for researchers to code</td>
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2.5.3.2.1 24-hour dietary recall

For the purposes of this thesis, we used a web-based 24-hour dietary recall platform to analyze the self-report diet records. Although we used this web-based platform for dietary analysis retrospectively, a brief description of the intended use of a typical 24-hour recall is provided below.

A 24-hour recall asks respondents to report consumption of all food and beverages in the preceding 24-hours. In the past, a 24-hour recall was conducted by a trained interviewer using a structured interview format known as the automated multiple pass method (AMPM)[101]. The AMPM is a five step dietary interview designed with multiple passes and probing questions to cue an individual’s memory. Recently, self-administered web-based 24-hour dietary recalls have been identified as a feasible cost-effective alternative to interview-based recalls. Thus, in recent years, several web-based 24-hour dietary recalls have been created.

2.5.3.3 Web-based automated 24-h recall

Specifically, the web-based automated 24-h recall platform (R24W) was used to analyze dietary data collected from self-report diet records for this thesis. The R24W was specifically developed [102] and validated [103] for the French-Canadian population inspired by the AMPM of the United States Department of Agriculture (USDA) [101]. In short, the R24W includes an organized list of foods and beverages, a search engine and suggestions for frequently forgotten foods. Portion sizes are represented by up to 8 pictures, with the option to select multiplicative or a fraction of each portion selected. The platform contains a database of 2865 food items with 687 pre-determined recipes for mixed dishes, including a variety of ethnic dishes [102]. The platform allows for automatic coding of nutrient intakes and diet quality scores using the 2010 Canadian Nutrient File [104] or the USDA Nutrient Database for Standard Reference [105] for the few items that are unavailable in the Canadian Nutrient File. Consequently, the program can automatically calculate a plethora of dietary information including EI, diet quality scores, food groups and specific nutrients.
2.5.4 Diet quality

In the past, nutritional research has primarily relied on a reductionist approach when examining the relationship between nutrition and health outcomes [106], primarily emphasizing the role of single nutrients in the development of disease. Though, in reality, single nutrients are not typically consumed in isolation, rather, humans consume diverse combinations of food and beverages. Correspondingly, nutrients have complex interactions when consumed together which can make it difficult to study the effect of a single nutrient on disease [107, 108]. Thus, the notion of diet quality represents a more comprehensive evaluation of one’s diet. While the definition of diet quality can vary within the literature, it is generally accepted that diet quality reflects how well an individual’s diet conforms to a set of dietary recommendations [109]. Diet quality is quantified with a multidimensional approach involving the selection of dietary components and respective cut-off values and scores (described below) [110]. A high diet quality score is thought to reflect a healthy, balanced diet with adequate levels of food and nutrients required to achieve optimal health for the prevention of disease [111, 112]. Accordingly, the relationship between diet quality and several health outcomes, including anthropometric measures of obesity, has emerged in recent years. Therefore, diet quality, and not just diet quantity, could offer a potential explanation for some of the interindividual variability observed for anthropometric measures in response to exercise.

2.5.4.1 Diet quality, WC and BW

To date, no study has examined the association between diet quality and interindividual variability for any trait, let alone change WC or BW, in response to exercise. However, studies that have examined the relationship between diet quality and change in anthropometry at the group level provide some insight. Specifically, the link between diet quality and anthropometric measures was recently highlighted in a series of systematic reviews examining the relationship between dietary patterns and health outcomes conducted by the USDA [25]. Evidence from numerous prospective epidemiological studies support the notion that higher diet quality index scores are associated with decreased BW, BMI,
and WC [113-116]. Furthermore, the association between diet quality and WC was independent of EI for the studies (n=4) contained within this review.

To my knowledge only two lifestyle-based interventions have examined the effects of both diet quality and exercise on change in WC and BW. In 2009, Jacobs et al. examined whether change in dietary patterns over 1 year would modify CVD and diabetes risk among 219 (men: 198, female: 21) participants with cardiometabolic risk factors from the Oslo Diet and Exercise Study [113]. Briefly, the participants were randomized into one of four groups: control, diet, exercise or diet and exercise combined. Both diet groups received 3 individualized dietary counseling sessions over the course of the year, whereas the exercise groups were prescribed 1 hour group exercise sessions 3 times a week. Attendance of exercise sessions averaged 1.8hr/wk. The study revealed that increased diet scores, which reflect a healthful diet, were associated with improvements in BW, WC and a variety of common cardiometabolic measures, independent of EI and the intervention assigned (ie. exercise only, diet only etc.). However, the negative energy balance was not standardized across groups and consequently, the findings attributed to diet could have been confounded by differences in negative energy balance overall. In addition, measurement of EI and energy expenditure was poor. Exercise and PA performed outside of the exercise regimen was not objectively measured and dietary intake was assessed with the use of the food frequency questionnaire, a tool which is not designed to derive EI [117].

In a secondary analysis, Nazare et al. examined the contribution of diet quality and PA on anthropometric and body composition measures among 93 abdominally obese men over the first year of a lifestyle-based intervention (SYNERGIE study) [118]. The study aimed to induce a daily deficit of 500 kcal with dietary counselling in addition to targeting 160 min of PA per week. The study revealed both PA amount and diet quality score (DASH derived diet quality score) were independently associated with changes in BMI, percent fat mass and visceral adipose tissue, beyond EI. Upon stratification of participants into high and low PA and diet quality, it was evident that those with the highest levels of both PA and diet quality obtained greater reductions in WC compared to those with both the lowest PA and diet quality. These findings, however, also suggested that PA may be the primary driver of the change in
WC compared to diet quality. Similar with Jacobs et al., this study is limited by the measurement tools used for diet and PA assessment. Furthermore, this study failed to include a control group.

Given the evidence that diet quality appears to influence both WC and BW change at the group level, the investigation of diet quality as a determinant of variability at the individual level is warranted.

2.5.4.2 Mechanisms

A potential explanation for the inverse association between diet quality and WC measures lies within the concept of food synergy [5], the additive influences of different food and nutrients that comprise one’s diet. Accordingly, diet quality may influence the change in anthropometric measures through a multitude of direct and indirect mechanisms.

First, a high diet quality is associated with high consumption of foods that are nutrient rich and low in energy density (ED) such as fruits and vegetables [119, 120]. For a given volume of food consumption, the greater consumption of lower ED food compared to higher ED food has been associated with less WC and BW gain [120]. Reductions in both WC and BW could be mediated by a reduction in EI due to a high consumption of low ED foods. Furthermore, the combined effects of single nutrients could alter metabolism and consumption behaviour [121, 122]. Food composition has been found to have a large influence on satiety [67, 123, 124] which can subsequently effect snacking behaviour and thus, potentially alter total EI. For instance, fiber has been shown to increase satiety and decrease gastric emptying [125] and food with a low glycemic index has been associated with reduced hunger and EI [126, 127]. Therefore, there are multiple synergistic pathways through which components of a high-quality diet can influence energy balance, and thus alter WC and BW.

2.5.4.3 Diet quality indices

To evaluate the contribution of diet quality to the interindividual variability for change in WC and BW in response to exercise, the assessment of diet quality is required. To date, a multitude of dietary indices have been developed and adapted to quantify diet quality [128].
In general, indices are constructed by using a theoretically defined dietary pattern or an empirically-derived pattern [129]. The first approach involves the development of a predefined index using current nutritional knowledge such as national dietary recommendations or recognized diets/dietary patterns (ie. Dietary Approaches to Stop Hypertension (DASH), Mediterranean diet). The second approach uses statistical analyses (ie. factor or cluster analysis) to determine scores for nutritional components after the nutritional data is already collected. The vast majority of indices have been developed based on nutritional guidelines or dietary patterns such as the Diet Quality Index (DQI), Healthy Eating Index (HEI), Healthy Diet Indicator (HDI), Mediterranean Diet Score (MDS) and Mediterranean Score to name a few. Specifically, the HEI [130-132] and MDS [133] are among the most widely used indices for assessing diet quality, and several adaptations of these have been tailored for specific populations, including Canadians [134]. For the purposes of this thesis, two dietary quality indices were used to evaluate diet quality. The Canadian-Healthy Eating Index (C-HEI) allowed for the assessment of diet quality based on national guidelines and the MedScore allowed for the assessment of diet quality based on an established dietary pattern that has been recently highlighted for its health benefits [135].

2.5.4.3.1 Canadian Healthy Eating Index (C-HEI)

The C-HEI [134] is adapted from the 2005 American HEI [131] and incorporates two aspects of diet quality: adequacy and moderation. Adequacy measures whether there is a sufficiency of intake for certain nutrients and foods, and moderation measures whether certain foods are overconsumed. Adequacy and moderation are comprised of 8 and 3 sub-components respectively with different weighted scores for each component (Table 3). A total C-HEI score can range from 0-100. A higher C-HEI score (100) reflects high adherence to Canada’s Food Guide which recommends a high intake of whole fruits and vegetables, dark green and orange vegetables, whole grains, nuts, legumes, unsaturated oils, low-fat dairy, poultry and fish and low intake of red meat, sugar-sweetened foods and beverages, high sodium content foods and moderate alcohol consumption [136]. Details on recommended serving sizes from Canada’s food guide used for the development of the C-HEI are provided in Table 3.
<table>
<thead>
<tr>
<th>Component</th>
<th>Range of Scores</th>
<th>Scoring criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequacy†</td>
<td>0 to 60 points</td>
<td></td>
</tr>
<tr>
<td>Total vegetables and fruit</td>
<td>0 to 10 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 4 to 10 servings*</td>
</tr>
<tr>
<td>Whole fruit</td>
<td>0 to 5 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 0.8 to 2.1 servings (21% of recommendation for total vegetables and fruit)*</td>
</tr>
<tr>
<td>Dark green and orange vegetables</td>
<td>0 to 5 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 0.8 to 2.1 servings (21% of recommendation for total vegetables and fruit)*</td>
</tr>
<tr>
<td>Total grain products</td>
<td>0 to 5 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 3 to 8 servings*</td>
</tr>
<tr>
<td>Whole grains</td>
<td>0 to 5 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 1.5 to 4 servings (50% of recommendation for total grain products)*</td>
</tr>
<tr>
<td>Milk and alternatives</td>
<td>0 to 10 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 2 to 4 servings*</td>
</tr>
<tr>
<td>Meat and alternatives</td>
<td>0 to 10 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 1 to 3 servings (75 to 225 grams)*</td>
</tr>
<tr>
<td>Unsaturated fats</td>
<td>0 to 10 points</td>
<td>Minimum: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 30 to 45 grams*</td>
</tr>
<tr>
<td>Moderation‡</td>
<td>0 to 40 points</td>
<td></td>
</tr>
<tr>
<td>Saturated fats</td>
<td>8 to 10 points</td>
<td>Minimum 7% to 10% of total EI</td>
</tr>
<tr>
<td></td>
<td>0 to 8 points</td>
<td>10% to maximum 15% of total EI</td>
</tr>
<tr>
<td>Sodium</td>
<td>8 to 10 points</td>
<td>Adequate intake to tolerable upper intake level</td>
</tr>
<tr>
<td></td>
<td>0 to 8 points</td>
<td>Tolerable upper intake level to twice tolerable upper intake level</td>
</tr>
<tr>
<td>“Other food”</td>
<td>0 to 20 points</td>
<td>Minimum: 5% or less of total EI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 40% or more of total EI</td>
</tr>
</tbody>
</table>

*according to age and sex, as specified in Canada’s Food Guide [136]

†for adequacy components, 0 points for minimum of less, 5 to 10 for maximum or more, and proportional for amounts between minimum and maximum

‡ for moderation components, 10 or 20 points for minimum of less, 0 for maximum or more, and proportional for amounts between minimum and maximum

Table taken from Garriguet, Didier (2009): 41. [134]. (Permission found in Appendix A)
2.5.4.3.2 Mediterranean Score (MedScore)

A typical Mediterranean diet is associated with daily consumption of non-refined grain products, fruits and vegetables, olive oil, low-fat dairy products and weekly consumption of fish, nuts and some poultry [137]. The Mediterranean Diet Score (MDS) was the first index developed to quantify the Mediterranean diet [133]. This index consisted of summed scores from eight dietary components resulting in a total score ranging from 0 to 16. A higher score (16) indicated greater adherence to the Mediterranean diet. Since then, numerous adaptions to this index have been constructed (ie. alternative-MDS, Mediterranean Score, MedScore).

Of interest to a Canadian population, Goulet and colleagues developed the MedScore in 2003 to examine the effects of a Mediterranean diet intervention for French-Canadian women [138]. For the purposes of this thesis, the MedScore was used to quantify diet quality. Like other indices, the MedScore is based on the Traditional Healthy Mediterranean Diet Pyramid components [137]. The index assigns adjusted partial scores (0-4 points) for 11 components of the Mediterranean pyramid including: grains, fruits, vegetables, legumes, nuts and seeds, olive oil, dairy products, fish, poultry, eggs, sweets and red meat/processed meat. The total score ranges from 0 to 44 points. A score of 44 would imply that an individual’s food pattern is fully consistent with the traditional Mediterranean diet. More details of the MedScore calculation are provided in Table 4.
<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole grain products&lt;sup&gt;1&lt;/sup&gt;</td>
<td>&lt; 1 portion/day</td>
<td>1-2 portions/day</td>
<td>3-4 portions/day</td>
<td>5-6 portions/day</td>
<td>≥ 7 portions/day</td>
</tr>
<tr>
<td>Vegetable consumption&lt;sup&gt;2&lt;/sup&gt;</td>
<td>&lt; 1 portion/day</td>
<td>1 portion/day</td>
<td>2 portions/day</td>
<td>3 portions/day</td>
<td>≥ 4 portions/day</td>
</tr>
<tr>
<td>Fruit consumption&lt;sup&gt;3&lt;/sup&gt;</td>
<td>&lt; 1 portion/day</td>
<td>1 portion/day</td>
<td>2 portions/day</td>
<td>3 portions/day</td>
<td>≥ 4 portions/day</td>
</tr>
<tr>
<td>Legumes, nuts and seed consumption&lt;sup&gt;4&lt;/sup&gt;</td>
<td>&lt; 0.5 portion/day</td>
<td>0.5 portion/day</td>
<td>1 portion/day</td>
<td>2 portions/day</td>
<td>&gt; 2 portions/day</td>
</tr>
<tr>
<td>Olive oil, olives and margarine made of olive oil consumption&lt;sup&gt;5&lt;/sup&gt;</td>
<td>&lt; 1 time/day</td>
<td>1 time/day</td>
<td>2 times/day</td>
<td>3 times/day</td>
<td>≥ 4 times/day</td>
</tr>
<tr>
<td>Milk and dairy products consumption&lt;sup&gt;6&lt;/sup&gt;</td>
<td>&lt; 1 portion/day or &gt; 4 portion/day</td>
<td>4 portions/day</td>
<td>1 portion/day</td>
<td>2-3 portions/day</td>
<td>2-3 portions/day</td>
</tr>
<tr>
<td>Fish and seafood (other than breaded)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Never</td>
<td>&lt;1 portion/week</td>
<td>1 portion/week</td>
<td>2 portions/week</td>
<td>≥ 3 portions/week</td>
</tr>
<tr>
<td>Poultry (other than breaded)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Never</td>
<td>&lt;1 portion/week</td>
<td>1 portion/week or ≥ 4 portion/week</td>
<td>2 portions/week</td>
<td>3 portions/week</td>
</tr>
<tr>
<td>Eggs</td>
<td>≥ 7/week</td>
<td>5-6/week</td>
<td>0-4/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweets&lt;sup&gt;8&lt;/sup&gt;</td>
<td>≥ 7 times/week</td>
<td>5-6 times/week</td>
<td>3-4 times/week</td>
<td>1-2 times/week</td>
<td>&lt; 1/week</td>
</tr>
<tr>
<td>Red meat/processed meat&lt;sup&gt;7&lt;/sup&gt;</td>
<td>≥ 7 portions/week</td>
<td>5-6 portions/week</td>
<td>3-4 portions/week</td>
<td>1-2 portions/week</td>
<td>&lt; 1 portions/week</td>
</tr>
</tbody>
</table>
1 For grain products, 1 portion = 1 slice of bread, half a cup of pasta, rice or couscous, 30 g of cereals. Maximum of 1 point for refined grain products.

2 For vegetables, 1 portion = half a cup or one medium vegetable. Maximum of 1 point for total number of vegetable juice portions.

3 For fruit, 1 portion = half a cup or 1 medium fruit. Maximum of 1 point for total number of fruit juice portions.

4 For legumes, nuts and seeds, 1 portion = half a cup of legumes, quarter of a cup of nuts/seeds or 100 g of tofu.

5 For olive oil, 1 point was given for each using of the oil. Maximum of 1 point for canola oil or margarine made with this oil.

6 For milk and dairy products, 1 portion = 1 cup of milk or enrich soy beverages, 50 g of cheese or 175 g of yoghurt.

7 For meat/processed meat, poultry, or fish, 1 portion = 50 to 100 g.

8 For sweets, 1 portion = 1 regular chocolate bar, 1/12 of cake or 1/6 of pie.

Table taken from Goulet, et al. (2003) (Permission found in Appendix A)
2.5.4.3.3 Limitations of dietary indices

In response to increased attention on the assessment of diet quality, numerous indices have been developed over the last two decades. However, with such a variety of indices, it can become difficult to make comparisons across studies. As mentioned above, indices can be derived from a variety of predefined nutritional recommendations (i.e., national guidelines vs Mediterranean pattern)[129]. Furthermore, indices differ in the selection of components. In general, indices consist of only nutrients, only food groups or a combination of both [129]. For instance, the C-HEI uses both nutrients and food groups for component scores, while the MedScore utilizes food groups alone.

Cut-off values and scoring methodology differ among indices as well [139]. While some indices assign a score based off a single a cut-off value, others like the C-HEI and MedScore assign proportional scores based on the degree of compliance to a particular dietary recommendation. It is likely that specific nutrients or foods do not contribute equally to health. While some indices attempt to address this issue by assigning adjusted proportional scores, these scores are arbitrarily decided and still may not be the most accurate [139]. Clearly, diet quality is a complex concept, and capturing the essence of one’s diet quality in a composite measure can be difficult and at times arbitrary. Further research is needed to identify optimal cut-off scores and components for the sufficient quantification of diet quality. Finally, as with other research indices, the measurement instrument is only as good as the information provided. Thus, like all nutritional assessment instruments, diet quality indices can potentially suffer in their ability to adequately assess diet if a participant is a poor self-reporter. Despite these limitations, diet quality indices have proved to be valuable tools for the assessment of diet quality. Since the development of these indices, numerous studies have been able to successfully identify relationships between diet quality and various anthropometric and cardiometabolic health outcomes [25].
2.5.5 Summary

It is unknown whether individual variability for a given trait in response to exercise truly exists. Prior trials investigating interindividual variability have almost exclusively performed analysis without incorporation of a control group, and consequently have not accounted for the random variability over time for the given trait under study. Absent from the literature is a study that adequately quantifies interindividual variability in response to exercise for any trait. A study that addresses the design and analytical flaws of prior trials will help clarify the notion of interindividual variability in response to exercise.

Both, WC and BW are significant predictors of morbidity and mortality and thus, represent traits of considerable clinical interest [18, 40]. In fact, no investigation has examined whether interindividual variability in response to exercise exists for WC change and, hence remains a significant gap in knowledge.

Correspondingly, potential determinants of individual variability in WC and BW deserve further investigation, assuming ‘true’ variability due to exercise exists. Indeed, it is plausible that differences in incidental PA, EI or diet quality could help explain variability in WC, beyond that of sex and initial baseline values. With the link between diet quality and WC recently highlighted, diet quality represents a novel concept that has yet to be investigated as a potential determinant of individual variability in response to exercise for any trait. An understanding of the factors that could alter one’s response to exercise could allow for the development of a more thoughtful and effective personalized approach when recommending lifestyle-based strategies for the management of abdominal obesity in a clinical setting.
Chapter 3

Exploration of interindividual variability for change in waist circumference and body weight in response to standardized exercise

3.1 Abstract

BACKGROUND: Substantial interindividual variability in response to a standard dose of exercise exists independent of the trait under investigation. Whether interindividual variability attributed to exercise exists after accounting for random variability is unknown.

OBJECTIVE: To determine the magnitude of the interindividual variability in response to exercise for waist circumference (WC) and body weight (BW) after accounting for random variability and, the extent to which the variability is explained by lifestyle behaviors.

METHODS: Participants were 181 (61% female) sedentary, abdominally obese adults (mean, (SD); 53, (7.5) years) who completed a 24-week intervention. Participants were randomly assigned to: control (n=44) or 5 weekly sessions of low amount, low intensity (LALI) (180 and 300kcal/session for women and men respectively at 50% VO2peak, n=46); high amount, low intensity (HALI) (360 and 600kcal/session for women and men respectively at 50% VO2peak, n=53); or high amount, high intensity (HAHI) (360 and 600kcal/session for women and men respectively at 75% VO2peak, n=38). Adherence was ≥ 80% in all exercise groups. Physical activity (PA) performed outside of the prescribed exercise was measured by accelerometer. Daily self-report diet records were used to derive EI (kcal) and diet quality (Canadian-Healthy Eating Index-2010, Mediterranean Score). The variability in response to exercise (SDR) was determined by separating the random variability from the intervention variability by comparing standard deviations (SD) from both the control and intervention groups.

RESULTS: WC and BW were substantially reduced at 24 weeks in all exercise groups compared to control (P<0.01). The variability due to exercise (SDR) for change in WC was 3.1, -0.3 and 3.1 cm for
LALI, HALI and HAHI groups respectively. Corresponding values for BW were 3.8, 2.0 and 3.5 kg for LALI, HALI and HAHI respectively. No dietary or PA variable was identified as a determinant of the interindividual variability in response to exercise for WC or BW (p>0.05).

**CONCLUSION:** A substantial interindividual variability in response to exercise was observed for change in WC and BW after accounting for the random variability. The determinants of the heterogeneity in response to exercise remain to be determined.
3.2 Introduction

It is well established that individuals exhibit a wide range of response to standardized exercise regardless of the trait examined. Bouchard and colleagues were among the first to demonstrate that for a given dose of exercise, the magnitude of response appears to vary, where some individuals appear to experience substantial improvements in a trait, while others do not [9, 10, 26, 27]. Research to date has focused on the variability of CRF response to exercise [9, 11-13], while measures of body composition such as WC and BW have received less attention. In fact, to our knowledge no study has examined individual variability for WC response to exercise in adults, and few have investigated the response for change in BW [14-16]. Despite a growing body of evidence, in recent years the veracity of the approach to measuring interindividual variability in response to exercise has been questioned [21-24]. Prior investigations have incorrectly assumed that the variability in response for a given trait is solely a consequence of exercise thereby ignoring the individual variability derived from numerous sources including the random variability from both day-to-day biological fluctuations and measurement error. Critics assert that consideration of the control group variability is necessary to adequately quantify interindividual variability in response to exercise [21-23]. Without exception, prior trials investigating individual response have ignored the variability observed within the control group, and consequently have not accounted for the contribution of random variability over time for the given trait under study.

Assuming ‘true’ variability due to exercise exists, the exploration of determinants could help elucidate why some individuals respond to a greater or lesser extent compared to another. It is possible that changes in behaviour outside of the intervention, including dietary consumption or incidental physical activity, may explain some of the variability for the change in anthropometric measures of obesity in response to exercise. An understanding of the variability in individual response for body composition measures, and what may explain it, is important for the development of a more personalized approach for the management of obesity when using lifestyle-based strategies.
Accordingly, the objective of this study was twofold. First, to determine the existence of interindvidual variability for change in WC and BW in response to standardized exercise and second, to identify potential determinants of interindvidual variability for change in WC and BW in response to standardized exercise. Our findings will provide clarification into the existence of interindvidual variability in response to exercise, and will provide insight into potential determinants of the variability for WC and BW response to exercise.

3.3 Methods

Setting and Participants

Details of the trial design and methods [140] and the primary findings have been published elsewhere [4]. Briefly, we conducted a 24-week, single-center, RCT with a parallel group design between September 1, 2009 to May 31, 2013. The primary objective of the original investigation was to determine the separate effects of exercise amount and intensity on WC and glucose tolerance among sedentary, abdominally obese men and women (n=300). 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, or if they were diabetic. All participants provided informed consent before participation. This study was approved by the Queen’s University Health Sciences Research Ethics Board (Appendix B). The manual of operating procedures is shown in Appendix C.

The objective of this secondary analysis was to determine the existence of interindvidual variability in WC and BW reduction in response to standardized exercise and to identify potential determinants of the individual variability in response to exercise. Of the participants originally randomized (n=300), participants were excluded from this study if they did not complete the 24-week trial (n=83), did not have both WC and BW measurements at week 24 (n=2), had an exercise adherence
(number of exercise sessions attended) of less than 80% (n=26) and did not have any dietary intake data (n=8). This resulted in a final sample of 181 participants.

**Exercise intervention**

Participants in this study were initially randomized to one of four groups: (1) no-exercise control (n=44); low amount/low intensity (LALI; n=46) (180 and 300 kcal/session for women and men, respectively, at 50% of VO\(_2\)peak), high amount/low intensity (HALI; n=53) (360 and 600 kcal/session for women and men, respectively, at 50% of VO\(_2\)peak); and high amount/ high intensity (HAHI; n=38) (360 and 600 kcal/session for women and men, respectively, at 75% of VO\(_2\)peak). All participants preformed primarily walking or jogging exercise on a treadmill for the time required to achieve the desired energy expenditure (kcal per session) 5 times per week at the required intensity (relative to CRF [V0\(_2\)peak]) for 24 weeks [4]. Using heart rate and oxygen consumption data obtained from the baseline exercise test, the heart rate corresponding to 50% of maximum oxygen consumption (LALI and HALI), and approximately 75% (HAHI) was assigned for each participant. At these exercise intensities, the energy expenditure targets (exercise amount) for women and men were 180 and 300 kcals, respectively for LALI, and 360 and 600 kcals respectively for both HALI and HAHI. Follow-up V0\(_2\)peak exercise tests were conducted at weeks 4, 8 and 16 to verify the heart rate-V0\(_2\) relationship. Continual adjustment of the heart-rate V0\(_2\) relationship accounted for improvement in CRF which adjusts the time required to achieve the prescribed energy expenditure. Heart rate was continuously monitored at every session to ensure adherence to prescribed exercise intensity. All exercise sessions were supervised by trained personnel and all exercise participants were asked not to engage in any structured exercise outside of the supervised sessions.

**Accelerometry**

PA performed outside of the prescribed exercise regimen was monitored using ActiGraph GT3X accelerometers for 7-day periods at approximately weeks 0, 8, 16 and 25. Participants were required to
wear the accelerometer for at least 4 days, 10 hours/day each monitoring period. Established accelerometer cut points were used to classify and estimate average duration of incidental physical activity (>100 counts per minute) [81].

**Dietary Regimen**

During a 1-week run-in period, all participants were instructed to maintain their BW and record their daily consumption of self-selected foods. During the intervention, participants were instructed to maintain the target daily EI derived from the run-in period and were prescribed a balanced diet (approximately 50 to 55% carbohydrate, 15–20% protein and 30% fat).

All participants were asked to complete daily self-report diet records for the duration of the intervention as a strategy to help ensure compliance with the dietary regimen [2, 3, 141]. The prescribed target EI was revisited and adjusted if need be if a participant’s BW change deviated from the predicted BW loss induced from the intervention arm by more than 1 kg. All dietary procedures were conducted and supervised by the intervention nutritionist.

**Selection of diet records**

Three-day diet records (two weekdays and one weekend day) were randomly selected from the run-in period (baseline), and weeks during the intervention that corresponded to the weeks wherein accelerometry data were obtained (week 8, 16, and 25) (Appendix D). In cases where 3-day diet records were unavailable at these time points, the next closest 7-day period was used. When diet records were not complete for criterion weekdays and weekend day, available data (ie. 2 weekdays) was analyzed at baseline (n=15), week 8 (n=1), week 16 (n=4) and week 24 (n=8).

**Dietary intake analysis**

The selected diet records for each participant were entered into a newly developed web-based automated 24-h recall platform (R24W). Details of the R24W development [102] and validation [103]
have been published elsewhere. Briefly, the R24W was initially developed for the French-Canadian population and was inspired by the Automated-Multiple Pass Method (AMPM) of the US Department of Agriculture (USDA)[101]. Portion sizes are represented by up to 8 pictures, with the option to select multiplicative or a fraction of each portion selected. The R24W allows for automatic coding of nutrient intakes and diet quality scores using the 2010 Canadian Nutrient File [104] or the USDA Nutrient Database for Standard Reference [105] for the few items that are unavailable in the Canadian Nutrient File. Example images from the R24W platform are displayed in Appendix E.

EI, macronutrient and diet quality scores (Canadian Healthy Eating Index [C-HEI] and Mediterranean Score [MedScore]) were averaged from the 3-day diet records. The C-HEI is an adaption of the 2005 American HEI [131] for Canada’s dietary recommendations. Briefly, the C-HEI consists of 8 adequacy (total vegetables and fruit, whole fruit, dark green and orange vegetables, total grain products, whole grains, milk and alternatives, meat and alternatives) and 3 moderation (saturated fats, sodium, other food) components. The 11 individual components are summed to produce a single score between 0 and 100, with higher scores indicating greater adherence to Canada’s Food Guide [142]. The definition and calculation of the C-HEI score is presented in Chapter 2, Table 3.

The MedScore is based on the Traditional Healthy Mediterranean Diet Pyramid [137] components and is described by Goulet and colleagues [138] elsewhere. The MedScore assigns adjusted partial scores (0-4 points) for 11 components of the Mediterranean pyramid including: grains, fruits, vegetables, legumes, nuts and seeds, olive oil, dairy products, fish, poultry, eggs, sweets and red meat/processed meat. The total score ranges from 0 to 44 points. A score of 44 would imply that an individual’s food pattern is fully consistent with the traditional Mediterranean diet. More details of the MedScore calculation are provided in Chapter 2, Table 4.

**Quality of reporting**

To determine the quality of reporting, all diet records were evaluated and characterized as follows: excellent (quantities and descriptions for all items are complete, no apparent missing data), good
(quantities and descriptions are generally complete, <5% of data missing), fair (quantities and
descriptions are fairly complete, <10% of data missing) or poor (majority of quantities and descriptions
are incomplete, >10% of data missing). Examples of diet records with varying quality of reporting scores
are displayed in Appendix F.

Cardiorespiratory Fitness

Cardiorespiratory fitness was assessed using standard open-circuit spirometry techniques
(SensorMedics) during a graded exercise test in which participants walked on a treadmill at a self-selected
speed at zero elevation for 3 minutes, after which the incline was increased by 5% for 2 minutes, then by
2% every subsequent 2 minutes until volitional fatigue [4].

Anthropometry

WC was measured at the superior edge of the iliac crest at baseline, 8, 16 and 24 weeks for all
participants in an exercise group, and at baseline, 16 and 24 for participants in the control group. BW was
measured using a calibrated scale.

Statistical analysis

A 1-way analysis of variance was performed to compare variables between groups at baseline. A
chi-square test was performed to compare the sex distribution between groups. To examine between-
group differences for change in anthropometric, dietary and PA variables, a linear mixed model for
repeated measures over time was applied. The mixed model procedure included intervention group, time
and their 2-factor interactions; sex and its interaction with time; and age as a covariate. The mixed model
was extended to include the 2-way interaction of sex by group and 3-way interactions of sex by group by
time to verify that the effect of treatment did not vary by sex. An unstructured covariance matrix was
imposed for the mixed model. Change in WC and BW between baseline and 16 and 24 weeks were
estimated and compared by using contrasts constructed from the 2-way interaction of group by time
within the mixed model. Change in dietary and PA variables between baseline, 8, 16 and 24 weeks were estimated and compared by using contrasts constructed from the 2-way interaction of group by time within the mixed model.

To quantify interindividual variability in response to exercise, the variation due to random variability was separated from the variation due to the intervention alone by using the following equation described by Atkinson and Batterham [23]: \( SD_R = \sqrt{SD_I^2 - SD_C^2} \). In this equation, \( SD_R \) represents the standard deviation (SD) of the interindividual variation in response due to treatment after adjustment for random variability, \( SD_I \) and \( SD_C \) represent the standard deviations of the change in the intervention and control \( SD_C \) group respectively.

If the \( SD_R \) value was greater than or equal to the pre-determined MCID, then further exploration of potential determinants was performed. A MCID of 2 cm for WC and 2 kg for weight was selected based on evidence of the association between differences in WC and BW with cardiometabolic risk factors and mortality [40].

A linear mixed model procedure was used to identify potential determinants of interindividual variability for change in WC and BW. The model used restricted maximum likelihood estimation. The intervention groups and control group were entered as both a fixed and random effect. As a random effect, they were coded as dummy variables and entered to allow for the extra variance in the exercise groups to be isolated from the reference group (control). Baseline value, sex, change in EI, diet quality scores, change in PA, and an interaction term between each effect and group were added to the model separately to identify potential determinants of individual variability in response to exercise. If the variable accounted for some of the variability in response to exercise then the extra variance for that exercise group, beyond that in the control, would be attenuated. To increase statistical power, the same analysis was performed collapsed across exercise groups. **Appendix G** displays an annotated output.

For exploratory purposes, we broadened our approach and also performed simple and stepwise multiple regression to determine whether any of the same variables, with the addition of total energy
expenditure, influenced the variability due to an exercise intervention in general for WC and BW, regardless of the random variability.

A one-way analysis of variance was performed to determine whether change in WC or BW differed between groups with various diet record compliance (amount of completed diet records). Participants were classified into three groups: excellent compliance (3-day diet records were complete for baseline, week 8, 16 and 24) (n=97), good compliance (3-day diet records were complete for 3 of the 4 time periods) (n=29), poor compliance (3-day diet records only complete for 1 or 2 of the 4 time periods)(n=11). An independent samples t-test was performed to determine whether change in WC or BW differed between groups with high or low diet quality reporting. Participants were classified into two groups: high (good or excellent scores)(n=98) or low quality reporting scores (acceptable or poor scores)(n=39). Quality of reporting scores were described in detail above.

A 2-sided α of 0.05 was used to determine statistical significance, and no adjustment was made for multiple comparisons. All analyses were performed using SAS, version 9.4 (SAS Institute) and SPSS software, version 24.0 (SPSS Inc).

### 3.4 Results

Participant characteristics are summarized in Table 1. With the exception of MedScore, there were no significant between group differences for any baseline characteristic (p>0.05).

Table 2 and Table 3 show the separate effects of exercise amount and intensity on change in anthropometric, diet and PA variables at 24 weeks. Reductions in WC were greater in the LALI (adjusted mean difference, -4.7 cm, [CI, -6.4 to -3.0]), HALI (-5.3cm, [-7.0 to -3.6]), and HAHI (-5.6cm, [-7.6 to -4.0]) groups compared to control (P<0.05), but did not differ from each other (P>0.05). Reductions in BW were greater in the LALI (adjusted mean difference, -4.0 kg, [CI, -5.7 to -2.3]), HALI (-5.1 kg [-6.7 to -3.4]), and HAHI (-5.2 kg [-7.0 to -3.4]) groups compared to control (P<0.05), but were not different from each other (P>0.05). Change in C-HEI was greater for the LALI (7.2 [0.1 to 14.0]) group compared to the control (P<0.05) Change in EI and MedScore did not differ between groups at 24 weeks (P>0.05). With
the exception of HALI (3.1 [0.2 to 5.9]), the change in amount of PA (% of day) performed outside of the 
exercise prescribed was not significant compared to control (p>0.05).

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=181)</th>
<th>Control (n=44)</th>
<th>LALI (n=46)</th>
<th>HALI (n=53)</th>
<th>HAHI (n=38)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>52.7 (7.5)</td>
<td>52.0 (7.7)</td>
<td>53.4 (7.1)</td>
<td>1.1 (50.5)</td>
<td>52.8 (7.4)</td>
<td>0.84</td>
</tr>
<tr>
<td>Sex ratio (F:M)</td>
<td>111:70</td>
<td>27:17</td>
<td>28:18</td>
<td>33:20</td>
<td>23:15</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Anthropometric</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC (cm)</td>
<td>110.2 (11.3)</td>
<td>109.3 (10.6)</td>
<td>109.9 (11.2)</td>
<td>110.3 (11.9)</td>
<td>111.8 (11.9)</td>
<td>0.79</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>94.9 (16.6)</td>
<td>95.0 (17.2)</td>
<td>92.8 (14.0)</td>
<td>95.1 (19.2)</td>
<td>97.2 (15.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>33.1 (4.5)</td>
<td>33.1 (4.7)</td>
<td>33.0 (4.1)</td>
<td>33.2 (5.2)</td>
<td>32.9 (3.7)</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Dietary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EI* (kcal/day)</td>
<td>2053.9 (511.6)</td>
<td>2116.8 (461.2)</td>
<td>2054.2 (462.9)</td>
<td>1996.2 (491.6)</td>
<td>2053.7 (664.8)</td>
<td>0.75</td>
</tr>
<tr>
<td>C-HEI*</td>
<td>57.6 (13.7)</td>
<td>57.5 (13.6)</td>
<td>56.9 (12.7)</td>
<td>14.1 (2.1)</td>
<td>53.5 (13.5)</td>
<td>0.12</td>
</tr>
<tr>
<td>MedScore*</td>
<td>16.4 (4.8)</td>
<td>17.1 (5.1)</td>
<td>17.0 (4.3)</td>
<td>16.7 (4.1)</td>
<td>14.2 (5.4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>79.7 (24.6)</td>
<td>82.7 (23.4)</td>
<td>82.9 (28.2)</td>
<td>75.5 (20.2)</td>
<td>77.5 (27.3)</td>
<td>0.41</td>
</tr>
<tr>
<td>(%)</td>
<td>34.9 (5.6)</td>
<td>35.1 (5.9)</td>
<td>36.1 (6.8)</td>
<td>34.1 (4.1)</td>
<td>34.2 (5.5)</td>
<td>0.36</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>239.6 (69.6)</td>
<td>248.3 (61.0)</td>
<td>229.8 (60.4)</td>
<td>240.4 (70.7)</td>
<td>239.2 (89.8)</td>
<td>0.70</td>
</tr>
<tr>
<td>(%)</td>
<td>44.9 (6.4)</td>
<td>45.4 (6.6)</td>
<td>43.1 (6.7)</td>
<td>46.2 (5.5)</td>
<td>44.6 (6.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>85.7 (22.1)</td>
<td>87.5 (20.7)</td>
<td>85.0 (20.8)</td>
<td>84.8 (22.5)</td>
<td>85.8 (25.7)</td>
<td>0.94</td>
</tr>
<tr>
<td>(%)</td>
<td>16.9 (3.0)</td>
<td>16.7 (2.8)</td>
<td>16.8 (3.2)</td>
<td>17.2 (2.9)</td>
<td>17.1 (3.2)</td>
<td>0.90</td>
</tr>
<tr>
<td>DR quality score</td>
<td>2.4 (0.7)</td>
<td>2.3 (0.7)</td>
<td>2.6 (0.5)</td>
<td>2.3 (0.7)</td>
<td>2.2 (0.9)</td>
<td>0.13</td>
</tr>
<tr>
<td>CRF§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(L/min)</td>
<td>2.7 (0.7)</td>
<td>2.8 (0.8)</td>
<td>2.6 (0.6)</td>
<td>2.7 (0.7)</td>
<td>2.8 (0.7)</td>
<td>0.64</td>
</tr>
<tr>
<td>(mL/kg/min)</td>
<td>28.8 (5.3)</td>
<td>29.5 (5.8)</td>
<td>28.3 (5.4)</td>
<td>28.9 (5.0)</td>
<td>28.5 (5.0)</td>
<td>0.71</td>
</tr>
<tr>
<td>PA†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(min/day)</td>
<td>298.3 (80.9)</td>
<td>308.0 (86.9)</td>
<td>301.6 (78.1)</td>
<td>295.8 (72.2)</td>
<td>285.8 (89.8)</td>
<td>0.68</td>
</tr>
<tr>
<td>(% of day)</td>
<td>32.3 (7.8)</td>
<td>33.4 (8.4)</td>
<td>32.3 (8.1)</td>
<td>31.9 (7.0)</td>
<td>31.3 (7.6)</td>
<td>0.66</td>
</tr>
</tbody>
</table>

Values are presented as means (SD) unless otherwise indicated. Sample size are shown unless otherwise indicated. M = male; F = female; WC = waist circumference; BW = body weight; BMI = body mass index; EI = energy intake; C-HEI = Canadian – Healthy Eating Index; MedScore = Mediterranean diet score; DR = diet record; CRF = cardiorespiratory fitness; PA = total physical activity performed outside of the exercise regimen; LALI = low amount, low intensity exercise; HALI = high amount, low intensity exercise; HAHI = high amount, high intensity exercise.
* Control (n = 42), LALI (n = 40), HALI (n = 46), HAHI (n = 30)

§ Control (n = 44), LALI (n = 46), HALI (n = 53), HAHI (n = 38)

† Control (n = 41), LALI (n = 44), HALI (n = 47), HAHI (n = 34)
Table 2. Differences between exercise groups and control for change in anthropometric, dietary and PA 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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value (CI)</td>
<td>P value</td>
<td>Value (CI)</td>
</tr>
<tr>
<td><strong>Anthropometric</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC (cm)</td>
<td>-4.7 (-6.4 to -3.0)</td>
<td>&lt;.0001*</td>
<td>-5.3 (-7.0 to -3.6)</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>-4.0 (-5.7 to -2.3)</td>
<td>&lt;.0001*</td>
<td>-5.1 (-6.7 to -3.4)</td>
</tr>
<tr>
<td><strong>Dietary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EI (kcal)</td>
<td>-44.6 (-273.7 to 184.5)</td>
<td>0.702</td>
<td>148.3 (-73.6 to 370.3)</td>
</tr>
<tr>
<td>C-HEI</td>
<td>7.2 (0.1 to 14.3)</td>
<td>0.048*</td>
<td>-1.4 (-8.3 to 5.4)</td>
</tr>
<tr>
<td>MedScore</td>
<td>2.3 (-0.3 to 4.8)</td>
<td>0.088</td>
<td>1.4 (-1.1 to 3.9)</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of day</td>
<td>2.2 (-0.8 to 5.1)</td>
<td>0.148</td>
<td>3.1 (0.2 to 5.9)</td>
</tr>
</tbody>
</table>

Values are presented as least-squares estimated means (95% CIs) adjusted for age and sex.

* indicates significant difference between groups at p<0.05.

WC = waist circumference; BW = body weight; C-HEI = Canadian – Healthy Eating Index; MedScore = Mediterranean Score;

Physical activity = total physical activity performed outside of the exercise regimen; LALI = low amount, low intensity exercise;

HALI = high amount, low intensity exercise; HAHI = high amount, high intensity exercise.
Table 3. Differences between exercise groups for change in anthropometric, dietary and PA variables at 24 weeks

<table>
<thead>
<tr>
<th>Variable</th>
<th>HALI vs LALI</th>
<th>HAHI vs LALI</th>
<th>HAHI vs HALI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value (CI)</td>
<td>P value</td>
<td>Value (CI)</td>
</tr>
<tr>
<td><strong>Anthropometric</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC (cm)</td>
<td>-0.6 (-2.3 to 1.1)</td>
<td>0.467</td>
<td>-1.1 (-2.9 to 0.7)</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>-1.1 (-2.7 to 0.5)</td>
<td>0.186</td>
<td>-1.3 (-3.0 to 0.5)</td>
</tr>
<tr>
<td><strong>Dietary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EI (kcal)</td>
<td>192.9 (-26.6 to 412.4)</td>
<td>0.085</td>
<td>88.2 (-161.0 to 337.3)</td>
</tr>
<tr>
<td>C-HEI</td>
<td>-8.6 (-15.4 to -1.8)</td>
<td>0.013*</td>
<td>-5.1 (-12.8 to 2.7)</td>
</tr>
<tr>
<td>MedScore</td>
<td>-0.9 (-3.3 to 1.6)</td>
<td>0.498</td>
<td>0.3 (-2.5 to 3.1)</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of day</td>
<td>0.9 (-1.8 to 3.6)</td>
<td>0.513</td>
<td>0.6 (-2.4 to 3.6)</td>
</tr>
</tbody>
</table>

Values are presented as least-squares estimated means (95% CIs) adjusted for age and sex.

* indicates significant difference between groups at p<0.05.

WC = waist circumference; BW = body weight; C-HEI = Canadian – Healthy Eating Index; MedScore = Mediterranean Score;

Physical activity = total physical activity performed outside of the exercise regimen; LALI = low amount, low intensity exercise;

HALI = high amount, low intensity exercise; HAHI = high amount, high intensity exercise.
**Figure 1** and **Figure 2** illustrate the individual change values for WC and BW at 24 weeks. For change in WC at 24 weeks, the SD$_R$ values were 3.1, -0.3 and 3.1 cm for LALI, HALI and HAHI respectively. For change in BW at 24 weeks, the SD$_R$ values were 3.8, 2.0 and 3.5 kg for LALI, HALI and HAHI respectively.

**Table 4** and **Table 5** show the results of the analysis performed to identify the determinants of interindividual variability for change in WC and BW. No dietary or PA variable accounted for interindividual variability for change in WC or BW for any exercise group (p>0.05). Baseline values accounted for approximately 19% and 16% of the interindividual variability for both change in WC and BW, respectively, in response to exercise for LALI alone (p<0.05). Sex accounted for about 13% of the interindividual variability for WC within the LALI group only (p<0.05). Sex did not account for interindividual variability in any group for change in BW (p>0.05).

We further examined the contribution of potential determinants of interindividual variability for change in WC and BW in response to exercise collapsed across groups (**Table 6**). No dietary or PA variable accounted for interindividual variability for change in WC or BW in response to exercise (p>0.05). Sex accounted for about 13% of the interindividual variability for the change in WC (p<0.05) and approached significance for change in BW (p=0.06). Baseline values did not account for the variability in WC (p>0.05), but approached significance for change in BW (p=0.06).
Figure 1. Change in WC at 24 weeks for each participant per group

Bars represent change in WC (cm) for each participant. WC = waist circumference; SD<sub>R</sub> = standard deviation (SD) of the interindividual variation in response due to treatment after accounting for random error, a (−) SD<sub>R</sub> value indicates the random variability was greater than the variability due to treatment; LALI = low amount, low intensity exercise; HALI = high amount, low intensity exercise; HAHI = high amount, high intensity exercise
Figure 2. Change in BW at 24 weeks for each participant per group

Bars represent change in BW (kg) for each participant. BW = body weight; SD_{R} = standard deviation (SD) of the interindividual variation in response due to treatment after accounting for random error; LALI = low amount, low intensity exercise; HALI = high amount, low intensity exercise; HAHI = high amount, high intensity exercise
Table 4. Potential determinants of interindividual variability for change in WC in response to exercise

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>LALI</th>
<th>HALI</th>
<th>HAHI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>Mean (CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Baseline WC</td>
<td>44</td>
<td>46</td>
<td>-0.158 (-0.32 to 0.00)</td>
<td>0.05*</td>
</tr>
<tr>
<td>Sex</td>
<td>44</td>
<td>46</td>
<td>3.883 (0.29 to 7.47)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Change in EI†</td>
<td>35</td>
<td>37</td>
<td>-0.016 (-0.06 to 0.03)</td>
<td>0.47</td>
</tr>
<tr>
<td>C-HEI</td>
<td>40</td>
<td>46</td>
<td>-0.066 (-0.23 to 0.10)</td>
<td>0.43</td>
</tr>
<tr>
<td>MedScore</td>
<td>40</td>
<td>46</td>
<td>-0.215 (-0.70 to 0.27)</td>
<td>0.39</td>
</tr>
<tr>
<td>Change in PA</td>
<td>31</td>
<td>37</td>
<td>-0.150 (-0.45 to 0.15)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Values are presented as estimated means (CIs). All estimated means represent the average change in WC (cm) per 1 unit increase in the corresponding variable compared to the control group, unless otherwise noted. WC = waist circumference; SD<sub>r</sub> = the standard deviation (SD) of the interindividual variation in response to treatment after adjustment for random error (control); SD<sub>r</sub> = SD<sub>r</sub> value before accounting for potential determinants (used as a reference); SD<sub>r</sub> group = SD<sub>r</sub> value after accounting for a potential determinant; WC = waist circumference (cm); EI = energy intake (kcal); C-HEI= Canadian-Healthy Eating Index, MedScore = Mediterranean Score, PA = total physical activity performed outside of exercise regimen (% of day).

¶ All variables represent interaction terms (Group x variable)

* indicates variable predicts change in WC differently from change in reference group at p ≤ 0.05

† estimated means represent the average change in WC (cm) per 10 unit increase in the corresponding variable compared to the control group.
Table 5. Potential determinants of interindividual variability for change in BW in response to exercise.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>LALI</th>
<th>HALI</th>
<th>HAHI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>Mean (CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Baseline BW</td>
<td>44</td>
<td>46</td>
<td>-0.145 (-0.26 to -0.03)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Sex</td>
<td>44</td>
<td>46</td>
<td>3.000 (-0.54 to 6.54)</td>
<td>0.10</td>
</tr>
<tr>
<td>Change in EI</td>
<td>35</td>
<td>37</td>
<td>-0.031 (-0.08 to 0.01)</td>
<td>0.17</td>
</tr>
<tr>
<td>C-HEI</td>
<td>40</td>
<td>46</td>
<td>-0.134 (-0.30 to 0.03)</td>
<td>0.11</td>
</tr>
<tr>
<td>MedScore</td>
<td>40</td>
<td>46</td>
<td>-0.258 (-0.74 to 0.22)</td>
<td>0.29</td>
</tr>
<tr>
<td>Change in PA</td>
<td>31</td>
<td>37</td>
<td>-0.220 (-0.52 to 0.08)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Values are presented as estimated means (CIs). All estimated means represent the average change in WC (cm) per 1 unit increase in the corresponding variable compared to the control group, unless otherwise noted. BW = body weight; SD<sub>R</sub> = standard deviation (SD) of the interindividual variation in response to treatment after adjustment for random error (control), SD<sub>R</sub> = SD<sub>R</sub> value before accounting for potential determinants (used as a reference); SD<sub>R</sub> group = SD<sub>R</sub> value after accounting for a potential determinant; EI = energy intake (kcal); C-HEI= Canadian-Healthy Eating Index, MedScore = Mediterranean Score, PA = total physical activity performed outside of exercise regimen (% of day).

¶ All variables represent interaction terms (Group x variable)

* indicates variable predicts change in weight differently from change in reference group at p≤0.05

† estimated means represent the average change in weight (kg) per 10 unit increase in the corresponding variable compared to the control group.


<table>
<thead>
<tr>
<th>Variable‡</th>
<th>Control</th>
<th>WC§</th>
<th>BW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>Mean (CI)</td>
</tr>
<tr>
<td>Baseline value</td>
<td>44</td>
<td>84</td>
<td>-0.12 (-0.3 to 0.0)</td>
</tr>
<tr>
<td>Sex</td>
<td>44</td>
<td>84</td>
<td>3.25 (0.1 to 6.4)</td>
</tr>
<tr>
<td>Change in EI†</td>
<td>35</td>
<td>59</td>
<td>-0.01 (-0.1 to 0.0)</td>
</tr>
<tr>
<td>C-H EI</td>
<td>40</td>
<td>83</td>
<td>0.00 (-0.1 to 0.1)</td>
</tr>
<tr>
<td>MedScore</td>
<td>40</td>
<td>83</td>
<td>-0.05 (-0.4 to 0.3)</td>
</tr>
<tr>
<td>Change in TPA</td>
<td>31</td>
<td>67</td>
<td>-0.14 (-0.4 to 0.2)</td>
</tr>
</tbody>
</table>

Values are presented as estimated means (CIs). All estimated means represent the average change in WC (cm) or weight (kg) per 1 unit increase in the corresponding variable collapsed across all exercise groups compared to the control group, unless otherwise noted. SDg = the standard deviation (SD) of the interindividual variation in response to treatment after adjustment for random error (control); SDg = SDg = SDg value before accounting for potential determinants (used as a reference); SDg group = SDg value after accounting for a potential determinant; EI = energy intake (kcal); C-H EI = Canadian-Healthy Eating Index, MedScore = Mediterranean Score, TPA = total physical activity performed outside of exercise regimen (% of day).

‡ All variables represent interaction terms (Group x variable)

§ all analyses for change in WC were performed collapsed across LALI and HAHI groups only

* indicates variable predicts change in WC (cm) or weight (kg) differently from change in reference group at p≤0.05

† estimated means represent the average change in WC (cm) or weight (kg) per 10 unit increase in the corresponding variable compared to the control group.
For exploratory purposes, we broadened our approach and simply examined whether any of the same variables, with the addition of total energy expenditure, influenced change in WC and BW for the control and exercise groups separately, regardless of the random variability. No variable was associated with change in WC or BW in the control group (p>0.05). Table 7 and Table 8 present the associations between the selected variables and change in WC and BW respectively collapsed across exercise groups. Baseline WC and BW, sex, change in EI, and total energy expenditure (kcal) over the 24 weeks were associated with change in WC and BW (p ≤ 0.05). In stepwise regression, sex and change in EI alone entered in the model for change in WC (r²=0.15, p<0.05). For change in BW, baseline BW, MedScore and total energy expenditure alone entered in the model (r²=0.20, p<0.05). Appendix H, Figure 1 and Appendix H, Figure 2 presents scatterplots for each variable with change in WC and BW respectively collapsed across exercise groups.

To examine whether potential adjustments in EI targets during the early weeks of the trial influenced the relationship between change in EI and change in WC and BW, the relationship between change in EI from week 8 to week 24 and change in WC and BW was assessed (Appendix I, Table 1). The association between change in EI and change in WC was no longer significant (p>0.05), while the association between change in EI and change in BW (r=0.21) remained significant (p<0.05).

Appendix I, Table 2 and Appendix I, Table 3 presents the change WC and BW across groups differing in diet record compliance (amount of diet records completed) and quality of reporting respectively collapsed across groups. Change in WC and BW did not differ between groups with different amounts of compliance (excellent, good or poor) (p>0.05). Change in WC and BW did not differ between groups with high quality reporting (excellent and good scores) and low quality reporting scores (acceptable and poor scores)(p>0.05).
Table 7. Associations between sex, baseline, dietary, PA and energy expenditure variables with change in WC

<table>
<thead>
<tr>
<th>Variable</th>
<th>Simple Regression for Δ WC (cm)</th>
<th>Stepwise Multiple Regression for Δ WC (cm)</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>B</td>
<td>R²</td>
<td>Sig.</td>
</tr>
<tr>
<td>Baseline WC</td>
<td>137</td>
<td>-0.064</td>
<td>0.028</td>
<td>0.052</td>
</tr>
<tr>
<td>Sex</td>
<td>137</td>
<td>2.358</td>
<td>0.067</td>
<td>0.002</td>
</tr>
<tr>
<td>Change in EI</td>
<td>100</td>
<td>-0.003</td>
<td>0.08</td>
<td>0.004</td>
</tr>
<tr>
<td>Change in PA</td>
<td>109</td>
<td>-0.068</td>
<td>0.011</td>
<td>0.279</td>
</tr>
<tr>
<td>C-HEI</td>
<td>135</td>
<td>-0.029</td>
<td>0.005</td>
<td>0.405</td>
</tr>
<tr>
<td>MedScore</td>
<td>135</td>
<td>-0.026</td>
<td>0.001</td>
<td>0.795</td>
</tr>
<tr>
<td>Total energy expenditure</td>
<td>137</td>
<td>-6.60E-05</td>
<td>0.064</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Variables offered for stepwise multiple regression: Baseline waist circumference, Sex, Change in EI, Change in TPA, HEI, C-HEI, Medscore and Total energy expenditure.

*B= unstandardized beta; WC = waist circumference (cm); EI = energy intake; PA = total physical activity performed outside of exercise regimen (% of day); C-HEI = Canadian – Healthy Eating Index; Sex, males=0, females=1; R² = variance explained

*significant associations (p ≤0.05)
### Table 8. Associations between sex, baseline, dietary, PA and energy expenditure variables with change in BW

<table>
<thead>
<tr>
<th>Variable</th>
<th>Simple Regression for ∆ BW (kg)</th>
<th>Stepwise Multiple Regression for ∆ BW (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>B</td>
</tr>
<tr>
<td>Baseline BW</td>
<td>137</td>
<td>-0.071</td>
</tr>
<tr>
<td>Sex</td>
<td>137</td>
<td>2.487</td>
</tr>
<tr>
<td>Change in EI</td>
<td>100</td>
<td>-0.003</td>
</tr>
<tr>
<td>Change in PA</td>
<td>109</td>
<td>-0.121</td>
</tr>
<tr>
<td>C-HEI</td>
<td>135</td>
<td>-0.043</td>
</tr>
<tr>
<td>MedScore</td>
<td>135</td>
<td>-0.09</td>
</tr>
<tr>
<td>Total energy expenditure</td>
<td>137</td>
<td>-7.9x10⁻⁵</td>
</tr>
</tbody>
</table>

Variables offered for stepwise multiple regression: Baseline BW, Sex, Change in EI, Change in TPA, C-HEI, MedScore and Total energy expenditure.

*B* = unstandardized beta; BW = body weight (kg); EI = energy intake; PA = total physical activity performed outside of exercise regimen (% of day); C-HEI = Canadian – Healthy Eating Index; Sex, males=0, females=1; R² = variance explained

*significant associations (p ≤ 0.05)
3.5 Discussion

The primary and novel finding of this study is substantial interindividual variability in response to exercise independent of amount or intensity was observed for change in WC and BW after accounting for the random variability. However, we were unable to demonstrate that any dietary or PA behaviours performed outside of the intervention were determinants of the variability observed in our sample. The current findings underscore the presence of substantial heterogeneity in response to standardized exercise beyond that attributed to random variation, and support the need for further investigation into determinants that may help to explain the individual response to exercise for WC and BW.

To our knowledge, this is the first study to quantify interindividual variability for change in WC and BW in response to standardized exercise after accounting for the random variability of the control group. Since the early observations of Bouchard and colleagues [10, 27], a growing body of evidence has supported the observation that substantial variability exists for numerous traits in response to a standard dose of exercise. [9, 11, 12, 15, 42]. However, without exception, prior studies have assumed the variability was a result of exercise alone. A failure to consider the variability due to day-to-day biological fluctuations and measurement error (random variability) precludes the accurate quantification of interindividual variability for a given trait. To address this, our study applied the approach suggested by Atkinson and Batterham that distinguishes the random variability from the intervention variability by comparing standard deviations (SD) from both the control and intervention groups [23]. By adequately quantifying the magnitude of interindividual variability in response to exercise, our investigation overcomes the limitations of prior trials and extends the observations of years of research on individual variability due to exercise, confirming the notion that each individual responds uniquely to a standardized treatment.
While the $SD_R$ value proposed by Atkinson and Batterham represents a straightforward way to isolate the variability due to treatment from the random variability, this approach is not immune to limitations. The underlying assumption of the $SD_R$ equation is that the random variability present in the control group is similar to that of the intervention group, and thus the remaining variability in the intervention group is attributed to exercise. However, the utility of this equation is questioned in instances wherein the variability in the exercise group is, in fact, homogenized due to treatment or where the control group is contaminated with other sources of variability, beyond that of random variability [143-145]. For instance, the finding that the HALI group had less variability for change in WC than the control group highlights the limitations of the $SD_R$ value as it is unlikely that variability in individual response for WC existed for only two of the three exercise groups. Though this finding remains unexplained, that the HALI group experienced substantial variability in BW and not WC, indicates this observation may, perhaps, be due to chance. While we concede that the $SD_R$ approach is a useful tool to partition some of the random variability from the variability due to treatment, the accurate quantification of interindividual variability due to treatment remains somewhat elusive.

With few exceptions, no determinants were identified for change in WC and BW in any group. However, for a few of the variables, we observed a large effect size despite the confidence intervals (CI) containing the null hypothesis ($P>0.05$) which suggests that our analysis may have been underpowered to detect such differences of differences.

For example, the results for the HAHI group, indicate that a female lost on average ~2.5 kg less than a male in that group relative to control, despite a p-value >0.05. Such a large difference in BW reduction is of clinical importance and should not be dismissed. Furthermore, despite collapsing across groups in an attempt to increase sample size, the results remained unchanged. That we were unable to identify determinants of variability despite our relatively large sample size suggests that much larger samples are needed, which may not be practical. For instance, if we were to investigate whether the effect of treatment differed between sex in a
simple 2 x 2 factorial study, we calculate that it would take approximately 126 individuals per group to detect a moderate effect size of the treatment effect to achieve 80% power at a two-sided $\alpha=0.05$ [146]. A total sample size (n=504) of that magnitude is not pragmatic nor feasible for most research groups. Therefore, we emphasize the need to develop pragmatic solutions, whether in initial study design or statistical approach to elucidate potential determinants of interindividual variability in the future.

Our study has several limitations. While the SD$_R$ approach accounts for random variability, it does not separate the within-subject variability from the interindividual variability due to exercise, and consequently, the response due to exercise is not completely isolated from all other sources of variability. Limitations associated with self-report diet records including self-representation and reactivity bias, may have prevented us from accurately assessing the influence of individual differences in both diet quality and change in EI on WC and BW change. It has been previously reported that self-report can underestimate EI and other macronutrients such as protein as much as 4-37% when compared to recovery biomarker studies [96-98]. Additionally, our sample is limited to sedentary, abdominally obese adult men and women who are primarily Caucasian. Thus, our results may not apply to other populations differing in age and ethnicity.

The principle strengths of this study include rigorously controlled exercise prescriptions with supervised exercise and frequent fitness tests. In addition, PA performed outside of the intervention was measured objectively using accelerometers at multiple times throughout the trial.

In summary, our study supports the existence of substantial interindividual variability in response to exercise for change in WC and BW after accounting for random variability, though we were unable to identify any lifestyle-based factors as determinants of the heterogeneity in response to exercise. These findings underscore the need for the appropriate and pragmatic quantification of individual variability for other health-related traits and support the continued exploration of determinants that may explain the substantial variability in response to exercise.
Chapter 4. General Discussion

4.1 Summary of Key Findings

The primary finding of this study is that substantial interindividual variability in response to exercise independent of amount or intensity was observed for change in WC and BW after accounting for random variability. However, we were unable to identify any differences in dietary or PA behaviours as determinants of the variability observed. To our knowledge, this is the first study to quantify interindividual variability for change in WC and BW in response to standardized exercise after accounting for the random variability of the control group. Furthermore, we are the first to assess the contribution of diet quality, as measured by index scores, on individual exercise response.

Since the initial observations made in the early 1980’s, substantial interindividual variability in response to a standard dose of exercise has been reported for a myriad of traits. [9, 11, 12, 15, 42]. However, prior studies have assumed exercise to be the sole source of the observed heterogeneity of response. A failure to account for other sources of variability due to day-to-day biological fluctuations and measurement error (random variability) precludes the accurate quantification of interindividual variability for a given trait. Correspondingly, to date, no prior study had adequately quantified the interindividual variability in response to exercise beyond that of the random variability. In response, our study applied the statistical approach suggested by Atkinson and Batterham, that distinguishes the random variability from the intervention variability by comparing standard deviations (SD) from both the control and intervention groups [23]. Consequently, our investigation overcomes the limitations of prior studies and extends the literature on variability in exercise response. The current findings highlight the existence of substantial heterogeneity in response to standardized exercise beyond
that attributed to random variation, and support the need for further investigation into determinants that may help to explain the individual response to exercise for WC and BW.

4.2 Key strengths and Limitations

The principle strengths of our study include the rigorous control of exercise prescriptions. We ensured participants performed the prescribed exercise amount and intensity by supervising all exercise sessions and included multiple fitness tests throughout the duration of the trial. In addition, our study included multiple objective measures of PA performed outside of the prescribed exercise regimen using accelerometers. Furthermore, daily dietary intake was assessed throughout the duration of the trial.

Despite the large sample size of this study, the primary limitation of this investigation is that we were likely underpowered to detect the contribution of potential determinants of individual variability in response to exercise. Our study was also limited by using self-report diet records for the derivation of EI and diet quality. The limitations of self-report are well-documented with reports suggesting an underestimation of EI and other macronutrients such as protein as much as 4-37% when compared to recovery biomarker studies.

4.3 Directions for future research

Our findings highlight the need for further investigation into several areas of clinical interest including the need for the appropriate quantification of interindividual variability, the identification of determinants of individual response and the accurate assessment of dietary intake.

Though the results of this study provide novel insight into individual variability in response to exercise for WC and BW, further investigation is necessary to confirm our
observations. Furthermore, the question remains whether ‘true’ variability exists for other traits. As the majority of research has focused on CRF, it would be of great interest to examine whether the observed variability in prior studies exists beyond that of random variability as well.

Additionally, no prior study has teased out the magnitude for which within-subject differences contribute to variability in response. The quantification of within-subject variability requires a repeated cross-over study design. While this type of investigation may not be feasible to carry out on a large scale, small cross-over trials may provide valuable insight in regards to the contribution of within-subject variability and subsequently allow for further isolation of the ‘true’ variability in response to exercise.

The fact that we were likely underpowered to detect potential determinants of individual variability in response to exercise calls for a reconsideration of the approach used to identify determinants of individual variability in response to exercise. While we await an RCT with a large enough sample size to detect determinants of individual response, the development of novel statistical approaches may be required to tease out the contributing factors for the time being.

The identification of lifestyle-based determinants not only requires the appropriate statistical approach and study design, but necessitates the accurate assessment of behaviours performed outside of the intervention. As such, the need for objective measures of dietary intake remains a significant limitation for nutritional research. To date, only a few biomarkers have been identified for specific components of dietary intake and thus more research is needed to develop a comprehensive measurement of dietary intake.

4.4 Contributions to the field

Our study was the first to quantify interindividual variability in response to exercise for any trait after accounting for random variability. Our observations provide initial support for the existence of substantial variability in exercise response for WC and BW and correspondingly
highlight the need for further investigation into whether ‘true’ variability due to exercise exists for other traits as well.

A noteworthy issue that arose during our study was that we were unable to detect any lifestyle-based determinants of individual variability. This observation suggests that the limitations in the current design and/or statistical approach need to be addressed in future studies. While the SD_R approach suggested by Atkinson and Batterham is a straightforward means to isolate the variability due to exercise from the random variability [23], our finding that one of our exercise groups had less variability than the control group suggests that this approach may be limited. This observation alludes to notion that the various sources of variability may be of different magnitudes between groups which challenges the implicit assumptions of the SD_R approach. Thus, we encourage the exploration and development of methods to quantify the different sources of variability in an intervention.

To note, that we were unable to identify any lifestyle-based variable as a determinant of individual response does not discount the importance of such behaviours for good health. In fact, the benefits of a healthful diet have been recently highlighted in large scale RCT and we may not have been powered to detect any contributions of diet to individual response for WC and BW.

4.5 Summary and Conclusions

In summary, our study supports the existence of substantial interindividual variability in response to exercise for change in WC and BW after accounting for random variability, though we were unable to identify any lifestyle-based factors as determinants of the heterogeneity in response to exercise. These findings underscore the need for the appropriate and pragmatic quantification of individual variability for other health-related traits and support the continued exploration of determinants that may explain the substantial variability in response to exercise.
References


Appendix A: Permissions

Chapter 2, Figure 1

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Changes in Weight, Waist Circumference and Compensatory Responses with Different Doses of Exercise among Sedentary, Overweight Postmenopausal Women

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Abstract

Background: It has been suggested that exercise training results in compensatory mechanisms that attenuate weight loss. However, this has only been examined with large doses of exercise. The goal of this analysis was to examine actual weight loss compared to predicted weight loss (compensation) across different doses of exercise in a controlled trial of sedentary, overweight or obese postmenopausal women (n = 411).

Methodology/Principal Findings: Participants were randomized to a non-exercise control (n = 94) or 1 of 3 exercise groups: exercise energy expenditure of 4 (n = 139), 8 (n = 85), or 12 (n = 93) kcal/kg/week (KWW). Training intensity was set at the heart rate associated with 50% of each woman's peak VO2 and the intervention period was 6 months. All exercise was supervised. The main outcomes were actual weight loss, predicted weight loss (exercise energy expenditure/7000 kcal per kg), compensation (actual minus predicted weight loss) and waist circumference. The study sample had a mean (SD) age 57.2 (6.3) years, BMI of 31.7 (3.8) kg/m², and was 63.5% Caucasian. The adherence to the intervention was >99% in all exercise groups. The mean (95% CI) weight loss in the 4, 8 and 12 KKW groups was −1.4 (−2.0, −0.8), −2.1 (−2.9, −1.4) and −1.5 (−2.2, −0.8) kg, respectively. In the 4 and 8 KKW groups the actual weight loss closely matched the predicted weight loss of −1.0 and −2.0 kg, respectively, resulting in no significant compensation. In the 12 KKW group the actual weight loss was less than the predicted weight loss (−2.7 kg) resulting in 1.2 (0.5, 1.9) kg of compensation (P<0.05 compared to 4 and 8 KKW groups). All exercise groups had a significant reduction in waist circumference which was independent of changes in weight.

Conclusion: In this study of previously sedentary, overweight or obese, postmenopausal women we observed no difference in the actual and predicted weight loss with 4 and 8 KKW of exercise (72 and 136 minutes respectively), while the 12 KKW (194 minutes) produced only about half of the predicted weight loss. However, all exercise groups had a significant reduction in waist circumference which was independent of changes in weight.

Trial Registration: ClinicalTrials.gov NCT 00011193


Edition: Thorild S. Soenksen, Institute of Preventive Medicine, Denmark

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Chapter 2, Figure 3

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August 03, 2017

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School of Kinesiology & Health Studies
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ROMEO/TRAQ: #6021510
Department Code: PHE-170-17
Study Title: Exploration of interindividual variability in waist circumference and weight reduction in response to standardized exercise
Co-Investigators: Dr. R. Ross
Review Type: Delegated
Date Ethics Clearance Issued: August 03, 2017
Ethics Clearance Expiry Date: August 03, 2018

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- HSREB Approval – Original Study – PHE-093-09
- Information/Consent Form – Original Study

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,

[Signature]

Chair, Health Sciences Research Ethics Board

The HSREB operates in compliance with, and is constituted in accordance with, the requirements of the Tri-Council 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 C: Manual of Operating Procedures

1.1 Anthropometry

A comprehensive set of anthropometric measurements will be collected at weeks 0, 8, 16 and 24. At the OGTT, height and weight will be measured. Note: Control participants will be assessed at 0, 16, 24. Anthropometric measurements should be recorded on the Anthropometric Data Collection Form located in the RA filing cabinet.

Personnel

- Research Assistants

Training Program

Prior to gathering anthropometric data on SERENA study participants, each Research Assistant must demonstrate an acceptable intra-measurer (multiple measures on same site by same Research Assistant) and intermeasurer (comparison between Research Assistants) error. The intra- and inter-measure range of errors for each measure is provided below in brackets.

List of Measured Variables (intra- and inter-measurement error)

Weight and Height

- Weight (0.2 kg; 0.2 kg)
- Standing Height (0.2 cm; 0.2 cm)

Circumferences

- Hip (2 cm; 2 cm)
- Waist (iliac crest, mid-point, last rib) (1.0 cm; 1.0 cm)
- Bicep (1.0 cm; 1.0 cm)
- Proximal thigh (1.0 cm; 1.0 cm)
- Midthigh (1.0 cm; 1.0 cm)
- Calf (1.0 cm; 1.0 cm)

Measurement Devices

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

Measurement Procedures:

Weight and height:

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

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

**Circumference Measures:**

For all circumferences, position the tape directly around the body part so that the inferior edge of the tape is at the level of the landmarked point. Ensure there is no clothing under tape (except in Hip Measurement).

**Hip procedure:**

At the level of farthest posterior protrusion of the buttocks. Be sure tape does not sag. Ensure the participant is standing with their feet together.

**General waist procedure:**

*Note:* It is mandatory that all assessors first view the WC measurement video prior to collecting any WC data.

1. Clear the client’s abdomen of all clothing and accessories. If you find resistance to the suggestion to fully remove shirt, roll up the shirt to allow free access to measurement sites and hold in place with a clip (i.e. hair clip).
2. Position the client with feet shoulder width apart and arms crossed over the chest in a relaxed manner.
3. Take a position to the right side of the client’s body on one knee.
4. Position the tape directly around the abdomen so that the inferior edge of the tape is at the level of the landmarked point. Use a cross-handed technique to bring the zero line of the tape in line with the measuring aspect of the tape. Ensure that the measuring tape is positioned in a horizontal plane around the abdomen. Apply tension to the tape to ensure it is snug, without causing indentation to the skin. Walk around the participant to ensure the tape is straight all around the abdomen. Alternatively, if a mirror is available – use this to ensure proper tape alignment.
5. At the end of a normal expiration, take the measurement.

**Waist (iliac crest):** top of the iliac crest

To find this landmark, palpate the upper right hipbone and draw a line where you locate the uppermost lateral border of the iliac crest.

**Waist (last rib):** bottom of rib cage on right side

To find this landmark, palpate the lower right rib cage and draw a line where you locate the lowest lateral border of the ribs.

**Waist (midpoint between iliac crest and last rib):** midpoint between the bottom of the rib cage and the top of the iliac crest

Use the landmarks from the previous two waist circumference measures to locate this
1.2 Cardiorespiratory Fitness Test

Participants in the SERENA study will perform 5 maximal graded exercise tests on a treadmill: at weeks 0, 4, 8, 16, and 24. Note: Control participants will only be evaluated at 0, 16, and 24.

Personnel

- Research Assistants

Training Program:
Prior to performing a VO\textsubscript{2}max 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 VMx 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 VO\textsubscript{2} 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\textsubscript{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\textsubscript{2}max. A successful test should meet at least 3 of the above criteria.

i. Plateau in VO\textsubscript{2} (oxygen uptake) with increasing work rate (increasing treadmill incline, speed or both). For our purposes we will define plateau in VO\textsubscript{2} as $\Delta$VO\textsubscript{2} <0.05 L/min at VO\textsubscript{2peak} 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\textsubscript{2}max testing never reach a true plateau.

ii. RQ > 1.10: This suggests non-metabolic production of CO\textsubscript{2} and reliance on anaerobic metabolism.

iii. 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)

iv. Borg scale=10. This gives the perception of effort by the participant during the test.

1.3 Exercise Procedures

Calculating Exercise Prescription:

i. Determine Quality of VO\textsubscript{2} Results

To calculate exercise prescription, the exercise monitors must receive a baseline VO\textsubscript{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\textsubscript{2}, Relative VO\textsubscript{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 determine (physiological or mechanical) and a repeated test should be considered after a consultation with the principal investigator and the RAs.

ii. Create Participant Electronic File

Based on the VO\textsubscript{2} results and randomization to determine group assignment, which determines individual daily caloric expenditure an individualized exercise prescription of duration and target heart rate, are determined for each participant.

iii. Calculating Exercise Prescription

1. Using the participant’ electronic file, 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 test as well. If not you may have to do this manually.
3. From the participants VO\textsubscript{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 VO₂ 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:

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

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 VO₂max 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.

**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.
Cases of non-compliance resulting in deviation from expected weight loss:
In cases where a participant weight begins to deviate outside of the tolerable range of expected weight loss we must take the appropriate action to correct it. First, the nutritionist must be notified and a discussion should take place to examine their overall compliance to both the exercise and nutrition portions of the program (Have they been exercising 5 days/week? Have they been handing in daily food records? Are they consuming the caloric target that was established at baseline?). From this discussion a course of action must be taken, it may involve placing demands on the participant to be more compliant or making an adjustment to the caloric target for an individual. In addition, a new projected weight loss should be calculated and shown on the weight loss graph in the participant’s electronic physical activity record. It will show the participants current weight and the weight change needed to achieve the target final weight calculated at baseline from the participant’s initial weight and the expected caloric expenditure based on the exercise prescribed. The purpose of the new trendline is to provide the participant, exercise monitors and nutritionist with new targets and a progression to correct the amount of weight change in the participant. This ensures that the participant is remaining compliant with the protocol. This can be used to provide more useful feedback and progress reports to the participant.

1.4 Accelerometry
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 24. 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

Measurement Device
• GT3X Actigraph Activity Monitor (Pensacola, FL)

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.
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.
1.5 Nutritional Assessment & Counselling

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.

The materials given to the participant during this first session include: a 3-ring binder to hold the materials, a Nutrition Facts leaflet from Health Canada, a handout demonstrating common portions and measurements, a T-Factor or H book, a handout on dietary fat, a ‘handy’ serving guide handout, blank daily food intake records, an instruction sheet summarizing the steps required to fill out the food records and lastly a sheet where the participant can record their frequently used foods.

First visit with the nutritionist
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

2. 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)
Note: if some people prefer to do it on their computer you can send them the file
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. **Add up calories** – How close are you to your recommended target? (If you are over or under, what adjustments can you make?)

3. The Nutritionist will review measurements and proper portions

**Measurements and Portions: (give measurement handout)**

- Try to make this component as interactive as possible.
- Use poster/handout out with thumb/finger guidelines
- thumb tip = a teaspoon (helpful for butter, mayo servings, etc)
  - Note: 3 thumb tips = tablespoon (useful for peanut butter, dressings etc)
- thumb = 25g therefore 2 thumbs = 50 grams which is cheese serving
- palm = 3-4 oz serving of meat
- fist = a cup
- Use measuring cups and spoons to remind people what ½ cup, 1 cup, 1 tsp and 1tbsp look like (use food models here to show 1 tsp of butter and 1tbsp of peanut butter)
- Using dishware may want to show participant different sizes of glasses (1/2 cup, 1 cup and very large glass) so they can estimate liquids
- Other measurements that might be useful: Open slot ladle = ¼ cup; heaping = ½ cup, Closed ladle = ½ cup liquids
- Some tips that people find helpful while trying to estimate the amount:
  - Pour/ put what usually have in bowl/ plate/ glass, then transfer to measuring cup to see how much you are having
  - Measure out 1 cup of cereal/ juice for example and then put it in a bowl/ glass/plate and notice where it fills the bowl up (can eye ball it after)
- If they can’t find it anywhere they may have to compare it to a similar item and make an educated guess (they can also leave it and ask you when they see you but try to encourage them to fill out everything).
4. The Nutritionist will explain where to find the calories and fat that needs to be recorded on the food diaries by introducing the Nutrition Facts tables, working with the T-Factor book and using internet calorie counting sites (if relevant to the participant).

**How to read labels:**
- Make sure they know that the information in the Nutrition Facts table is based on the specific amount of food listed. They then need to compare this to the amount they have eaten.
- Go through some examples with the participant having them tell you how many calories they would have gotten if they had half the serving or double the serving etc. (Make sure they are comfortable with this).
- The serving size amount may be listed in grams, cups, ML or pieces of the item (example bread, crackers, cookies, chips etc). Watch for some snack items that don’t include the whole package.
- The information is always listed in the same order so they will always be able to find calories and fat in the same place (point them both out). Explain that we want them to record the Total Fat which is the first fat # listed.
- If they are eating a food with a label have them use that information (don’t look it up in booklet or on internet) as the table will be the most accurate.

**How to look information up in booklet:**
- Give participant a few common single items to look up (make sure they know where to find the calories and fat listed and also note the serving size – need to compare that to what they have had)
- Give an example of a combined meal and breakdown the foods used and work with participant to look them up (i.e. Spaghetti dinner, homemade pizza, casserole or large salad with meat, nuts, cheese, veggies etc)

**How to use Internet sites to obtain calorie and fat info (if applicable):**
- Can give them a list of websites that you recommend, e.g. http://www.calorieking.com/
- Look up some examples with them (if you have access to a computer)
- Note that those types of websites are “dieting” type sites – remind participant that this is not a dieting study! The reason they need to record their food

**Subsequent visits with the nutritionist**
An appointment is scheduled for a return visit within the next 7-8 days to assess diet records, measure body weight and prescribe calorie and fat targets. Canada’s Food Guide is also given and discussed during this visit. Participants are instructed to hand in their food records the day before the second visit so that the Nutritionist has a chance to assess them.

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.
Appendix D: Intervention timeline for WC, dietary and PA measurements

Red boxes indicate the selected weeks for diet record analysis
Appendix E: Web-based dietary recall

Dietary questionnaire (24-Hour Recall)

Log In
Username
bhammond
Password
*******
Log In
I forgot my password
Example: Selection of 3-day (2 weekdays, 1 weekend day) diet records for a participant at week 16
Example: Selection of meals and snacks

Example: Meal Entry (Breakfast)
Example: Selection of quantity for different food and beverages
**Example:** Complete 1-day entry

**Summary of your day : Thursday, March 18, 2010**

<table>
<thead>
<tr>
<th>Time</th>
<th>Meal Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00 a.m.</td>
<td>Breakfast: Filtered/instant coffee - 250 ml (1 cup) (1 small) + 10% cream - 45 ml (3 Tbsp) English muffin with egg and cheese (mayonnaise excluded) - 1 English muffin</td>
</tr>
<tr>
<td>12:00 p.m.</td>
<td>Lunch: Chicken/poultry leg - 2 X 115 gr. cooked (145 gr. raw) (1 small leg) Fried potatoes/home fries - 180 gr. (3 cups) + Mayonnaise - 45 ml (3 Tbsp) (3 packets) + Brown gravy - 125 ml (1 1/4 cup) Water - 500 ml (2 cups) (1 small bottle)</td>
</tr>
<tr>
<td>5:00 p.m.</td>
<td>Supper: Lamb roast/shoulder roast - 90 gr. cooked (130 gr. raw) Brown gravy - 66 ml (1 1/4 cup) Fried potatoes/home fries - 1/4 X 60 g (1 cup) Carrot, cooked - 60 ml (1/4 cup) Water - 500 ml (2 cups) (1 small bottle)</td>
</tr>
<tr>
<td>7:00 p.m.</td>
<td>Snack: Pepperoni/other deli meat pizza, regular crust - 1/4 pizza 12-inches</td>
</tr>
</tbody>
</table>
Appendix F: Example Diet Record

Example: Excellent diet record quality score

<table>
<thead>
<tr>
<th>February 2, 2012</th>
<th>Calories</th>
<th>Carbs</th>
<th>Fat</th>
<th>Protein</th>
<th>Cholest</th>
<th>Sodium</th>
<th>Sugars</th>
<th>Fiber</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breakfast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imperial - Cinnamon Spread, 2 tsp</td>
<td>70</td>
<td>5g</td>
<td>5g</td>
<td>0g</td>
<td>0mg</td>
<td>20mg</td>
<td>5g</td>
<td>0g</td>
</tr>
<tr>
<td>Old Mill - Cinnamon Raisin Bagel (Pre-Sliced), 1 Bagel (85 g)</td>
<td>230</td>
<td>45g</td>
<td>2g</td>
<td>9g</td>
<td>0mg</td>
<td>410mg</td>
<td>6g</td>
<td>2g</td>
</tr>
<tr>
<td>Quaker - Instant Oatmeal (Original) Cln Pkg, 2 Packet</td>
<td>200</td>
<td>38g</td>
<td>4g</td>
<td>8g</td>
<td>0mg</td>
<td>150mg</td>
<td>0g</td>
<td>6g</td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wonder + - Enriched White Bread - 13 Essential Nutrients, 4 slices (76g)</td>
<td>380</td>
<td>72g</td>
<td>4g</td>
<td>14g</td>
<td>0mg</td>
<td>540mg</td>
<td>8g</td>
<td>6g</td>
</tr>
<tr>
<td>French's (Canada) - Prepared Mustard, 10 ml</td>
<td>0</td>
<td>0g</td>
<td>0g</td>
<td>0g</td>
<td>0mg</td>
<td>110mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td>San Daniele Mortadella Light - Meat, 8 slices(56g)</td>
<td>200</td>
<td>0g</td>
<td>12g</td>
<td>20g</td>
<td>60mg</td>
<td>900mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chicken - Drumstick, meat and skin, cooked, roasted, 4 drumstick, bone removed</td>
<td>449</td>
<td>0g</td>
<td>23g</td>
<td>59g</td>
<td>8mg</td>
<td>18mg</td>
<td>18mg</td>
<td>0g</td>
</tr>
<tr>
<td>Generic - Sweet Potato , 132 g (1/2 cup)</td>
<td>114</td>
<td>27g</td>
<td>9g</td>
<td>2g</td>
<td>0mg</td>
<td>74mg</td>
<td>6g</td>
<td>4g</td>
</tr>
<tr>
<td>B&amp;O's - Pickled Sliced Beets, 15 slices (30g)</td>
<td>75</td>
<td>15g</td>
<td>0g</td>
<td>2g</td>
<td>0mg</td>
<td>425mg</td>
<td>15g</td>
<td>5g</td>
</tr>
<tr>
<td><strong>Snacks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight Watchers Recipe - Blueberry Cranberry Oatmeal Muffin, 3 muffin</td>
<td>375</td>
<td>110g</td>
<td>3g</td>
<td>10g</td>
<td>0mg</td>
<td>41mg</td>
<td>195mg</td>
<td>35g</td>
</tr>
<tr>
<td>Baby Carrots - Vegetable, 15 pieces</td>
<td>35</td>
<td>0g</td>
<td>0g</td>
<td>0g</td>
<td>0mg</td>
<td>0mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td>Baby Carrots - Vegetable, 15 pieces</td>
<td>35</td>
<td>0g</td>
<td>0g</td>
<td>0g</td>
<td>0mg</td>
<td>0mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td><strong>TOTAL:</strong></td>
<td>2,183</td>
<td>312g</td>
<td>63g</td>
<td>121g</td>
<td>297mg</td>
<td>3,071mg</td>
<td>76g</td>
<td>30g</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>February 3, 2012</th>
<th>Calories</th>
<th>Carbs</th>
<th>Fat</th>
<th>Protein</th>
<th>Cholest</th>
<th>Sodium</th>
<th>Sugars</th>
<th>Fiber</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breakfast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imperial - Cinnamon Spread, 2 tsp</td>
<td>70</td>
<td>5g</td>
<td>5g</td>
<td>0g</td>
<td>0mg</td>
<td>20mg</td>
<td>5g</td>
<td>0g</td>
</tr>
<tr>
<td>Old Mill - Cinnamon Raisin Bagel (Pre-Sliced), 1 Bagel (85 g)</td>
<td>230</td>
<td>45g</td>
<td>2g</td>
<td>9g</td>
<td>0mg</td>
<td>410mg</td>
<td>6g</td>
<td>2g</td>
</tr>
<tr>
<td><strong>Lunch</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wonder + - Enriched White Bread - 13 Essential Nutrients, 4 slices (76g)</td>
<td>380</td>
<td>72g</td>
<td>4g</td>
<td>14g</td>
<td>0mg</td>
<td>540mg</td>
<td>8g</td>
<td>6g</td>
</tr>
<tr>
<td>French's (Canada) - Prepared Mustard, 10 ml</td>
<td>0</td>
<td>0g</td>
<td>0g</td>
<td>0g</td>
<td>0mg</td>
<td>110mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td>San Daniele Mortadella Light - Meat, 8 slices(56g)</td>
<td>200</td>
<td>0g</td>
<td>12g</td>
<td>20g</td>
<td>60mg</td>
<td>900mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td><strong>Dinner</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider's - Mini Sizzlers, 8 sausages</td>
<td>760</td>
<td>12g</td>
<td>72g</td>
<td>24g</td>
<td>120mg</td>
<td>1,480mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td>Kraft - Diner, 1/2 box</td>
<td>420</td>
<td>72g</td>
<td>3g</td>
<td>14g</td>
<td>0mg</td>
<td>700mg</td>
<td>12g</td>
<td>2g</td>
</tr>
<tr>
<td>Delmonte - Peas &amp; Carrots, 1/2 cup</td>
<td>60</td>
<td>11g</td>
<td>0g</td>
<td>2g</td>
<td>0mg</td>
<td>360mg</td>
<td>4g</td>
<td>2g</td>
</tr>
<tr>
<td>Generic - Sweet Potato , 66 g (1/2 cup)</td>
<td>57</td>
<td>13g</td>
<td>0g</td>
<td>1g</td>
<td>0mg</td>
<td>37mg</td>
<td>3g</td>
<td>2g</td>
</tr>
<tr>
<td><strong>Snacks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baby Carrots - Vegetable, 15 pieces</td>
<td>35</td>
<td>0g</td>
<td>0g</td>
<td>0g</td>
<td>0mg</td>
<td>0mg</td>
<td>0g</td>
<td>0g</td>
</tr>
<tr>
<td>Generic - Celery Raw 7&quot; Stalk, 2 stalks (cut up)</td>
<td>12</td>
<td>4g</td>
<td>0g</td>
<td>1g</td>
<td>0mg</td>
<td>7mg</td>
<td>0g</td>
<td>4g</td>
</tr>
<tr>
<td><strong>TOTAL:</strong></td>
<td>2,474</td>
<td>307g</td>
<td>100g</td>
<td>92g</td>
<td>212mg</td>
<td>4,817mg</td>
<td>61g</td>
<td>23g</td>
</tr>
</tbody>
</table>
Example: Good diet record quality score

<table>
<thead>
<tr>
<th>Time</th>
<th>Food Description</th>
<th>Calories</th>
<th>Fat (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>Coffee (brewed)</td>
<td>21.5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2% milk</td>
<td>160</td>
<td>8</td>
</tr>
<tr>
<td>Lunch</td>
<td>Bread (white)</td>
<td>65</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Ham</td>
<td>115</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Tomato</td>
<td>26</td>
<td>0.4</td>
</tr>
<tr>
<td>Dinner</td>
<td>Mixed salad greens</td>
<td>35</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>Bacon</td>
<td>40</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Mandarin orange</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>Snacks</td>
<td>Frozen coffee cream</td>
<td>52</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Pecans</td>
<td>150</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Please include source book and page
or reference number (e.g. T-5 = T-factor, page 5)

T = T-factor
P = Photocopied book
* = Food label
? = Best guess

Fat calories: (B) x 9 kcal/g fat
% kcal from fat: (C/A) x 100
Example: Fair diet record quality score

<table>
<thead>
<tr>
<th>Time</th>
<th>Source</th>
<th>Amount</th>
<th>Food</th>
<th>Calories</th>
<th>Fat (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td></td>
<td></td>
<td><strong>Cereal (min-wheats)</strong></td>
<td>250</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>7-36</td>
<td>2</td>
<td><strong>fried eggs</strong></td>
<td>208</td>
<td>15.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td><strong>coffee with milk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Breakfast Subtotals:</strong></td>
<td>466</td>
<td>18.2</td>
</tr>
<tr>
<td>Lunch</td>
<td></td>
<td></td>
<td><strong>Lasagna</strong></td>
<td>761</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>7-91</td>
<td>1</td>
<td><strong>caesar salad</strong></td>
<td>80</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>7-42</td>
<td>2</td>
<td><strong>garlic bread</strong></td>
<td>70</td>
<td>25.2</td>
</tr>
<tr>
<td></td>
<td>4-26(52)</td>
<td>2</td>
<td><strong>Rum &amp; coke (homemade)</strong></td>
<td>396</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td><strong>Apple pie (homemade)</strong></td>
<td>358</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Dinner Subtotals:</strong></td>
<td>1518</td>
<td>70</td>
</tr>
</tbody>
</table>

Please include source book and page or reference number (e.g. T-5 = T-factor, page 5)

T = T-factor
P = Photocopied book
* = Food label
? = Best guess

Fat calories: \((B) \times 9\) kcal/g fat

% kcal from fat: \((C/A) \times 100\)

Canada's Food Guide Checklist:
Grains: 1 7 3 2 4 5 6 7 8 9 10 11 12
F & V: 1 2 3 4 5 6 7 8 9 10
Milk: 1 2 3 4
Meat: 1 2 3

Total:

117
Example: Poor diet record quality score

<table>
<thead>
<tr>
<th>Source</th>
<th>Amount</th>
<th>Food</th>
<th>Calories</th>
<th>Fat (g)</th>
</tr>
</thead>
</table>
| Breakfast |       | 4 cups  
ka i
milk | 24       | (0)     |
| Lunch  |        |                      |          |         |
| Dinner |        | 4 cups  
ka i
milk |          |         |
| Snacks |        |                      |          |         |

Please include source book and page
or reference number (eg. T-5 = T-factor, page 5)
T = T-factor
P = Photocopied book
* = Food label
? = Best guess

Fat calories: (B) x 9 kcal/g fat
% kcal from fat: (C/A) X 100 =

Canada's Food Guide Checklist:
Grains: 1 2 3 4 5 6 7 8 9 10 11 12
F & V: 1 2 3 4 5 6 7 8 9 10
Milk: 1 2 3 4
Meat: 1 2 3
Appendix G: Example Statistical Output

MODEL 2: Simple mixed model set up to show "extra variance" in non-control groups
This virtually the same as model 1

The Mixed Procedure

<table>
<thead>
<tr>
<th>Model Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Set</td>
<td>WORK.REP.CH</td>
</tr>
<tr>
<td>Dependent Variable</td>
<td>With24</td>
</tr>
<tr>
<td>Covariance Structure</td>
<td>Variance Components</td>
</tr>
<tr>
<td>Subject Effect</td>
<td>ID</td>
</tr>
<tr>
<td>Estimation Method</td>
<td>REML</td>
</tr>
<tr>
<td>Residual Variance Method</td>
<td>Profile</td>
</tr>
<tr>
<td>Fixed Effects SE Method</td>
<td>Model-Based</td>
</tr>
<tr>
<td>Degrees of Freedom Method</td>
<td>Between-Within</td>
</tr>
</tbody>
</table>

restriction maximum likelihood

<table>
<thead>
<tr>
<th>Class Level Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
</tr>
<tr>
<td>-------</td>
</tr>
</tbody>
</table>
| ID    | 181    | S001  
S002  
S003  
S026  
S029  
S038  
S040  
S042  
S045  
S055  
S061  
S062  
S067  
S069  
S070  
S073  
S076  
S081  
S088  
S100  
S106  
S109  
S118  
S125  
S126  
S129  
S130  
S131  
S136  
S159  
S160  
S163  
S165  
S167  
S174  
S176  
S179  
S196  
S200  
S202  
S204  
S307  
S312  
S315  
S325  
S352  
S364  
S379  
S386  
S393  
S408  
S411  
S412  
S431  
S438  
S443  
S471  
S481  
S493  
S498  |
|        |       | S492  
S517  
S522  
S524  
S547  
S560  
S565  
S566  
S569  
S570  
S578  
S579  
S581  
S582  
S590  
S596  
S611  
S613  
S615  
S617  
S618  
S619  
S621  
S624  
S626  
S629  
S677  
S687  
S695  
S698  
S700  
S707  
S710  
S712  
S715  |
|        |       | S721  
S722  
S723  
S724  
S727  
S730  
S733  
S735  
S738  
S741  
S743  
S744  
S746  
S750  
S753  
S764  
S768  
S772  
S776  
S809  
S812  |
|        |       | S817  
S818  
S820  
S823  
S840  
S844  
S848  
S849  |
| Gender | 2      | Female Male |
| Group  | 4      | HVLI HVII LVLI Control |
| ExGroup| 2      | Exercises Control |

<table>
<thead>
<tr>
<th>Dimensions</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Covariance Parameters</td>
<td>4</td>
</tr>
<tr>
<td>Columns in X</td>
<td>15</td>
</tr>
<tr>
<td>Columns in Z per Subject</td>
<td>3</td>
</tr>
<tr>
<td>Subjects</td>
<td>181</td>
</tr>
<tr>
<td>Max Obs per Subject</td>
<td>1</td>
</tr>
</tbody>
</table>
MODEL 2: Simple mixed model set up to show "extra variance" in non-control groups
This virtually the same as model 1

The Mixed Procedure

<table>
<thead>
<tr>
<th>Number of Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Observations Read</td>
</tr>
<tr>
<td>Number of Observations Used</td>
</tr>
<tr>
<td>Number of Observations Not Used</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Iteration</th>
<th>Evaluations</th>
<th>-2 Res Log Like</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>1009.01887588</td>
<td>0.00000000</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1001.06614389</td>
<td>0.00000000</td>
</tr>
</tbody>
</table>

\[ SD_{R} = \sqrt{SD_{x}^2 - SD_{e}^2} \]
\[ 'extra' \text{ variance} = SD_{x}^2 - SD_{e}^2 \]
\[ \text{ie. HVHI} \]
\[ SD_{R} = \sqrt{10.5^2 - 3.2^2} \]

Covariance Parameter Estimates

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Subject</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Z Value</th>
<th>Pr &gt;</th>
<th>Alpha</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>HVHI(ID)</td>
<td></td>
<td>10.5135</td>
<td>5.6146</td>
<td>1.87</td>
<td>0.0300</td>
<td>0.05</td>
<td>4.3987</td>
<td>43.4751</td>
</tr>
<tr>
<td>HVLI(ID)</td>
<td></td>
<td>3.1239</td>
<td>3.8899</td>
<td>0.85</td>
<td>0.1986</td>
<td>0.05</td>
<td>0.7317</td>
<td>436.41</td>
</tr>
<tr>
<td>ESVLI(ID)</td>
<td></td>
<td>12.5726</td>
<td>5.7736</td>
<td>2.26</td>
<td>0.0120</td>
<td>0.05</td>
<td>6.1695</td>
<td>38.2396</td>
</tr>
<tr>
<td>Residual</td>
<td></td>
<td>11.0143</td>
<td>2.4035</td>
<td>4.58</td>
<td>&lt;.0001</td>
<td>0.05</td>
<td>7.4883</td>
<td>17.7933</td>
</tr>
</tbody>
</table>

Fit Statistics

| -2 Res Log Likelihood | 1001.1 |
| AIC (Smaller is Better) | 1009.1 |
| AICC (Smaller is Better) | 1009.3 |
| BIC (Smaller is Better) | 1021.9 |

Solution for Fixed Effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Gender</th>
<th>Group</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>DF</th>
<th>t Value</th>
<th>Pr &gt;</th>
<th>Alpha</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
<td></td>
<td>-1.3941</td>
<td>0.8049</td>
<td>173</td>
<td>-1.73</td>
<td>0.0851</td>
<td>0.05</td>
<td>-2.9820</td>
<td>0.1946</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td></td>
<td>0.02004</td>
<td>1.0275</td>
<td>173</td>
<td>0.02</td>
<td>0.9845</td>
<td>0.05</td>
<td>-0.0681</td>
<td>2.0482</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>HVHI</td>
<td></td>
<td>-4.2159</td>
<td>1.1640</td>
<td>173</td>
<td>-3.54</td>
<td>&lt;.0001</td>
<td>0.05</td>
<td>-8.5133</td>
<td>-3.9185</td>
</tr>
</tbody>
</table>
### MODEL 2: Simple mixed model setup to show "extra variance" in non-control groups

This virtually the same as model 1, but consider differences in gender, age, and other factors that may contribute to variance.

#### Mixed Procedure

- **Level of Significance:** Use a significance level of 0.05.
- **The effect of gender does differ:** Between groups, gender is a significant factor.
- **Interpretation example:** A female in the group 1 has on average a score less than a male (compared to control).

#### Table of Fixed Effects

<table>
<thead>
<tr>
<th>Gender</th>
<th>Group</th>
<th>Effect</th>
<th>DF</th>
<th>Num</th>
<th>VAF</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>LVLI</td>
<td></td>
<td></td>
<td>173</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>LVLI</td>
<td></td>
<td></td>
<td>173</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Control</td>
<td></td>
<td></td>
<td>173</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>Control</td>
<td></td>
<td></td>
<td>173</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Table of Random Effects

<table>
<thead>
<tr>
<th>Group</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>DF</th>
<th>Value</th>
<th>Pr &gt;</th>
<th>Alpha Lower Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVLI</td>
<td>-5.8114</td>
<td>0.7165</td>
<td>9</td>
<td>-8.14</td>
<td>&lt;.001</td>
<td>-7.218 to -4.404</td>
</tr>
<tr>
<td>Control</td>
<td>-5.8114</td>
<td>0.7165</td>
<td>9</td>
<td>-8.14</td>
<td>&lt;.001</td>
<td>-7.218 to -4.404</td>
</tr>
</tbody>
</table>

#### Notes:

- The model was fit with random effects of gender and group to account for variability in the response variable.
- The significance levels were determined using a t-test for fixed effects and an ANOVA for random effects.
How to interpret the statistical output?

1. **Does interindividual variability in response to exercise for change in BW exist?**

   The ‘covariance parameter estimate’ represents the ‘extra’ variance in the exercise group after accounting for the variance of the control

2. **Identify potential determinants of the interindividual variability in response to exercise for change in BW**

   First, it must be established whether the potential determinant significantly predicts change in BW differently across groups by examining the interaction terms in the Solutions for fixed effects and the Type 3 tests of fixed effects tables. In this case, the gender by group interaction term was not significant and thus, we cannot reject the null hypothesis. Therefore, gender is not a determinant of the interindividual variability in response to exercise. If the interaction term was significant, then we would re-examine the ‘covariance parameter estimate’ values (see example below). If gender accounted for some of the variability in response to exercise then the ‘extra’ variance for that exercise group (covariance parameter estimate) beyond that in the control, would be attenuated compared to the reference variances (when no additional variable is added to the model).

For example:

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Subject</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Z</th>
<th>Pr &gt;</th>
<th>Alpha</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>HVHI</td>
<td>ID</td>
<td>11.9727</td>
<td>5.7757</td>
<td>2.07</td>
<td>0.0190</td>
<td>0.05</td>
<td>5.9877</td>
<td>41.3484</td>
</tr>
<tr>
<td>HVL1</td>
<td>ID</td>
<td>3.9541</td>
<td>1.7065</td>
<td>2.10</td>
<td>0.0190</td>
<td>0.05</td>
<td>1.0736</td>
<td>105.97</td>
</tr>
<tr>
<td>LVLI</td>
<td>ID</td>
<td>14.5249</td>
<td>5.8192</td>
<td>2.50</td>
<td>0.0062</td>
<td>0.05</td>
<td>7.2507</td>
<td>38.8214</td>
</tr>
<tr>
<td>Residual</td>
<td></td>
<td>10.7538</td>
<td>2.3282</td>
<td>4.64</td>
<td>&lt;0.0001</td>
<td>0.05</td>
<td>7.3484</td>
<td>17.2788</td>
</tr>
</tbody>
</table>

Examine whether the addition of gender accounted for some variance (have to check whether gender by group interaction is significant 1st).

It went from 11.97 to 10.51 (very small amount - not significant)
Appendix H: Supplementary Figures

Figure 1. Scatterplots for change in BW and potential determinants
Figure 2. Scatterplots for change in WC and potential determinants
Appendix I: Supplementary Tables

Table 1. Association between change in EI from week 8 to 24 and change in WC and BW

<table>
<thead>
<tr>
<th>Change in WC</th>
<th>Change in WC</th>
<th>Change in BW</th>
<th>Change in EI (week 0 to 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in WC</td>
<td>Pearson Correlation</td>
<td>1</td>
<td>.836**</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0</td>
<td>0</td>
<td>0.004</td>
</tr>
<tr>
<td>N</td>
<td>137</td>
<td>137</td>
<td>100</td>
</tr>
<tr>
<td>Change in BW</td>
<td>Pearson Correlation</td>
<td>.836**</td>
<td>1</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0</td>
<td>0</td>
<td>0.004</td>
</tr>
<tr>
<td>N</td>
<td>137</td>
<td>137</td>
<td>100</td>
</tr>
<tr>
<td>Change in EI (week 0 to 24)</td>
<td>Pearson Correlation</td>
<td>-.283**</td>
<td>-.287**</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0.004</td>
<td>0.004</td>
<td>100</td>
</tr>
<tr>
<td>N</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Change in EI (week 8 to 24)</td>
<td>Pearson Correlation</td>
<td>-0.142</td>
<td>-.215*</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0.135</td>
<td>0.023</td>
<td>0</td>
</tr>
<tr>
<td>N</td>
<td>112</td>
<td>112</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2. Change in anthropometry for groups with high or low quality of reporting

<table>
<thead>
<tr>
<th>Variable</th>
<th>High (n=128)</th>
<th>Low (n=53)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in WC</td>
<td>-5.0 (5.1)</td>
<td>-4.2 (3.9)</td>
<td>0.31</td>
</tr>
<tr>
<td>Change in BW</td>
<td>-5.3 (5.0)</td>
<td>(-4.3) (3.8)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

WC = waist circumference; BW = body weight

High quality of reporting = received an average rating of excellent or good for the diet records

Low quality of reporting = received an average rating of fair or poor for the diet records
Table 3. Change in anthropometry for groups varying in compliance (amount of diet records complete)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Excellent (n=141)</th>
<th>Good (n=26)</th>
<th>Poor (n=8)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in WC</td>
<td>-5.1 (4.9)</td>
<td>-4.9 (4.4)</td>
<td>-2.0 (4.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>Change in BW</td>
<td>-5.4 (4.9)</td>
<td>-4.3 (3.7)</td>
<td>-2.0 (3.4)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

WC = waist circumference; BW = body weight

Excellent compliance = diet records completed for baseline, week 8, 16 and 24

Good compliance = diet records completed for 3 of the time periods (baseline, week 8, 16 or 24)

Poor compliance = diet records completed for only 1 or 2 of the time periods (baseline, week 8, 16 or 24)