Intervention factors associated with reduction in metabolic syndrome score during a lifestyle intervention program

by

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Abstract

Background:

Metabolic syndrome (MetSyn) is a cluster of risk factors associated with increased incidence of diabetes and cardiovascular disease. Personalized lifestyle interventions using diet and exercise are effective approaches to reverse metabolic syndrome, but have not been well adopted by Canadians. The Canadian Health Advanced By Nutrition and Graded Exercise (CHANGE) demonstration project focused on implementing a physician-led lifestyle intervention program in the primary care setting. Understanding how dietitian and kinesiologists sessions impact patient outcomes may help the implementation of other lifestyle intervention programs.

Methods:

A retrospective pre-post cohort study was conducted using data collected prospectively as part of the CHANGE demonstration project. Patients in the CHANGE demonstration project were adults diagnosed with metabolic syndrome in one of three Canadian primary care clinics. All 305 patients were provided a one year intensive personalized diet and exercise program through a multidisciplinary approach involving their family physician, a dietitian and a kinesiologist. Metabolic syndrome severity was measured using a continuous metabolic syndrome score standardized to have a standard deviation of one. Half a standard deviation change in metabolic syndrome score represents a moderate effect size. Robust multiple linear regression with multiple imputation was the method used to model the association between the exposures and outcomes while controlling for potential confounders and precision variables. A mediation analysis was also conducted where warranted and the statistical significance was tested by bootstrapping of the imputed sample.

Results:

The mean decrease in metabolic syndrome score was 0.5 after three months of intervention. The number of kinesiologist visits was not significantly associated with change in metabolic syndrome score but each dietitian visit was associated with a -0.048 [CI -0.09, -0.01] change in metabolic syndrome score.
Although statistically significant, only 12.5% of the improvement in the metabolic syndrome score associated with dietitian contacts was partially mediated by the Healthy Eating Index.

**Conclusion:**

In the context of a multi-modal primary care-based lifestyle intervention program, increasing dietitian contacts appears to be associated with an improvement in metabolic syndrome score. More research is needed to understand what mediates the treatment effect of dietitian visits.
Co-Authorship

This thesis is the work of Roger Leung in collaboration with co-supervisors Dr. Daren Heyland, Dr. Hélène Ouellette-Kuntz and Andrew Day.
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>CHANGE</td>
<td>Canadian Health Advanced By Nutrition and Graded Exercise</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>DASH</td>
<td>Dietary Approaches to Stop Hypertension</td>
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<tr>
<td>ESHA</td>
<td>Elisabeth Stewart Hands and Associates</td>
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<tr>
<td>HDL-C</td>
<td>High-Density Lipoprotein Cholesterol</td>
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<td>HEI</td>
<td>Healthy Eating Index</td>
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<td>MetSyn</td>
<td>Metabolic Syndrome</td>
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<tr>
<td>SD</td>
<td>Standard Deviation</td>
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<tr>
<td>SE</td>
<td>Standard Error</td>
</tr>
<tr>
<td>VO₂max</td>
<td>Maximal Oxygen Consumption</td>
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Chapter 1: Introduction

Cardiovascular disease represents a significant burden in Canada. In 2007, 1.3 million Canadians reported being diagnosed with heart disease, which is likely an underestimate [1]. Cardiovascular disease accounted for almost a third of all-cause mortality in Canada [2] and in 2005 represented an annual economic cost of $20.9 billion for direct and indirect health care costs as well as productivity losses [3]. This cost is projected to rise to $28.3 billion by 2020 [3]. Diabetes affected 2.5 million Canadians in 2010 with another 1.2 million expected to be diagnosed by 2020 [4]. The economic burden of diabetes was expected to be $12.2 billion in 2010 and is projected to rise to $16.9 billion by 2020 [4]. Metabolic syndrome (MetSyn), a constellation of risk factors (hypertension, hyperglycemia, dyslipidemia and high visceral adipose tissue) [5, 6], is associated with increased risk of cardiovascular disease and diabetes [5-8] and affects 22% of all Canadian adults [9].

1.1 Treatment of Metabolic Syndrome

Lifestyle intervention studies have demonstrated that diet and exercise programs can reverse MetSyn status [10-13]. Despite the strong evidence supporting lifestyle interventions, most patients do not meet recommended diet and exercise guidelines. The Canadian Health Measures Survey conducted between 2007 and 2009 utilized accelerometers to determine a person’s physical activity level [14]. In this representative sample of the Canadian population, only 17% of men and 14% of women met the recommendations of the Canadian and World Health Organization guidelines of 150 minutes per week of moderate-to-vigorous physical activity [14-16]. The Canadian Community Health Survey, Cycle 2.2 Nutrition (2004) found similar issues with Canadians consuming excessive total fat and sodium and inadequate levels of some vitamins and minerals [17, 18].

While guidelines exist, their adherence may require support for lifestyle changes from professionals. While we know that diet and exercise work in a “research setting”, there appears to be little
uptake of these behaviors in “real practice” settings [6, 14, 17-19]. Interdisciplinary primary care teams are an ideal setting to implement lifestyle interventions [20].

1.2 The CHANGE Demonstration Project

The Canadian Health Advanced By Nutrition and Graded Exercise (CHANGE) demonstration project focuses on determining how to optimally implement a lifestyle intervention for adult patients with MetSyn in the primary care setting [21]. The CHANGE project is an ongoing prospective pre-post cohort study without a control group. It follows participants for twelve months. The objectives of the CHANGE project are to develop and implement a program through family doctors supported by kinesiologists and dietitians to show that a regimen of nutritional modification and graded exercise over a one year period will:

a. Reduce components of the metabolic syndrome (hypertension, hyperglycemia, dyslipidemia and high visceral adipose tissue);

b. Reduce reliance on pharmacological drug use;

c. Evaluate the feasibility of team-based approach to manage metabolic syndrome.

Patients were excluded if they had significant co-morbidities (type 1 diabetes, uncontrolled type 2 diabetes, renal failure, cognitive impairment, cancer, terminal illness, and/or chronic inflammatory disease), were pregnant/lactating, or had a body mass index > 35 kg/m². Patients were enrolled in the program through their primary care physician.

Enrolled patients work with a dietitian and a kinesiologist to create personalized diet and exercise plans. The patients meet with their dietitian and kinesiologist weekly for three months and then monthly for the following nine months. The family physician follows up with the patient every three months to track the patient’s progress. Nutrition and fitness assessments including a treadmill test and a 24-hour food recall are completed at baseline as well as at the month three and twelve follow-ups to obtain Maximal Oxygen Consumption (VO₂ max) and Healthy Eating Index (HEI) scores respectively. “Change
“change in VO2 max” provides an overall measure of change in aerobic health [22-24] and “change in HEI” gives an overall measure of change in diet quality [25-27].

1.2.1 Transtheoretical Model

The Transtheoretical model was used in the CHANGE project to determine the patient’s intention to change which was incorporated into the diet plan. The Transtheoretical model describes the readiness for change as a continuum, where individuals may be more or less ready to change a particular behaviour [28]. The stages of change are depicted as a spiral as patients often relapse regressing to an earlier stage [28]. Despite this, patients usually never regress all the way back to where they began because they learn from their past experiences [28].

The diet intervention in the CHANGE project has been described in detail by Royall [29]. It utilizes an integrative model comprised of education, skill building and a combination of behavioural strategies as identified by Michie [30]. The behavioural strategies chosen depend on the patient’s needs and may include strategies based on the Transtheoretical model [28], motivational interviewing [31] and cognitive behavioural therapy. The integrative model has three primary determinants of intention that drive behaviour: 1) attitude (overall favourableness, favorableness of performing the behaviour); 2) perceived norms (social pressures to adopt or not adopt a behaviour), and 3) self-efficacy (necessary skills to perform the behaviour) [32].

1.2.2 Recruitment and Outcome

The CHANGE demonstration project recruited 305 patients across three sites (Edmonton, Toronto and Laval) between June 2012 and December 2014 [21]. The final patient completed the study in January 2016. Preliminary analysis showed that 15.6% of patients reversed their MetSyn status (for definition of MetSyn reversal see section 2.4) after three months of intervention and 24.1% reversed their MetSyn status after twelve months of intervention (results not published). Overall, 37.4% of patients no longer met at least one of the MetSyn criteria (hypertension, hyperglycemia, dyslipidemia or high visceral
adipose tissue) after three months of intervention and 49.4% no longer met at least one of the MetSyn components after twelve months of intervention (results not published).

Although there were clear signs of improvement, there were questions regarding the implementation of the program. Patients were expected to visit the kinesiologist and dietitian every week for the first three months and then monthly for the following nine months, but in actual practice, patients do not always follow this protocol. Study participants were allowed to have extra contacts with the dietitian and kinesiologist beyond what was expected, which included but was not limited to extra email and telephone contacts with the dietitian. This replicated what would have occurred in a regular clinic. In addition, patients may miss visits for a variety of reasons. This variation in dietitian contacts and kinesiologist visits may affect patient outcomes.

1.3 Rationale

It is not currently understood how program elements such as additional visits influence the CHANGE demonstration project. Understanding the relationship between the number of kinesiologist visits and dietitian contacts to a change in MetSyn score may guide the implementation of this program. Kinesiologist visits are more time intensive and expensive than the usual dietitian contacts, so unless there is a substantive benefit, it may be pragmatic to limit program visits. Conversely, the time for a dietitian to do a follow-up email or phone call might be economically justifiable if the patients in turn receive significantly greater improvement in MetSyn symptoms.

1.4 Objectives

This thesis is a secondary analysis of CHANGE project data. Since the intensity of the intervention changes after three months, the analysis was restricted to the first three months of the intervention.

The objectives of this thesis were:

1) To describe and interpret the observed change in MetSyn score within three months of the start of a lifestyle intervention.
2) To evaluate the association between the frequency of kinesiologist visits and change in metabolic syndrome score within three months of the start of a lifestyle intervention and to determine whether this association is mediated through a change in aerobic capacity.

3) To evaluate the association between the frequency of dietitian contacts and change in metabolic syndrome score within three months of the start of a lifestyle intervention and to determine whether this association is mediated through a change in the overall diet quality.

1.5 Thesis Organization

This thesis is organized into chapters as per the guidelines provided by the School of Graduate Studies at Queen’s University. The current chapter provided an overview of treatment of MetSyn, the CHANGE demonstration project, study rationale and objectives. Chapter 2 contains a literature review of MetSyn epidemiology, MetSyn pathophysiology, MetSyn treatment, measures of impact and measures of aerobic exercise and diet interventions. Chapter 3 presents the methods used including study design, study population, data collection, data measurements, study variables and statistical analysis. The results are presented in Chapter 4 with details of the patient characteristics, exposure variables (kinesiologist visits and dietitian contacts), outcome variable (MetSyn score), mediation variables (VO2max and HEI), the relationships between those variables, the regression models and the mediation models. Chapter 5 includes a discussion of the key findings in change in MetSyn score, kinesiologist visits, dietitian contacts, strengths, limitations, generalizability, and implications for future research.
Chapter 2: Literature Review

2.1 Metabolic Syndrome

2.1.1 MetSyn Criteria

Based on the harmonized guidelines across different health associations, metabolic syndrome is defined by the presence of at least 3 out of 5 criteria: high blood pressure, high fasting blood glucose, high triglyceride, low high-density lipids cholesterol (HDL-C), and high abdominal circumference[5, 6]; see Table 1. Patients with the syndrome have an almost 2-fold relative risk of cardiovascular disease within 5 to 10 years, and a 5-fold increased relative risk of diabetes [5, 7, 8]. Prevention and treatment of MetSyn may be key to decreasing the incidence of cardiovascular disease and diabetes [6].

Table 1: Criteria for the Clinical Diagnosis of Metabolic Syndrome [5, 6]

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Measure/Categorical Cut Points</th>
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| Elevated Blood Pressure | • Blood Pressure $\geq$ 130/85 mmHg  
• Or use of antihypertensives to treat hypertension |
| Elevated Fasting Blood | • Fasting blood glucose $\geq$ 100 mg/dL (5.6 mmol/L)  
• Or drug treatment of elevated glucose |
| Elevated Triglycerides | • Triglycerides $\geq$ 150 mg/dL (1.7 mmol/L)  
• Or drug treatment of elevated triglycerides |
| Reduced High-Density Lipoprotein Cholesterol (HDL-C) | • $< 40$ mg/dL (1.0 mmol/L) in males  
• $< 50$ mg/dL (1.3 mmol/L) in females |
| Elevated Abdominal Circumference | • Europids/Caucasian/Sub-Saharan Africans/ Mediterranean/Middle East (Arab) $\geq 94$ cm Males, $\geq 80$ cm Female.  
• Asian and South Central Americans $\geq 90$ cm Males and $\geq 80$ cm Females  
• US and Canadian $\geq 102$ cm Males, $\geq 88$ cm Females. |

† Ethnic categories are combined based on the categorical cut points
2.1.2 Epidemiology

MetSyn is highly prevalent, affecting 22% of all Canadian adults and 41% of those between the ages of 60 and 79 [9]. The prevalence of each MetSyn criteria (except HDL-C) increases with age in both men and women [33-35]. Males have significantly higher prevalence of elevated abdominal obesity, elevated triglycerides and elevated fasting blood glucose than women [36]. MetSyn affects 24% of males and 20% of females but this difference is stronger in elderly patients (ages 60 to 79) affecting 46% of males and 37% of females [9]. MetSyn also disproportionately affects those with less education and lower income. MetSyn affects 40.1% of Canadians with less than a secondary education and 34.4% of Canadians with a secondary education [36]. This is a substantial difference compared to the prevalence in Canadians with some post-secondary education and post-secondary graduation at 9.4% and 15.2% respectively [36]. This disparity is similar though less pronounced when comparing MetSyn prevalence by the income groupings of lowest income, lower-middle income, upper-middle income and highest income with prevalences of 21.3%, 31.6%, 20.5% and 15.2% respectively [36]. Working status itself is also associated with MetSyn based on a large cross-sectional study in France [37]. People who worked full time had a lower prevalence of MetSyn compared to people who were retired or never worked.

In addition to the above sociodemographic characteristics, clinical factors including BMI and depression have been shown to be associated with MetSyn. In the case of BMI, high BMI is significantly associated with an increased incidence of metabolic syndrome due to the effect of visceral fat on insulin resistance [38, 39]. As for depression, a meta-analysis showing that depression is associated with non-adherence to medications for hypertension and hyperlipidemia (OR 1.79 [CI 1.28-2.51]) suggests an increased risk for MetSyn [40].

2.2 Pathophysiology

The pathophysiology of MetSyn is a complex interplay between the environment, genetics, physiology and biochemistry [39]. Environmental factors such as decreased physical activity and increased energy intake can lead to hyperplasia and hypertrophy of adipose tissue due to the need to store
excess triglycerides [41]. Visceral (intra-abdominal) adipose specifically has been associated with increased insulin resistance and metabolic syndrome features [42]. Three scenarios have been proposed to explain adipose tissue’s relation to metabolic syndrome [43]. It is believed that all three happen simultaneously.

1) The hyperlipotic state of the adipose tissue increases portal circulation of free fatty acids and is insulin resistant [43]. Free fatty acids are substrates for triglycerides which cause hypertriglyceridemia and the production of very low density lipoproteins that clear high-density lipids [44]. Acute plasma free fatty acids have been shown to impair hepatic metabolic responses [43] and induce insulin resistance in skeletal muscle of healthy volunteers by inhibiting insulin-stimulated glucose uptake [44]. The free fatty acids also impair hepatic metabolic processes causing glucose intolerance (higher glucose production) and hyperinsulinemia through decreased insulin clearance [43]. Hyperinsulinemia may also induce hypertension by increasing renal reabsorption of sodium [45].

2) Adipose tissue has an endocrine function increasing the release of adipokines that increase insulin resistance, a pro-inflammatory state and a pro-thrombotic state [43]. Increases in adipose tissue is also correlated with increases in plasma angiotensin and aldosterone which have been shown to induce hypertension through the renin-angiotensin-aldosterone system [45].

3) Visceral adipose is partly a marker of dysfunctional adipose tissue which normally acts as a protective buffer for energy surplus [38]. This results in storage of triglycerides as ectopic fat that accumulates on the liver, heart, skeletal muscle and pancreas [43].

### 2.3 Treatment

Treatment of MetSyn is primarily through diet and exercise modifications in conjunction with pharmacotherapy to normalize each of the risk factors [6, 46]. Changes in diet and exercise can target specific MetSyn criteria or promote overall general health.
2.3.1 Treatment Through Exercise

There is consistent evidence of the benefits of different exercise programs to treat MetSyn [47-55]. There are three main forms of exercise treatment that have been shown to affect MetSyn: high aerobic exercise (at least 60% max capacity), moderate intensity aerobic exercise (i.e. walking) and strength/resistance training.

Aerobic exercise has consistently been shown to increase insulin sensitivity [49, 55] by increasing insulin-stimulated glucose transport-phosphorylation [54]. In a study of women with grade 1 essential hypertension randomized to 6 weeks of supervised high intensity aerobic exercise (45-60 min sessions, 5 times a week) versus only written recommended exercise, there was a significant improvement in blood pressure in the aerobic exercise group [48]. Moderate intensity aerobic exercise may be more suitable for elderly populations and can be incorporated into everyday life which may be more likely to produce sustained results [51]. Brisk walking is a low cost moderate exercise that can significantly reduce blood pressure [51], increase HDL-C [53] and reduce triglycerides [53]. Strength exercise has not traditionally been used to treat diabetes but a study of older patients with type 2 diabetes found significant improvements in insulin sensitivity and reductions in free fatty acids in patients randomized to 16 weeks of strength training plus standard of care versus standard of care alone [50].

The combined effect of intensive aerobic and resistance training was studied in a large randomized control trial of 691 patients who had type 2 diabetes mellitus and metabolic syndrome [47]. Patients were randomized to twice a week supervised aerobic/resistance exercise and exercise counselling, or to counselling alone for 12 months. There was significant improvement in the exercise group compared to the control (mean difference [95% confidence interval]): systolic blood pressure (-4.2 mmHg [CI -6.9, -1.6]); diastolic blood pressure (-1.7 mmHg [CI -3.3, -1.1]); HDL-C (3.7mg/dL [CI 2.2, 5.3]); LDL (-9.6mg/dL [CI -15.9, -3.3]); waist circumference (-3.6cm [CI -4.4, -2.9]); body mass index (-0.78 [CI -1.07, -0.49]) and in Homeostasis Model Assessment-Insulin Resistance (-0.36 [CI -0.94, -0.22]) [47]. Although randomized controlled trials use highly selected populations, a large (n=1776) 3-year pseudo-experimental cohort study in Norway demonstrated that a low-cost population-based exercise
program could increase physical activity levels and significantly improve blood pressure, triglycerides and glucose levels [52].

These studies align with the guidelines published by the World Health Organization and the Canadian Society for Exercise Physiology which recommend adults receive 150 minutes of moderate-to-vigorous aerobic exercise a week, in bouts of 10 minutes or more [15, 16]. In addition, it is recommended that muscle-strengthening activities should be done on major muscle groups at least two days per week [15, 16].

2.3.2 Treatment Through Diet

There are many different diets that have been reported to have positive effects on MetSyn as well as its downstream effects of cardiovascular disease and diabetes. The Mediterranean diet for example is characterized by high fruit, vegetable and fish intake, as well as less red meat consumption [56]. The PERIMED study was a multi-centered randomized controlled trial conducted in Spain to determine the effect of the Mediterranean diet on cardiovascular events (myocardial infarction, stroke and death due to cardiovascular disease) [56]. Almost 7,500 people at high risk for cardiovascular disease were randomized into one of three arms: a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control diet (advice to reduce dietary fat) for a median follow-up of 4.8 years. The combined multivariable-adjusted hazard ratio for both intervention arms was 0.71 [CI 0.56, 0.90] versus the control group, showing a reduction in cardiovascular event risk [56].

Most studies of diet interventions have only been able to demonstrate an effect on risk markers such as the MetSyn components as opposed to MetSyn status. The Dietary Approaches to Stop Hypertension or “DASH” diet is recommended by several associations including the Heart and Stoke Foundation [57] and the National Heart, Lung and Blood Institute [58] to treat hypertension. In a randomized controlled trial, 459 patients were randomized to: 1) a diet rich in fruits and vegetables; 2) a “combination” (DASH) diet rich in fruits and vegetables, low-fat dairy and reduced total fat/sodium; or 3)
a control diet typical of the average diet in the United States [59]. All patients received a control diet that was low in fruits, vegetables and dairy products with an average fat content for a United States diet during a three week run-in phase. The run-in phase was followed by the intervention phase where patients were randomized to one of the three arms described above. The “combination” diet offered benefits in addition to simply adding fruits and vegetables, showing an average reduction of systolic and diastolic blood pressure of 5.5 and 3.0 mmHg respectively versus the control. These results were replicated in hypertensive patients [60].

Caloric restriction is a standard method that has been shown to reduce both visceral and subcutaneous adipose and thus reduce waist circumference [61]. National clinical guidelines suggest caloric reductions of 500-1000 calories/day, with no more than 30% of daily calories from fat [62]. In a meta-analysis of weight reduction studies, triglycerides were reduced by 0.015 mmol/L for each kilogram of weight loss [63]. There were small increases in HDL-C levels as well for patients at stable weights after the weight reduction program. It should be noted that the patients on the Mediterranean diet in the PERIMED study reduced cardiovascular risk without caloric reduction.

These diet interventions align with the recommendations from Canada’s Food Guide [64] and Dietary Reference Intake [65].

2.3.3 Treatment Through Lifestyle Interventions

The combination of diet and exercise approaches is also known as a lifestyle intervention. Different lifestyle interventions have been studied but the results are similar to the individual diet and exercise literature. In a randomized controlled diabetes prevention trial, 1,711 patients with impaired glucose intolerance were randomized to an intensive lifestyle intervention program (individualized to maintain 7% weight loss and 150 min exercise per week), standard lifestyle recommendations plus metformin (850mg twice daily), or a control of standard lifestyle recommendations plus placebo (in place of the metformin) [13]. After a mean of 3.2 years of follow-up, the proportional hazard model showed that the lifestyle intervention group had a 41% [95% CI 28, 52] reduction in metabolic syndrome incidence compared to
the placebo group and a 29% [95% CI 13, 42] reduction compared to the metformin group [13]. The metformin group only had a 17% [95% CI 0, 31] reduction in metabolic syndrome incidence compared to the placebo group [13].

The D.E.S.I.R. study was a large epidemiological study in France that examined how lifestyle habits over 3 years impacted metabolic syndrome in 3986 men and women between 30 and 56 years of age [10]. It showed that physical activity including sports had benefits in the levels of insulin, HDL-C, triglycerides and waist circumference in men [10].

A diabetes prevention trial randomized 523 overweight patients with impaired glucose tolerance to either lifestyle advice (control) or seven sessions with a nutritionist for the first year to discuss weight reduction, consumption of saturated fat and increasing fibre in addition to lifestyle advice [12]. After the first year, the intervention (nutritionist) group had significant improvements in weight, waist circumference, glucose, triglycerides and blood pressure compared to the control (lifestyle advice) group [12].

However, such programs are not consistently offered to patients. Randomized controlled studies that had physicians and/or nurses deliver lifestyle interventions in the primary care setting showed modest benefits to MetSyn criteria [66-69]. A randomized controlled trial of 491 obese Canadians found that an intensive 2-year exercise program that was tailored to individual patients also showed modest benefits on MetSyn components such as waist circumference [70, 71]. The benefits were strongest after the initial intensive 6-month phase and then the benefit eroded over the course of the following 18 months [70, 71].

2.3.3.1 Primary Care Setting

When a random sample of all patients from three Family Health Networks in Ontario were surveyed, it was found that there were low rates of preventative counselling, 37% and 24% for diet and exercise counselling, respectively [72]. In addition, the majority of the counselling consisted of verbal advice only (61% and 78% for diet and exercise counselling respectively) followed by pamphlets or other written materials (34% and 18% for diet and exercise counselling respectively) [72]. Few clinics have the
resources to provide lifestyle interventions [21, 37]. A survey of family physicians in British Columbia cited time and compensation as the major barriers to offering nutrition counselling [73], as it is often not covered by health insurance policies.

Health professionals trained in diet and exercise can personalize lifestyle intervention programs to take into account various complex factors such as cultural differences, physical limitations, patient expectations and patient preferences [11]. Primary care physicians are generally not trained to provide these types of services and cite this lack of training as a barrier to patient care [19, 74].

The Canadian Clinical Practice Guidelines recommend that qualified health professionals such as dietitians and kinesiologists assess patients and aid delivery of care in multidisciplinary teams [46]. A randomized controlled trial in Italy evaluated in patients with at least two MetSyn criteria (instead of three) used such an approach [11]. All patients received verbal lifestyle advice as per standard of care but patients randomized into the intervention group received detailed individualized recommendations from nutritionists, endocrinologists and internal medicine physicians for a year [11]. The intervention group showed modest improvement to metabolic syndrome criteria and inflammatory markers [11]. In contrast, the control group had either no change or worse metabolic syndrome and inflammatory marker outcomes after a year [11]. A similar study in Sweden echoed the results from Italy [75]. Adult patients diagnosed with hypertension, type 2 diabetes, dyslipidemia or obesity were randomized to usual care or a program involving their physician, a physiotherapist and a dietitian [75]. Those in the intervention group had statistically significant but modest improvements in waist circumference and blood pressure when compared to the control group [75].

2.3.4 Professionals and Frequency of Contact

Attendance to a non-randomized lifestyle intervention study among patients with metabolic syndrome was evaluated in a study of 207 Japanese middle aged adults [76]. Patients were offered either 3 individual and 28 group counselling sessions on diet and exercise (intervention group), or only 7 health information letters by mail (control group). Attendance was calculated based on the total number of
counselling and group meeting sessions. Patients were categorized as high or low attendance depending if they were above or below the median attendance of 87.1% [76]. After 27 months, high attendance in males was associated with significantly lower odds for dyslipidemia (HDL-C < 1mmol/L, LDL-C ≥ 3.6 mmol/L, triglyceride ≥ 1.7 mmol/L) with an odds ratio of 0.11 [CI 0.02, 0.51] compared to the control group [76]. Compared to controls, low attendance was not associated with lower odds of dyslipidemia in males [76]. Among females, high attendance were associated with significantly lower BMI (≥25kg/m^2) and health behaviours like higher walking steps (≥6000 steps a day) with odds ratio of 0.24 [CI 0.07, 0.81] and 3.23 [CI 1.31, 7.95] respectively [76]. In females, lower attendance was not significantly associated with those outcomes compared to controls.

Similar results were found in a diabetic patient population. In a randomized controlled study of weight loss in 5,145 diabetic patients, an intensive diet and exercise intervention was compared to a control group that received usual care (diabetic support and education) [77]. Attendance was based on all the individual and group sessions attended by the patient over the twelve-month intervention [77]. The primary goal of the study was to achieve a weight loss of 7% of the patient’s initial weight but patients were instructed to aim for a personal weight loss goal of 10% of their initial weight [77]. An analysis comparing the quartile with the highest attendance to the lowest attendance showed that patients in the highest quartile were 5.8 [CI 4.0, 7.0] and 8.1 [CI 5.7, 11.5] times more likely to achieve their 7% and 10% goal respectively [77].

These studies showed that attendance was associated with changes to dyslipidemia, BMI and weight loss. BMI and weight can affect abdominal circumference. These outcomes would have an impact on MetSyn improvement and supports the association that increased attendance to a lifestyle intervention can improve MetSyn.

2.3.5 Patient Factors Associated with Adherence to Lifestyle Interventions

Demographic and clinical factors have been shown to be associated with adherence to lifestyle interventions. Increasing age [78], being male [79, 80], having a lower BMI [81], and not having a
diagnosis of depression [40] or diabetes [82] are associated with increased adherence. In a study of adherence to diet and physical activity recommendations in overweight and obese adults, increased age was associated with completion of the weight loss program [78]. Each incremental year increased the probability of successfully completing the weight loss program by 1.6% [78]. In a study of exercise, sex was associated with adherence [79]. This may be due to how sex affects health intentions and behaviours in regards to exercise and diet [80]. High BMI is inversely associated with adherence to a Mediterranean diet [81]. Depression in diabetics has been associated with non-adherence to self-care activities such as diet and exercise [40]. Patients with depression ate less fruits and vegetables, ate higher fat foods, and exercised less than patients without diabetes [40]. Diabetic patients in general have multifactorial reasons that affect their adherence to self-care including polytherapy, psychological factors and additional cost [82].

2.4 Measures of Impact

The majority of studies examine the impact of intervention through changes in individual metabolic syndrome components (blood pressure, fasting blood glucose, triglycerides, HDL-C and abdominal circumference) [12, 47-53, 56, 59-61, 63, 70, 71, 75]. The studies that have used the syndrome as the outcome of interest, have used a binary definition of MetSyn as either having the syndrome or not [7, 8, 10, 11, 83-85]. The use of this binary definition of MetSyn in epidemiology has been criticized as it does not accurately reflect the progressive risk of disease and is not sensitive to changes in individual MetSyn criteria [85-87]. For example, in a cohort study in France, a third of patients who were classified as presenting with metabolic syndrome at baseline were considered “normal” at the 3-year follow-up despite minimal changes in the absolute values of each criteria [83, 86]. Similar results were found in a randomized controlled trial of patients with at least two MetSyn criteria that compared the effectiveness of a yearlong group-based lifestyle intervention program to a control group who received standard of care from their family physicians [11].
As an alternative, Hillier described a single continuous metabolic syndrome score based on first principal component analysis, which described 50% of the total variance of waist circumference, (log) triglycerides, systolic blood pressure and glucose [86]. They used logistic regression to predict the incidence of diabetes, coronary heart disease and cardiovascular disease with the continuous MetSyn score as the exposure. Standardized odds ratios were used to describe the incident diabetes, coronary heart disease and cardiovascular disease per 1 standard deviation increase in MetSyn score.

2.5 Measures of Aerobic Exercise and Diet Interventions

Change maximal oxygen consumption (VO₂max) and change in Healthy Eating Index (HEI) are overall measures of aerobic exercise and diet, respectively. Maximal VO₂ is considered an important metric that defines the limits of the cardiopulmonary system [23]. It is commonly used to describe exercise capacity [23] as it is a stable measure over time that varies only due to exercise [22]. Change in VO₂max is able to show a cumulative change due to aerobic exercise [22].

HEI was originally created by the U.S. Department of Health and Human Services to measure adherence to dietary guidelines [88]. It is a validated measure of population health [26] that has been adapted to reflect Canadian guidelines [25, 27]. HEI can range between 0 and 100 with 100 representing a perfect diet. The Canadian HEI is based on eleven components that can be grouped as either an “adequacy component” (maximum score of 60) or a “moderation component” (maximum score of 40). The score represents a greater emphasis on eating a balanced diet over moderating certain foods. There are limitations to the use of HEI as a measure of overall diet quality. Although there is evidence that HEI has face and content validity, its predictive validity has not been shown at an individual level [25-27].
Chapter 3: Methods

3.1 Study Design

This is a retrospective pre-post cohort study using data collected from the Canadian Health Advanced By Nutrition and Graded Exercise (CHANGE): a demonstration project of lifestyle intervention offered to patients with metabolic syndrome. All patients were provided personalized diet and exercise interventions by registered dietitians and kinesiologists weekly for three months and then monthly for nine additional months. Each patient had follow-up assessments with their family doctor every three months. The study enrolled 305 adult patients across three Canadian centers. Enrollment started in October 2012 and the final follow-up was completed January 2016. Research ethics for the thesis was obtained by the Queen’s University Health Sciences Research Ethics Board (Appendix A).

3.2 Study Population

Recruiting sites (n=3) were primary care clinics in urban centers across three provinces in Canada: Edmonton (Alberta), Toronto (Ontario), and Laval (Quebec). Adult patients with metabolic syndrome were enrolled. Patients were screened during routine annual exams provided by the family physicians involved in the study. Screening data for patients enrolled in the study were not recorded due to the significant burden to the sites.

3.3 Data Collection and Measurements

Unless otherwise specified, all data was abstracted from the patient’s medical charts and entered into a secure online data capture system by research staff at each site. The data capture system implemented in REDCap (http://www.project-redcap.org/) included data restrictions and real time data integrity checks. Data required for the study was then abstracted from the data capture system into SAS (www.sas.com) datasets. These included data required to derive the levels of exposures of interest (kinesiologist visits and dietitian contacts), the outcome (change in MetSyn score), potential confounders (site, age, sex, and baseline clinical variables), mediation variables (change in VO₂max and change in
HEI), as well as precision (baseline medications) and auxiliary variables (change in readiness score, co-morbidity index).

3.3.1 Exposure Variables

**Kinesiologist visits** was the count of all face-to-face visits with the patient from baseline to the month three follow-up examination by the family physician. Similarly, the number of **dietitian contacts** was the sum of all face-to-face visits, emails and phone calls with the patient from baseline to the date of the month three follow-up examination by the family physician. To determine if this difference between the definition of kinesiologist visits and dietitian contacts would impact the results, a sensitivity analysis was conducted using the definition **dietitian visits** (face-to-face visits only).

Patients had a follow-up visit with dietitian, kinesiologist and family physician three months after baseline. These visits may not have occurred on the same calendar day. To ensure consistency, only kinesiologist visits and dietitian contacts that occurred on or prior to the month three follow-up with the family physician were counted because that was when the variables for the MetSyn score were collected. If a patient did not have a month three follow-up, the sum of kinesiologist visits and dietitian contacts that occurred on or before the week twelve visit were counted. Nutrition and fitness assessments were to be conducted at baseline and month three to collect the data for the Healthy Eating Index (HEI) and Maximal Oxygen Consumption (VO₂max). These assessments were considered additional visits even if they occurred on the same day as a regularly scheduled kinesiologist visit or dietitian contact.

3.3.2 Outcome Variable

The metabolic syndrome score was calculated with the equation provided by Hillier [86] and shown below. The MetSyn score was created based on a longitudinal cohort study in France of 5,024 adults aged 35 to 65 years [86]. Patients were recruited from volunteers insured by the French national Social Security system between 1994 and 1996 [86]. The French cohort had a mean abdominal circumference of 83.3 cm, mean fasting blood glucose of 5.4 mmol/L, mean triglycerides of 1.1 mmol/L, mean HDL-C of 1.6 mmol/L and mean systolic/diastolic blood pressure of 130/79 mmHg [9]. This is
similar to the Canadian population with a mean abdominal circumference of 90.3 cm, mean fasting blood glucose of 5.2 mmol/L, mean triglycerides of 1.22 mmol/L, mean HDL-C of 1.38 mmol/L and mean systolic/diastolic blood pressure of 109/69 mmHg [89, 90]. The main differences are a higher mean abdominal circumference and lower mean blood pressure in Canada.

The MetSyn score used the abdominal circumference, blood pressure, triglycerides and fasting blood glucose measurements collected at baseline and at the month three follow-up. Instructions were provided to study sites to standardize the collection of blood pressure and abdominal circumference measurements (see Appendix B).

\[
\text{Metabolic Syndrome Score} = 0.59 \times (\text{Abdominal Circumference} - 83.3) / 11.8 + 0.51 \times (\text{LOG Triglycerides} + 0.03) / 0.52 + 0.47 \times (\text{Systolic Blood Pressure} - 130) / 16 + 0.42 \times (\text{Fasting Blood Glucose} - 5.4) / 0.9
\]

Each variable was in the appropriate units before calculation: abdominal circumference (cm), triglycerides (mmol/L), systolic blood pressure (mmHg) and HDL-C (mmol/L). The adjusted weights, means and standard deviations were also from Hillier [86]. Hillier log-transformed the triglycerides to reduce skewness of distribution.

The MetSyn score was standardized based on the French cohort to have a standard deviation of one and a mean of zero [86]. The score has not been validated in a Canadian population. A half a standard deviation change is considered a moderate effect size and a full standard deviation change is considered a large effect size [91]. The MetSyn score can be used to describe the risk of incident diabetes, coronary heart disease and cardiovascular disease in nine years per one standard deviation increase in MetSyn score [86]. A description of how to convert the MetSyn score into odds ratios is provided in Appendix C.
3.3.3 Potential Confounders

The following potential confounders were chosen based on a combination of a literature review and expert opinion from the CHANGE operations committee. The confounders were either known to be or suspected to be associated with both the exposure (kinesiologist visits/dietitian contacts) and the outcome (change in MetSyn score) but not on the causal pathway.

1) Site: There were a total of three sites across three provinces. Site was coded using two dummy variables with Edmonton as the reference category.

2) Age: Age was coded as a continuous variable in years.

3) Sex: Sex was coded as a categorical variable with male as the reference category.

4) Baseline Body Mass Index (BMI): BMI was calculated based on the patient’s height and weight and coded as a continuous variable in kg/m².

5) Baseline Depression: Baseline depression was coded as a categorical variable based on the patient’s chart. Non-depression status at baseline was the reference category. The CHANGE demonstration project did not screen for depression.

6) Baseline Diabetes: Baseline diabetes was coded as a categorical variable and was also based on the patient’s chart. Non-diabetes status at baseline was the reference category.

7) Baseline working Status: The research site staff asked the patients about their working status at baseline. Baseline working status was coded as a categorical variable with the dummy variables “Unemployed” and “Other”. “Employed” at baseline was used as the reference category.

3.3.4 Precision Variables

Precision variables were added to the model. These variables explain some variance in the outcome but are not associated with the exposure. Adding these variables does not affect confounding, but results in smaller standard errors and thus greater precision and power.
1) Baseline MetSyn Medications (Prescribed): The baseline medications for glycemia, hypertension and hypertriglyceridemia were coded as three separate categorical variables with no medication use as the reference category for all three. The use of MetSyn medications directly affects the components that go into the MetSyn score. Medication adherence was not recorded in the CHANGE demonstration project. The only information available was the list of medications prescribed.

2) Baseline MetSyn Score: Baseline MetSyn score was calculated based on the systolic blood pressure, fasting blood glucose, triglyceride and abdominal circumference measurements at baseline and coded as a continuous variable. The magnitude of the change in MetSyn score will be highly correlated with the initial baseline score.

3.3.5 Mediation Variables

It is hypothesized that, 1) change in maximal oxygen consumption (VO_{2max}) may mediate the association (if present) between kinesiologist visits and change in MetSyn score, and 2) change in Healthy Eating Index (HEI) may mediate the association (if present) between dietitian contacts and change in change in MetSyn score.

1) Change Maximal Oxygen Consumption (VO_{2max}) between three months after the start of the intervention and baseline: VO_{2max} was coded as a continuous variable per unit (ml*kg^{-1}*min^{-1}). The CHANGE demonstration project used the treadmill walking test as described by Ebbeling et al. to estimate the VO_{2max} as it is more suitable for apparently healthy, non-athletic adults [24]. This method is endorsed by The Canadian Society for Exercise Physiology [92].

2) Change in Healthy Eating Index (HEI) between three months after the start of the intervention and baseline: HEI was coded as a continuous variable per unit of the index. The Healthy Eating Index was calculated using the United States Department of Agriculture’s multiple-pass method [93, 94] based on the average of two 24-hour food recalls conducted a week apart. The 24-hour food recalls were collected by the dietitians and then analyzed through diet analysis software
from the Elisabeth Stewart Hands and Associates (ESHA) Research by collaborators at the University of Guelph. Refer to Appendix D for the breakdown of the “adequacy” and “moderation” components and the ranges of each HEI component. The “adequacy components” were scored proportionally based on a patient’s recommended intake of grains, vegetables, fruits, milk and meat in a day [88]. The “moderation components” were scored based a patient’s recommended allowance of total fat, saturated fat, cholesterol, sodium and food variety [88]. The total scores for both the adequacy and moderation components were summed to produce the HEI score. The dietitian experts in the CHANGE demonstration project considered a five point change in HEI to be clinically significant.

3.3.6 Additional Descriptive Variables

Auxiliary variables were collected to provide additional baseline descriptive statistics. These variables were not used in the regression models but were used to inform the generation of the multiple imputation data sets.

1) Ethnicity: The ethnicity recorded was based on the judgment of the site investigator or research coordinator and not by self-identification. The category “US and Canadian Whites” was used as the reference category. There was not strong evidence that ethnicity was associated with a change in diet or exercise attendance so ethnicity was not included as a confounder.

2) Charlson co-morbidity index: This was coded as a continuous variable per unit of the index. The Charlson co-morbidity index was used to indicate the patient’s health status by quantifying co-morbid conditions. The index has been shown to predict a patient’s relative risk of hospital mortality in longitudinal studies [95]. The index was revised in 1994 to account for age [96]. The Charlson co-morbidity index is based on a specific list of conditions. It was determined that the only condition that would be clinically related to a difference in MetSyn score was diabetes which was already a confounder. Thus the Charlson co-morbidity index was not included as a confounder.
3) Stage of Readiness: The Stage of Readiness is an indicator of a patient’s readiness to change his/her behaviour[28]. In the CHANGE study, the Stage of Readiness was based on the physician’s assessment at screening and not on a self-assessment by the patient. This was coded as a categorical variable including “Pre-contemplative”, “Contemplative”, and “Action/Maintenance” phases; the latter was used as a reference category. The Stage of Readiness is based on the Transtheoretical model [28]. The association between Stage of Readiness and a change in MetSyn score is likely mediated by a change in diet contacts. Stage of Readiness was thus not included as a confounder.

3.4 Analysis

All statistical analyses were conducted using SAS® (Version 9.3, SAS Institute Inc., Cary North Carolina). Unless otherwise indicated, continuous variables are described by means and standard deviations and categorical variables are presented using counts and percentages. The study used a robust regression method (bisquare weight) with multiple imputation as its modelling strategy for all regression analyses including the mediation analysis. Robust regression was used because the data contained some outliers that violated the normality assumption and could have too large of an influence on regular ordinary least squares regression. The Robust regression method is more efficient than the ordinary least squares in the presence of influential observations [97, 98]. The ordinary least square method was initially used to check linearity assumptions and perform diagnostics for influential observations [99]. Collinearity diagnostics were also conducted to determine potential collinearity between kinesiologist visits and dietitian contacts using the ordinary least square model.

Multiple imputation was used because many patients were missing some or all of their outcomes but the missing outcomes were correlated with other non-missing variables. This increases the statistical efficiency and reduces potential bias [100]. The multiple imputation used the Markov chain Monte Carlo method [101-103] to randomly impute missing values. One hundred imputations of the robust regression were conducted and the resulting datasets were used for the analyses. The multiple imputations were
informed based on the following covariates: site, age, sex, ethnicity, body mass index, Charlson co-
morbidity index, diabetes status, depression status, working status, Stage of Readiness, baseline waist
circumference, month 3 waist circumference, baseline blood pressure, month three blood pressure,
baseline fasting blood glucose, month three fasting blood glucose, baseline triglycerides, month three
triglycerides, baseline VO₂max, month three VO₂max, baseline HEI, month three HEI and baseline
medication prescriptions for elevated blood pressure, elevated fasting blood glucose and elevated
triglycerides. Each of the 100 imputed datasets were analyzed separately and then the estimates were
combined into a single set of estimates using Rubin’s rules [104]. This approach accounts for the
uncertainty due to missing data in the standard error (and thus confidence interval and p-value) estimates.

3.4.1 Descriptive Statistics

Descriptive statistics were used to present the baseline patient characteristics as well as the
MetSyn criteria across the study population. Descriptive statistics for the exposure variables (kinesiologist
visits, dietitian contacts) were also provided. The relationship between kinesiologist visits and dietitian
contacts was examined graphically. The outcome, change in MetSyn score, was presented along with
changes in MetSyn components. The determination of the effect size of the MetSyn changes were based
on the work of Fleming [20]. Baseline and month three values were presented and differences tested using
the paired t-test. The 95% confidence interval around the mean change in MetSyn score was provided.
For mediation variables, change in VO₂max and change in HEI, in addition to presenting means, baseline
and month three values were given and differences tested using the paired t-test; 95% confidence intervals
around the mean changes are provided. The relationships between changes in VO₂max and HEI to their
respective baselines were examined by plotting the values. The relationships between kinesiologist visits,
change in VO₂max and change in MetSyn score were examined graphically. The relationships between
dietitian contacts, change in HEI and change in MetSyn score were also examined graphically.
3.4.2 Regression Modelling

A multiple linear regression model was created to compare the kinesiologist visits and dietitian contacts to the change in MetSyn. The model adjusted for the confounders and precision variables as shown in the conceptual model (Figure 1). The conceptual depiction of the models distinguishes covariates included to reduce confounding (confounders) from covariates included to increase precision of the estimates (precision variables) although they are handled in the same way in the modelling process.

There were three models: crude unadjusted, partially adjusted (adjusted for kinesiologist visits or dietitian contacts) and fully adjusted (adjusted for the confounders and precision variables listed in Figure 1).
Figure 1: Conceptual Model
3.4.2.1 Missing Data Description

A patient flow diagram outlining the degree of missing data was created. Patients who had all month three data available were considered “Complete Cases”. Patients who had at least one variable missing at month three (VO₂max, HEI and/or a component used to calculate the MetSyn score) were considered “Incomplete Cases”. Finally patients who had no month three data were considered to have “Dropped Out” of the study. Differences in baseline variables across categories of missing data were tested using Chi-square. Continuous variables were tested using one way ANOVA.

3.4.3 Mediation Analysis

Where either kinesiologist visits or dietitian contacts (model 1 and 2 respectively) were found to be significantly associated with the outcome, a mediation analysis was conducted to determine if the association was mediated through a change in VO₂max (an overall measure of aerobic exercise intervention) or a change in HEI scores (a measure of overall diet quality) (model 3 and 4 respectively) (Figure 1). The Baron and Kenny method was applied to the mediation analysis (Figure 2 and 3). The direct path (Path C) was tested with a simple model using either the kinesiologist visits or dietitian contacts as the independent variable and the change in MetSyn score as the dependent variable. The mediation models were only adjusted for the baseline MetSyn score and the baseline mediation variable because the change was highly dependent on the initial value. Patients who have a high initial VO₂max or HEI have less room for improvement. The mediation effect was examined based on three models as per Baron and Kenny [105]: 1) change in the mediation variable (VO₂max/HEI) as an outcome and kinesiologist visits/dietitian contacts as an exposure (Path A), 2) change in MetSyn score as an outcome and change in the mediation variable (VO₂max/HEI) as an exposure (Path B), and 3) change in MetSyn Score as an outcome and both the change in the mediation variable (VO₂max /HEI) as well as kinesiologist visits/dietitian contacts as an exposure (Path C prime). If the potential mediator met the criteria for all three mediation models, the amount of mediation or “indirect effect” was measured based on the difference in the effect of the exposure (kinesiologist visits or dietitian contacts) before and after
adjusting for the mediator variable (VO₂max/HEI). The mediation effect was also expressed as the percent decrease in the effect of the exposure after controlling for the mediation. Bootstrapping is the recommended standard to determine statistical significance of mediation [106, 107]. 10,000 bootstrap samples were drawn and applied to each of the first 10 multiple imputation samples. After the 10 multiple imputations were combined within each bootstrap sample using Rubin’s rules [104], the 10,000 bootstrap samples were used to estimate the distribution of the indirect effect. In particular, the 95% confidence intervals of the indirect effect were estimated by the 2.5th to 97.5th percentile of the bootstrap samples and the p-values were estimated by the Z-test using the standard deviation of the bootstrap samples to estimate the standard error of the indirect effect [108].

Figure 2: Kinesiologist Visit Mediation Models
3.4.4 Sensitivity Analysis

Three sensitivity analyses were conducted.

1) Dietitian Visits Versus Dietitian Contacts

To determine the impact of using dietitian visits (face-to-face only) as the exposure instead of dietitian contacts (which included face-to-face, telephone and web/email contact) a sensitivity analysis was conducted. Dietitian visits was plotted against kinesiologist visits and the primary regression model was reanalyzed using dietitian visits.

2) Different Modelling Methods

To determine the impact of the regression method as well as the use of multiple imputation, a sensitivity analysis was conducted. Four regression methods were compared: ordinary least square, ordinary least square with patients having a Cook’s D 0.016 or higher removed, robust regression using a bisquare weight and a robust regression using a bisquare weight with multiple imputation.

3) Missing Mediation Variables

The mediation variables had a high level of missing data. To determine the impact of imputing values in the mediation analysis, a sensitivity analysis was conducted using only complete cases (patients with both the mediator of interest and the change in MetSyn score).
Chapter 4: Results

4.1 Patient Characteristics

A total of 305 patients were enrolled in the study (Edmonton n=152, Toronto n=60, Laval n=93). As shown in Table 2, patients had a mean age of 59±9.7 years, 51.1% were women, and over three quarters were classified as “US and Canadian Whites”.

Patients had a mean weight of 90.6±14.9 kg, mean body mass index 31.8±3.4 kg/m² and mean waist circumference of 107.2±9.7cm (Table 2). They had few co-morbidities and had a mean Charlson co-morbidity index of 0.8±0.9 (range of 1-4). Type 2 diabetes was highly prevalent in this patient group at 51.8%. In terms of the Stage of Readiness, the majority of the patients were either in the “Contemplative” or “Action/Maintenance” phase (44.3% and 52.5% respectively).
Table 2: Patient Characteristics at Baseline

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Overall mean±SD or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>305 (100%)</td>
</tr>
<tr>
<td>Age (Range 35-76 years)</td>
<td>59.1±9.7</td>
</tr>
<tr>
<td>Ethnicity†</td>
<td></td>
</tr>
<tr>
<td>Europids, Whites, sub-Saharan Africans, Mediterranean, middle east/Arab*</td>
<td>52 (17.0%)</td>
</tr>
<tr>
<td>Asian and South Central Americans</td>
<td>15 (4.9%)</td>
</tr>
<tr>
<td>US and Canadian Whites</td>
<td>233 (76.4%)</td>
</tr>
<tr>
<td>Ethnicity unclear</td>
<td>5 (1.6%)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>90.6 ± 14.9</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>31.8± 3.4</td>
</tr>
<tr>
<td>Charlson Co-morbidity Score</td>
<td>0.8± 0.9</td>
</tr>
<tr>
<td>Diabetes (Type 2)</td>
<td>158 (51.8%)</td>
</tr>
<tr>
<td>Active Depression</td>
<td>29 (9.5%)</td>
</tr>
<tr>
<td>Metabolic Syndrome Score</td>
<td>2.2 ± 1.0</td>
</tr>
<tr>
<td>Working Status</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>181 (59.3%)</td>
</tr>
<tr>
<td>Retired</td>
<td>102 (33.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>22 (7.2%)</td>
</tr>
<tr>
<td>Stage of Readiness</td>
<td></td>
</tr>
<tr>
<td>Pre-contemplative</td>
<td>10 (3.3%)</td>
</tr>
<tr>
<td>Contemplative</td>
<td>135 (44.3%)</td>
</tr>
<tr>
<td>Action/Maintenance</td>
<td>160 (52.5%)</td>
</tr>
</tbody>
</table>

† Ethnicity categories were based on the groupings used to determine the appropriate abdominal circumference ranges to diagnose metabolic syndrome. Specific ethnic categories were not available.
**“Whites” in this category referred to Caucasians not from the US or Canada.

4.1.1 Baseline Metabolic Syndrome Criteria and Score

Table 3 describes baseline MetSyn criteria, the associated laboratory values and the use of pharmacotherapy. At baseline, 30.2% of patients had elevated blood pressure. At that time, 73.1% of all patients were prescribed antihypertensive medications taking a mean of 1.4 medications each. There were 77.4% with elevated fasting blood glucose with 40.7% prescribed glucose control medication taking on average 1.6 medications each. Few patients were on Fibrates (3.6%) to treat elevated triglycerides.
Almost all patients had a high abdominal circumference (95.7%). The mean MetSyn score was 2.2±1.0 at baseline.

Table 3: Baseline Metabolic Syndrome Criteria

<table>
<thead>
<tr>
<th>Metabolic Syndrome Criteria</th>
<th>Overall mean±SD or n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Pressure ≥ 130/85 mmHg</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>92 (30.2%)</td>
</tr>
<tr>
<td>Mean Systolic Pressure (mmHg)</td>
<td>133.6±14.5</td>
</tr>
<tr>
<td>Mean Diastolic Pressure (mmHg)</td>
<td>80.7±9.1</td>
</tr>
<tr>
<td><strong>Receiving Pharmacotherapy for elevated blood pressure</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>223 (73.1%)</td>
</tr>
<tr>
<td>Mean Antihypertensive Medications per patient (n=223)</td>
<td>1.4±0.7</td>
</tr>
<tr>
<td>Mean Diuretic Medications per patient (n=223)</td>
<td>0.5±0.6</td>
</tr>
<tr>
<td><strong>Fasting Blood Glucose &gt; 5.6 mmol/L</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>236 (77.4%)</td>
</tr>
<tr>
<td>Mean Fasting Blood Glucose (mmol/L)</td>
<td>6.6±1.5</td>
</tr>
<tr>
<td><strong>Receiving pharmacotherapy for elevated blood glucose levels</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>124 (40.7%)</td>
</tr>
<tr>
<td>Mean Glucose Control Medications per patient (n=124)</td>
<td>1.6±0.8</td>
</tr>
<tr>
<td><strong>Triglyceride of &gt; 1.7 mmol/L</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>188 (61.2%)</td>
</tr>
<tr>
<td>Mean triglycerides (mmol/L)</td>
<td>2.2±1.7</td>
</tr>
<tr>
<td><strong>Receiving pharmacotherapy for elevated triglycerides</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>11 (3.6%)</td>
</tr>
<tr>
<td>Mean Triglyceride Medications per patient (n=11)</td>
<td>1±0</td>
</tr>
<tr>
<td><strong>HDL-C &lt; 1.0 mmol/L Males and &lt;1.3 mmol/L females</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>143 (46.9%)</td>
</tr>
<tr>
<td>Mean HDL-C (mmol/L)</td>
<td>1.2±0.3</td>
</tr>
<tr>
<td><strong>High Abdominal Circumference</strong></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>292 (95.7%)</td>
</tr>
<tr>
<td>Mean abdominal circumference (cm)</td>
<td>107.2±9.7</td>
</tr>
</tbody>
</table>

Kinesiologist Visits and Dietitian Contacts

The majority of face-to-face visits/contacts occurred simultaneously. Patients had a mean of 9.3±3.3 visits (range 0-16) with the kinesiologist and a mean of 11.1±3.3 contacts with the dietitian (range 0-16) before the month three follow-up. Almost all patients had at least one face-to-face contact with the
dietitian, with a mean of 9.9±3.0 face-to-face contacts per person. Only 44.9% of patients had telephone contacts with the dietitian. The mean number of telephone contacts was 2.4±1.7 per person. Most patients had more dietitian contacts than kinesiologist visits (Figure 4).

![Figure 4: Kinesiologist Visits Versus Dietitian Contacts by Patient (n=305)](image)

### 4.2 Change in Metabolic Syndrome Score

For the 243 patients who had data available to calculate MetSyn score at both baseline and month three, the mean MetSyn score was 2.2±1.0 at baseline and 1.7±1.1 after three months of intervention. The mean change in metabolic syndrome score of -0.5±0.8 was significant (Table 4) but there was wide variation in the change. This drop in the score corresponds to a decrease in odds of incident diabetes of 43% (OR = 0.57) in men and 51% (OR = 0.49) in women over a 9-year period, this is considered a medium effect size. This change in MetSyn score also corresponds to a reduction in the odds of incident coronary heart disease and cardiovascular disease of 25% (OR = 0.75) in men and 33% (OR = 0.77) in women.
There was also a large statistically significant drop in the systolic blood pressure (-7.5 mmHg [CI -9.2, -5.9]) and small but statistically significant drops in fasting blood glucose (-0.2 mmol/L [CI -0.3, -0.0]), abdominal circumference (-2.9 cm [CI -3.5, -2.3]) and triglycerides (-0.3 mmol/L [CI -0.5, -0.2]).

Table 4: Change in Metabolic Syndrome Score

<table>
<thead>
<tr>
<th>Metabolic Syndrome Criteria</th>
<th>n†</th>
<th>Baseline mean±SD</th>
<th>Month 3 mean±SD</th>
<th>Change mean±SD</th>
<th>Change [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Metabolic Syndrome Score</td>
<td>243</td>
<td>2.2 ± 1.0</td>
<td>1.7 ± 1.1</td>
<td>-0.5 ± 0.8</td>
<td>[-0.6, -0.4]*</td>
</tr>
<tr>
<td>Mean Systolic Pressure (mmHg)</td>
<td>254</td>
<td>134.4± 14.9</td>
<td>126.8± 12.9</td>
<td>-7.5± 13.3</td>
<td>[-9.2, -5.9]*</td>
</tr>
<tr>
<td>Mean Fasting Blood Glucose (mmol/L)</td>
<td>255</td>
<td>6.5± 1.5</td>
<td>6.4±1.4</td>
<td>-0.2± 0.1</td>
<td>[-0.3, 0.0]*</td>
</tr>
<tr>
<td>Mean triglycerides (mmol/L)</td>
<td>259</td>
<td>2.2± 1.7</td>
<td>1.9±1.1</td>
<td>-0.3± 1.0</td>
<td>[-0.45, -0.20]*</td>
</tr>
<tr>
<td>Mean abdominal circumference (cm)</td>
<td>265</td>
<td>107.7± 9.3</td>
<td>104.8±9.4</td>
<td>-2.9± 4.7</td>
<td>[-3.5, -2.3]*</td>
</tr>
</tbody>
</table>

*P-value < 0.05 by paired t-test
† The n was based on patients with both baseline and month 3 data available.

4.3 Mediation Variables

Only 225 patients had both the change in VO₂ max and change in MetSyn score recorded and 190 patients had both the change in HEI and change in MetSyn score recorded. The overall VO₂ max was 32.7±7.0 at baseline and 35.5±7.0 at month three with a statistically significant mean paired change of 2.8±3.1 (Table 5). The overall mean HEI score was 58.1±14.3 at baseline and 69.4±12.4 at month three. There was a significant overall mean change in paired HEI of 11.4±14.9 (Table 5). The relationships between changes in VO₂ max and HEI to their respective baseline values were examined by plotting the values (Appendix E). Baseline VO₂ max and HEI were negatively correlated with the change in VO₂ max and HEI respectively.
Table 5: Paired Maximal Oxygen Consumption and Paired Healthy Eating Index

<table>
<thead>
<tr>
<th>Site</th>
<th>n†</th>
<th>Baseline mean±SD</th>
<th>Month 3 mean±SD</th>
<th>Change mean±SD</th>
<th>Change [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂ max</td>
<td>225</td>
<td>32.7±7.0</td>
<td>35.5±7.0</td>
<td>2.8±3.1</td>
<td>[2.4, 3.2]*</td>
</tr>
<tr>
<td>HEI</td>
<td>190</td>
<td>58.1±14.3</td>
<td>69.4±12.4</td>
<td>11.4±14.9</td>
<td>[9.1, 13.4]*</td>
</tr>
</tbody>
</table>

*P-value < 0.05 by paired t-test
† The n was based on patients with baseline and month three data available for the mediation variable (VO₂ max or HEI) and MetSyn Score

4.4 Relationship between kinesiologist visits, change in VO₂ max and change in MetSyn Score

When the number of kinesiologist visits was plotted against the change in MetSyn score (Figure 5), it was found to be weakly associated with an improvement (decrease) in MetSyn score. There was a positive relationship observed when the kinesiologist visits were plotted against the change in VO₂ max (r = 0.03) (Figure 6). Improvement (increase) in VO₂ max was associated with an improvement (decrease) in MetSyn score (Figure 7).

![Figure 5: Change in MetSyn Score Versus Kinesiologist Visits (n=305)](image)
Figure 6: Change in VO\textsubscript{2} max Versus Kinesiologist Visits (n=305)

![Graph showing the relationship between Kinesiologist Visits and Change in VO\textsubscript{2} max. The correlation coefficient is r = 0.10 with p = 0.12.]

Figure 7: Change in MetSyn Score Versus Change in VO\textsubscript{2} max (n=305)

![Graph showing the relationship between Change in VO\textsubscript{2} max and Change in MetSyn Score. The correlation coefficient is r = -0.10 with p = 0.12.]

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4.5 Relationship between dietitian contacts, change in HEI and change in MetSyn Score

The number of dietitian contacts (Figure 8) was weakly associated with an improvement (decrease) in MetSyn score. A positive relationship was observed between dietitian contacts and change in HEI (Figure 9). Improvement (increase) in HEI was associated with an improvement (decrease) in MetSyn score (Figure 10).

Figure 8: Change in MetSyn score Versus Dietitian Contacts (n=305)
Figure 9: Change in HEI Versus Dietitian Contacts (n=305)

Figure 10: Change in MetSyn Score Versus Change in HEI (n=305)
4.6 Regression Models

The studentized residuals were not normally distributed, violating one of the linear regression assumptions (Appendix F). Based on the QQ plot, this appeared to be due to a few significant outliers. Outlier and influential diagnostics revealed significant influential observations (Appendix G). Kinesiologist visits were collinear with dietitian contacts (Pearson’s Coefficient of 0.61) but variance inflation factor for both was about 1.5 and thus was not expected to substantially bias the model (Appendix H).

The parameter estimates for the fully adjusted regression model are provided in Table 6. Site, baseline body mass index (BMI) and MetSyn baseline score were highly significantly associated with change in MetSyn score. Patients in Laval had significantly better improvements (decrease) in MetSyn score than patients in Edmonton, but Toronto patients had worse MetSyn improvements compared to Edmonton patients. High BMI was associated with worse change in MetSyn score. Every unit increase in BMI was associated with a 0.06 [CI 0.04, 0.09] (worse) change in MetSyn score. A high baseline MetSyn score was significantly associated with the outcome. A one unit increase in baseline MetSyn score was associated with an additional -0.43 [CI -0.52, -0.34] improvement (decrease) in MetSyn score by month three. Age and depression were borderline significant and may be important predictors to explain the association between dietitian/kinesiologist contacts and the change in MetSyn score.

In the crude unadjusted model, kinesiologist visits were not significantly associated with a -0.031 [CI -0.07, 0.00] improvement (decrease) in MetSyn score per kinesiologist visit. The strength of this association decreased and was not statistically significant after adjustment for dietitian contacts (partially adjusted model) or after adjustment for a priori potential confounders and precision variables (fully adjusted model) (Table 6).

The number of dietitian contacts was significantly associated with an improvement (decrease) in MetSyn score (-0.06 [CI -0.10, -0.02] per dietitian contact in the crude model). The strength of association was similar to the partially adjusted model and weaker in the fully adjusted model. In the
fully adjusted model, MetSyn score decreased (improved) by an additional 0.048 [CI -0.09, -0.01] for every dietitian contact (Table 6).
Table 6: Robust Linear Regression Models with Multiple Imputation To Examine The Relationship Between Kinesiologist Visits/Dietitian Contacts and Change in Metabolic Syndrome Score

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Crude Unadjusted(^1)</th>
<th>Partially Adjusted(^2)</th>
<th>Fully Adjusted(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parameter [95% CI]</td>
<td>p</td>
<td>Parameter [95% CI]</td>
</tr>
<tr>
<td>(n=305)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinesiologist Visits</td>
<td>-0.031 [-0.07, 0.00]</td>
<td>0.09</td>
<td>0.006 [-0.04, 0.05]</td>
</tr>
<tr>
<td>Dietitian Contacts</td>
<td>-0.060 [-0.10, -0.02]</td>
<td>&lt;0.01</td>
<td>-0.064 [-0.11, -0.02]</td>
</tr>
<tr>
<td>Site: Toronto(^4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site: Laval(^5)</td>
<td></td>
<td></td>
<td>-0.34 [-0.57, -0.1]</td>
</tr>
<tr>
<td>Age (per year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex(^6)</td>
<td>-0.01 [-0.18, 0.15]</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>BMI (per unit)</td>
<td>0.06 [0.04, 0.09]</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Depression(^7)</td>
<td>0.25 [-0.07, 0.57]</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Diabetes(^8)</td>
<td>0.15 [-0.1, 0.39]</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Work: Unemployed(^9)</td>
<td>-0.05 [-0.24, 0.14]</td>
<td>0.63</td>
<td></td>
</tr>
<tr>
<td>Work: Other(^10)</td>
<td>0.25 [-0.66, 1.16]</td>
<td>0.59</td>
<td></td>
</tr>
<tr>
<td>Glucose Medication(^11)</td>
<td>0.08 [-0.17, 0.33]</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>Antihypertensive Medication(^12)</td>
<td>-0.12 [-0.32, 0.08]</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Triglyceride Medication(^13)</td>
<td>-0.15 [-0.6, 0.31]</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>MetSyn Baseline Score(^14)</td>
<td>-0.43 [-0.52, -0.34]</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) The crude model is unadjusted.
\(^2\) This model is adjusted for either kinesiologist visits or dietitian contacts
\(^3\) This model is adjusted for either kinesiologist visits or dietitian contacts as well as site, age, sex, BMI, depression status, diabetes status, working status, glucose control medication, antihypertensive medication, triglyceride medication and baseline MetSyn score
\(^4\) Reference site was Edmonton
\(^5\) Reference was male
\(^6\) Reference was no diagnosis of depression at baseline
\(^7\) Reference was no diagnosis of diabetes at baseline
\(^8\) Reference working status was employed
\(^9\) Reference was no medication use
\(^10\) MetSyn Score is standardized to have a mean of zero and a standard deviation of one
* CI stands for Confidence Interval
4.6.1 Missing Data

As shown in Figure 11, at the month three follow-up, 192 (63.0%) patients completed both the VO$_2$max and HEI assessments, 19 (6.2%) patients were missing VO$_2$max, 55 (18.0%) patients were missing HEI and 39 (12.8%) patients were missing both VO$_2$max and HEI. There were 175 (57.4%) patients with all month three data (VO$_2$max, HEI and MetSyn score). These were considered “Complete Cases”. Patients who had at least one variable missing at month three (VO$_2$max, HEI and/or a component used to calculate the MetSyn score) were considered “Incomplete Cases”, which accounted for 95 (31.1%) of the patients. Finally there were 35 (11.5%) patients who had no month three data and were considered to have “Dropped Out” of the study.

Comparative analysis of the patient baseline characteristics (Appendix I) and baseline MetSyn criteria (Appendix J) by the three missing data categories revealed that the characteristics and baseline MetSyn criteria were similar in all three groups with the exception of the presence of baseline active depression status and Stage of Readiness. A greater proportion of patients who “Dropped Out” of the study had active depression (22.9%) compared to patients in the “Complete Cases” group (8.0%) (p-value = 0.03). Stage of Readiness revealed that patients who “Dropped Out” of the study were more likely to be in the “Action/ Maintenance” phase than the “Complete Cases” and “Incomplete Cases” (71.4% compared to only 56.0% and 38.9% respectively, p-value <0.01). A final analysis of the patients’ history of cardiovascular disease and cardiovascular risk factors across the three groups of patients classified by their missing data showed that patients with active angina at baseline were statistically more likely to be “Incomplete Cases”; however this was only based on a total of seven active angina cases (Appendix K).

There was significant proportion of month three VO$_2$max and HEI data missing. Almost a third (30.8%) of the patients were missing a month three HEI and 19.0% of patients were missing a month three VO$_2$max (Figure 12).
Figure 11: Patient Flow Diagram
Figure 12: Month Three Follow-Up Data Availability
4.7 Mediation Models

There were 190 patients with complete data for the change in HEI mediation analysis (Figure 12). The regression model did not find a significant association between kinesiologist visits and change MetSyn score so the mediation analysis of VO₂max was not explored. Conversely there was a significant association between dietitian contacts and change in MetSyn score. The results of the mediation models of the Baron and Kenny approach are displayed in Figure 13. The change in HEI was scaled per point on the HEI scale.

The mediation models met the criteria set out by Baron and Kenny [105]. Both “Path A” and “Path B” were highly significant. Each dietitian contact was associated with an increased improvement in HEI score of 0.85 [95% CI 0.34, 1.5] (Path A) and for every point improvement on the HEI scale, the change in MetSyn score dropped by an additional 0.015 [95% CI 0.01, 0.02] (Path B). In the direct “Path C”, each dietitian contact was associated with an additional 0.056 [95% CI 0.02, 0.09] drop in MetSyn score. After adjusting for change in HEI, the association decreased to a 0.048 [95% CI 0.01, 0.08] improvement (decrease) in MetSyn score change. Based on the bootstrapped samples, the mediation effect was statistically significant, but small – 0.007 [CI –0.014, –0.002]. This corresponded to an approximately 12.5% decrease in the effect of the exposure after controlling for the mediation. HEI only mediated a small portion if any of the association between dietitian contacts and change in MetSyn score.
Figure 13: Mediation Analysis of Healthy Eating Index In The Relationship Between Dietitian Contacts and Change in MetSyn Score (with Multiple Imputation) (n=305)
4.7.1 Sensitivity Analyses

1) Dietitian visits vs. Dietitian contacts

The results of the modelling did not change significantly when only face-to-face dietitian visits were modelled (Appendix L). The parameter estimates for dietitian contacts and dietitian visits (face-to-face) were compared in the fully adjusted models (Appendix L). The strength and statistical significance of all predictors except site remained similar regardless of whether dietitian visits or contacts was used (dietitian visits -0.08 [-0.14, -0.02] compared to dietitian contacts -0.05 [CI -0.09, -0.01]). The change in the strength of association between the kinesiologist visits and the change in MetSyn score was minimal (0.02 [-0.02, 0.05] in the dietitian contacts model and 0.03 [-0.02, 0.08] in the dietitian visits model). The Laval site was significantly associated with a MetSyn improvement (decrease) compared to the Edmonton site when the number of dietitian contacts was the exposure. When dietitian visits was the exposure, the Laval site was no longer significant but the Toronto site patients showed worsening of MetSyn compared to patients at the Edmonton site.

2) Different Modelling Methods

Different modelling methods did not impact the conclusions of the regression models (Appendix M). The strength of the parameter estimates and the significance was nearly identical across all four modelling methods and across the three different models (crude unadjusted, partially adjusted and fully adjusted) (Appendix M).

3) Missing Mediation Variables

The magnitude of the mediation effect was identical in the imputed model (n=305) and the complete case model (n=190), but it was not statistically significant in the complete case model (– 0.007 [CI –0.024, 0.003]) (Appendix O). The parameter estimates of path C and C’ respectively were -0.056 and -0.048 in the imputed model and -0.069 and -0.061 in the complete case model.
Chapter 5: Discussion and Conclusion

This chapter will highlight the key findings, strengths, limitations, generalizability and implications for future research.

5.1 Key Findings

- In three months, the average decrease in MetSyn score was 0.5, which is about one half of the baseline (and follow-up) standard deviation.
- There were also improvements in the average VO₂ max and HEI over the three months.
- The number of kinesiologist visits was not associated with a change in MetSyn score.
- The number of dietitian contacts was significantly associated with a decrease in MetSyn risk score, and this association was partially mediated by a change in the HEI.

5.1.1 Change in MetSyn Score Components

The largest clinically significant change was in systolic blood pressure. The change after three months of intervention was higher than other lifestyle intervention studies that only demonstrated a moderate effect after twelve months of intervention [11, 47, 59]. Other lifestyle intervention studies also showed similar small effect sizes to the present study related to changes in fasting blood glucose, triglycerides and abdominal circumference [11, 47, 59].

5.1.2 Dietitian Contacts and Change in Metabolic Syndrome Score

Each additional dietitian contact was associated with an additional 0.048 [CI -0.09, -0.01] decrease in MetSyn score. To put this value into context, the overall mean change in MetSyn score was -0.5 [CI-0.6, -0.4]. To the best of our knowledge, the association between dietitian contacts and the change in MetSyn score has not been previously studied. The clinical effect of dietitian contacts on incident diabetes, coronary heart disease and cardiovascular disease is likely small.

5.1.2.1 Mediation Effect of the Healthy Eating Index
Change in the Healthy Eating Index (HEI) only mediated a small portion of the association between dietitian visits and change in MetSyn suggesting that there may be other factors done by dietitians that are not reflected by HEI that are impacting the outcome. Future research is needed to investigate if these other uncontrolled factors also mediate the association between dietitian contacts and a change in MetSyn score.

5.1.3 Sensitivity Analysis

1) The sensitivity analysis comparing the difference of dietitian visits versus dietitian contacts found no significant difference when the exposure was limited to face-to-face contacts (dietitian visits).

2) The different modeling methods as well as the use of multiple imputation did not affect the strength or significance of the associations. This suggests that the method chosen did not introduce bias into the study results.

3) Missing variables was not a significant concern for the mediation analysis. The magnitude and the significance of the effect estimate did not change in the sensitivity analysis.

5.2 Limitations

5.2.1 Missing Data

Although all baseline variables were available, many patients were missing month three follow-up data (VO2max, HEI and MetSyn components). The majority of baseline characteristics were similar between “Complete Cases”, “Incomplete Cases” and patients who “Dropped Out” with the exception of baseline depression status and Stage of Readiness. A disproportionate percent of patients were depressed at baseline and were on the “Action/Maintenance” phase in terms of their Stage of Readiness. Baseline depression is a known barrier to adherence to lifestyle interventions [40], but the Stage of Readiness finding was unexpected. It may be related to how the program was implemented. Most if not all in-person visits with the kinesiologist and dietitian occurred during traditional work hours (9am-5pm on weekdays)
which may conflict with patient schedules. Patients in the “Action/Maintenance” phase at baseline may be more likely to have already adopted new exercise and/or diet behaviours outside of the CHANGE demonstration program (such as obtaining a gym membership). If patients felt the time commitment for the CHANGE program was too onerous, they may have opted to drop the program and continue to exercise/diet on their own. Future studies should consider the timing of the intervention.

The significant missing month three data increased the noise in the multiple imputation model [100] and could introduce bias if the assumptions of the imputation model are not correct. Multiple imputation was used because many patients had at least some of the month three MetSyn components used to derive the MetSyn score that would be informative to imputing other month three MetSyn components. The mediator variables (change in VO2max and change in HEI) did not have variables available that would be highly informative to their imputation. Due to this limitation, it was important to conduct a sensitivity analysis to determine if complete cases analysis would provide different results than the imputed analysis.

5.2.2 Regression to the Mean

The CHANGE demonstration project recruited patients with MetSyn. This represented a portion of the population with overall high blood pressure, high fasting blood glucose, high triglycerides, low HDL-C and/or high abdominal circumference. Each of these measurements has a degree of random error. After some time, if the patients were to be retested for each of these variables, the values might be closer to the population mean. This statistical phenomenon is called regression to the mean [109]. With no control group (non-intervention group), it is not possible to determine the magnitude of the regression to the mean effect.

Based on a randomized controlled trial of a lifestyle intervention to a standard of care control group in patients with at least two MetSyn criteria, the effect of regression to the mean is expected to be minimal [11]. In that study, patients in the control group (no intervention) had small but statistically significantly worse abdominal circumference, systolic blood pressure and HDL-C after a year. The
control group had no statistically significant changes in fasting blood glucose and triglyceride levels after
a year.

5.2.3 Reverse Causality

The objectives of this study assumed that changing the frequency of kinesiologist visits and
dietitian contacts would change a patient’s MetSyn score. A reverse relationship whereby the patient
increases or decreases the frequency of visits and contacts based on results with the program is also
possible. Patients that self-monitor their loss in weight can visibly see and feel a change in waist
circumference and many patients routinely check their blood pressure and glucose levels. It is possible
that there was a reverse relationship given the literature on self-monitoring practices of diet, exercise and
weight which shows that self-monitoring has a positive impact on weight loss and weight loss
maintenance [110]. In a randomized controlled trial, adherence to self-monitoring of weight loss was
associated with better weight loss maintenance than the control group [111]. Weight and weight loss
maintenance are related to abdominal obesity. These studies suggest that self-monitoring may be a
potential confounder as opposed to a mechanism for reverse causality. Self-monitoring was not measured
in this study and was not controlled for in the analysis.

5.2.4 Timing of Exposure

This study has assumed that there is a linear relationship between change in MetSyn score and the
frequency of contacts with the dietitian/kinesiologist. It also assumed that the association of total number
of dietitian and kinesiologist contacts/visits to change in MetSyn score is the same regardless of when the
contacts/visits occurred. Based on this assumption, ten dietitian visits over two weeks is considered
equivalent to ten visits across three months. There does not seem to be strong variation in timing but this
should be accounted for in future studies.

5.2.5 Unmeasured Confounders
This study is dependent on secondary data and thus some critical elements were not measured. Some confounders of particular concern included:

1) Baseline Smoking Status: Smoking is associated with triglycerides, HDL and glucose levels [10, 37, 112]. Smoking status was only recorded in the study if it was in the patient’s medical chart. Since the patient was not asked directly, smoking status was not included due to the suspected poor quality of the data.

2) Education: In a randomized controlled trial of lifestyle intervention in MetSyn patients, education level was identified as an important confounder [11]. Educational level has an inverse relationship with household income which is related to available free time and motivation to comply with study visits as well as overall health [37]. Since education was not captured in the CHANGE demonstration project, it could not be included in the analyses.

3) Changes during the intervention: MetSyn Medication changes and new diagnosis that occurred during the study intervention window was not captured.

5.2.6 Measurements and Misclassification

Medical Charts

The majority of data elements were based on the patient’s medical charts which may be a source of misclassification, in particular for the confounder’s baseline depression status and baseline MetSyn medication use. New patients often do not have a complete medical history or may have multiple primary care physicians. The CHANGE demonstration project did not screen for active depression and may have missed undiagnosed patients. In addition, baseline MetSyn medication use was based on what was prescribed. This does not capture the patient’s actual adherence to MetSyn medications which was not ascertained.

Measurements Errors
The abdominal circumference conducted at baseline was usually completed by a family physician or nurse while the month three follow-up waist circumference was completed by the kinesiologist. The sites were provided specific instructions on how to measure the abdominal circumference but were not trained in person. There may have been inter-rater measurement error. Measurements of waist circumference have strong intra-rater reliability [113, 114] but weaker inter-rater reliability [115, 116].

**Procedural Issues**

The blood glucose measurements were based on the assumption that all patients fasted 8-12 hours before the blood sample was taken. Some of the influential outliers had a higher glucose measurement than baseline despite significant improvements in other MetSyn criteria. It is possible that these patients did not fast as instructed resulting in higher fasting blood glucose measurements; this could not be verified. These outliers would decrease model fit and attenuate the association between the dietitian contacts and kinesiologist visits to the change in MetSyn score.

**Lack of precise tracking of the intervention**

As previously mentioned, kinesiologists did not record email or telephone contacts they had with patients, only face-to-face visits were recorded by each site. The study protocol allowed patients to have extra visits/contacts with the kinesiologist beyond the weekly face-to-face visits prescribed. Other personalized exercise programs based on weekly and monthly telephone calls to monitor progress and answer questions have shown small but statistically significant improvements in HDL-C and triglyceride levels after a year of intervention compared to a control group [117]. Telephone follow-ups have been shown to be effective in maintaining monthly adherence rates in low intensity exercise programs for as long as two years [118]. Therefore unrecorded contacts with kinesiologists would likely attenuate the association between kinesiologist visits and change in MetSyn score.

**Sensitivity of the measures**

The measures chosen were not highly sensitive which would attenuate the associations. Although used in other studies [76, 77], the number of contact sessions such as the kinesiologist visits and dietitian
contacts are crude measures of adherence and do not account for what was done at each visit/contact.

Some patients for example could not perform many exercises due to illness or injury.

The HEI is based on multiple “adequacy” and “moderation” components (Appendix D) such as “whole fruit” or “saturated fat” intake [25, 88]. Each component of the HEI score may have different strengths of association with a change in MetSyn score. Sodium for example has well established effects on blood pressure [60], and is a component of the MetSyn score and is worth a maximum of ten points out of a hundred in the Healthy Eating Index. On the other hand “Milk and Alternatives” is also worth a maximum of 10 points but its degree of association to a change in MetSyn score is less clear. This lack of sensitivity would increase the noise and attenuate the mediation effect. Similarly, VO2max is a great overall measure of aerobic exercise but it does not reflect change due to resistance exercises [119].

**Validity of the MetSyn Score**

The MetSyn score was validated in a French population and has not been validated in Canada [86]. This may impact the calculation of the score and its interpretation. The MetSyn score is standardized based on the mean and standard errors of the abdominal circumference, systolic blood pressure, fasting blood glucose and triglyceride values from the cohort study in France [86]. The mean values from France are similar to the Canadian population but have a lower mean abdominal circumference and higher mean blood pressure [86, 89, 90]. The odds risk of MetSyn score on incident cardiovascular disease and diabetes were also based on the French cohort [86] and have not been studied in the Canadian context.

**5.3 Strengths**

To our knowledge, the CHANGE demonstration project was the first in Canada to be conducted in a primary care setting, with conditions and procedures that mimicked how dietitians and kinesiologists would typically work with their patients to provide individualized care. It captured the varying ways patient’s access health care across three different provinces in study centers with very different levels of resources. This improves the external validity of the study. The data was collected prospectively and had detailed data collection and analysis strategies. Multiple imputation was used to adjust for missing data
and sensitivity analysis were used to test assumptions in the study. The use of a continuous MetSyn score also provided increased precision than previous studies that relied on a binary definition of MetSyn [85-87]. The study was also well powered for its objectives (Appendix P).

5.3.1 Familiarity with the study

Roger Leung was intimately involved in the CHANGE demonstration project and has thorough understanding of the data. As the project assistant he created the case report forms, electronic data capture system, procedure manuals and various study tools used by the site and managed any procedural questions the study sites may have had. As the data manager and data analyst, Roger was also managed the quality of the data and generated periodic data analysis reports over the course of the demonstration project.

5.4 Generalizability

Although the goal of this study is to determine how to efficiently provide the CHANGE intervention to improve MetSyn, there are limitations to the generalizability of the conclusions:

1) Exclusion Criteria: There were many exclusion criteria which limited the generalizability of the findings. The CHANGE demonstration project did not keep records of all screened patients because the study sites considered it a significant burden. It is unclear how many patients met each of the exclusion criteria.

1) Ethnicity: Despite being conducted at three centers in three different provinces, half of the patients were recruited from Edmonton and at least 76% of the patients were “US and Canadian white”. These results may not be as applicable to a more multicultural population. Patients were included based on MetSyn status as per the harmonized guidelines [5, 6]. This may have been a source of misclassification. There were no instructions provided on how to differentiate ambiguous categories such as “Europid, white” versus “US and Canadian white”. Out of 305 patients, 233 patients (76.4%) were categorized as “US and Canadian whites” while 52 patients (17%) were categorized as “Europids, whites, Sub-Saharan Africans, Mediterranean, middle
east/Arab”. This limits the generalizability of the study findings. Furthermore, one of the criteria for MetSyn is abdominal circumference which has cut offs based on ethnicity [6]. If a patient was misclassified based on ethnicity, they may not have met the inclusion criteria for the study. This misclassification would not affect the MetSyn score which uses the continuous abdominal circumference measurement and is not adjusted for ethnicity.

2) Stage of Change: Stage of Readiness [28] was not an inclusion criteria, but investigators were instructed to counsel and “nudge” patients in the “pre-contemplative” stage until they were ready for action. The patients included may represent patients with high motivation to change at the onset.

5.5 Implications For Practice and Future Research

1) Month twelve follow-up data: The study should be repeated using month twelve data. The scope of this study was limited to the first three months of the intervention based on the availability of the data. The variation in kinesiologist visits and dietitian contacts will be greater over a year and there will be time for a greater change in MetSyn score. The results will not be directly comparable to the three month analysis because the intensity of the intervention changes after the first three months. Previous studies that analysed attendance focused on longer periods of intervention of one or two years [76, 77].

2) Cost effectiveness study: This study may provide the ground work for future studies to conduct cost-effectiveness studies with units in cost per change in MetSyn score. Kinesiologist visits tend to require a significant amount of resources in terms of personal time (an average visit takes 45 minutes to an hour) and equipment compared to dietitian visits which can be short telephone calls or emails.

3) Kinesiologist Contacts: If similar studies are conducted in the future, the telephone and email/web contacts with the kinesiologist should be recorded prospectively. This will allow direct comparisons to the impact of the number of dietitian contacts.
4) Mental Health: Mental health was identified as a barrier to completing the program by the research sites. Patients who dropped out of the study also had higher rates of depression. The Edmonton site was the only site to report having on site access to a mental health professional, but there were also significant wait times to access those services. Identification and treatment of mental health issues should be considered for future iterations of this program.

5) Macro and Micro Nutrients: The macro and micro nutrients were collected in the CHANGE demonstration project as a part of the nutrition assessment at baseline and every three months. These nutrients may be mediators between dietitian contacts and change in MetSyn score. Such detailed nutritional assessments were beyond the scope of the current analysis but should be investigated in future studies.

6) Types of Contacts: This study identified that there was variation in the type of dietitian contacts, namely face-to-face, telephone and email. Future studies should analyze this variation to determine if the type of contact affects the change in MetSyn score. This will aid in optimizing the efficiency of the intervention.

7) Motivational factors: Although the CHANGE project protocol was not designed based on a strong motivational framework, social factors that influence motivation should be recorded in future studies. An integrative model could be used to record the patients intentions which drive behaviour [32]. Adherence to exercise programs has been shown to be strongly correlated with intrinsic motivation [120].

8) Intensity Over Time: There was variation in the time frame patients could visit kinesiologists and contact dietitians. The current study assumes that ten dietitian visits in two weeks is equivalent to ten visits over thirteen weeks. This assumption should be tested in future studies that account for the timing between visits.
5.6 Conclusion

The dietitian visits provided through the CHANGE project contribute to an improvement in MetSyn risk among MetSyn patients within the first three months of the program. This effect may be partly due to the adoption of healthier diets, but it appears that only a small portion of the association between dietitian visits and change in MetSyn was explained by improvements in the HEI. The contribution of kinesiologist visits to MetSyn risk reduction was not elucidated by the data. Future research is needed to confirm the associations between kinesiologist visits and dietitian contacts with a change in MetSyn score at month twelve are similar to the associations at month three.
References


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103. Berglund, P.A. An Introduction to Multiple Imputation of Complex Sample Data using SAS® v9.2. 2010 [cited 2015 Jun 11]; Available from:


Appendix A
Queen’s University Ethics Approval

QUEEN’S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW
February 18, 2015

Mr. Roger Leung
Department of Medicine
Queen’s University

Dear Mr. Leung

Study Title: DMED-1772-15 Factors associated with reduction in metabolic risk score during a lifestyle intervention program
File # 6014744
Co-Investigators: Mrs. H. Ouellette-Kuntz, Dr. D. Heyland

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair’s signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post-review file # 6014744 in your Researcher Portal (https://researcher.queensu.ca/romeo_researcher)

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. Serious Adverse Event forms are located with your post-review file 6014744 in your Researcher Portal (https://researcher.queensu.ca/romeo_researcher)

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.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair’s signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Chair, Health Sciences Research Ethics Board
February 18, 2015

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.
Appendix B

Blood Pressure and Abdominal Instructions

The following instructions were provided to study sites:

**Blood Pressure Measurement Procedure**

1) Patient comfortably seated with feet on floor
2) Calibrated automatic monitor used
3) Monitor placed at the level of the heart
4) Regular cuff used if arm circumference is <31 cm, otherwise use large cuff
5) Discard first reading and then take 3 readings and average result

Automated blood pressure devices are allowed if calibrated properly.

**Abdominal Circumference Measurement Procedure**

1) Locate the top of the iliac crest
2) Position the tape in the horizontal plane around the abdomen at the top of the iliac crest
3) Fit tape snugly but do not compress the skin
4) Measure at end of normal expiration, with relaxed abdominal muscles.
Appendix C

Metabolic Syndrome Score

The MetSyn Score is based on a cohort study of insulin resistance syndrome in 5212 French patients [86]. Hillier used first principal component analysis to create a single continuous measure of metabolic syndrome or MetSyn score. Logistic regression was used to predict the incidence of diabetes, coronary heart disease and cardiovascular disease with the continuous MetSyn score as the exposure. Standardized Odds Ratios were used to describe the incident diabetes, coronary heart disease and cardiovascular disease per 1 standard deviation increase in MetSyn score. The MetSyn score is standardized to have a mean of zero and standard deviation of 1. Using the age adjusted odds ratios from the DESIR study, a patient’s risk of incident diabetes, coronary heart disease and cardiovascular risk in 9 years can be calculated based on the patients MetSyn score (Table 7).

Table 7: Age-Adjusted odds ratio associated with a one point increase in MetSyn score based on patients in the DESIR cohort study

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident diabetes</td>
<td>3.1 (2.2-4.4)</td>
<td>4.1 (2.6-6.4)</td>
</tr>
<tr>
<td>Incident Coronary heart Disease</td>
<td>1.8 (1.4-2.3)</td>
<td>1.4 (0.78-2.6)</td>
</tr>
<tr>
<td>Incident Cardiovascular Disease</td>
<td>1.7 (1.4-2.1)</td>
<td>1.7 (1.0-2.7)</td>
</tr>
</tbody>
</table>

If a male patient had a decrease in MetSyn score of 1 point, his odds of incident diabetes would be multiplied by $(3.1)^{-1}=0.32$ and his odds of CHD would be multiplied by $(1.8)^{-1}=0.56$ over a 9-year period. If a male patient decreased his MetSyn score by 0.5 point then his odds of incident diabetes would be multiplied by $(3.1)^{-0.5}=0.57$ and his odds of CHD would be multiplied by $(1.8)^{-0.5}=0.75$ over a 9-year period. Consistent with Cohen’s commonly used effect size conventions, we consider a 1 point change a large effect size and a 0.5 point change a moderate effect size [121].
Appendix D

Components of Canadian Adaptation of Healthy Eating Index Scoring

<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: 8-10 servings/day</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: 1.5-2.1 servings/day</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: 1.5-2.1 servings/day</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: 8 servings/day</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: 4 servings/day</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 servings/day</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: 3 servings/day</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: 3 servings/day</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 7-10% of total energy</td>
</tr>
<tr>
<td></td>
<td>0 to 8 points</td>
<td>10% to maximum 15% of total energy</td>
</tr>
<tr>
<td>Sodium</td>
<td>8 to 10 points</td>
<td>Adequate intake to TUL</td>
</tr>
<tr>
<td></td>
<td>0 to 8 points</td>
<td>Tolerable upper intake level (2300 mg) to 2x TUL (4500 mg)</td>
</tr>
<tr>
<td>Other Food</td>
<td>0 to 20 points</td>
<td>Minimum: 5% or less of total energy intake</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum: 40% or more of total energy intake</td>
</tr>
</tbody>
</table>

Figure 14: Components of Canadian Adaptation of Healthy Eating Index Scoring[25]
Appendix E

Baseline Versus Change in Mediator Variables

The relationships between changes in VO2 max and HEI to their respectively baseline values were examined by plotting the values.

Figure 15: Baseline Healthy Eating Index Versus Change in Healthy Eating Index

\[ r = -0.64 \]
\[ p < 0.01 \]
Figure 16: Baseline Maximal Oxygen Consumption Versus Change in Maximal Oxygen Consumption

$r = -0.22$  
$p < 0.01$
Appendix F

Linear Regression Assumptions

An ordinary least square squared linear regression model was used to determine the association of kinesiologist visits and dietitian contacts with a change in MetSyn score after three months. The linear regression assumptions were evaluated.

1) Linearity and additively assumption: The predictors were plotted against the change in MetSyn. The linearity assumption did not appear to be violated.

2) Statistical Independence: The studentized residual was plotted against the observation number (data not shown). No pattern was evident and it was assumed that the independence assumption was met.

3) Homoscedasticity: The individual errors were plotted against the predicted value (Figure 17). The variance of the errors of predicted values were fairly constant. It is therefore assumed that the homoscedasticity assumption is not violated.

Figure 17: Studentized Residuals Versus Predicted Values Of The Change in MetSyn Score
4) Normality of error distribution

The model violated the normality assumption with statistically significant Kolmogorov-Smirnov p-value of <0.01. The QQ plot revealed significant outliers that may have been the reason it is not normally distributed (Figure 18).

Figure 18: Quantile-Quantile (QQ) Plot Of The Studentized Residuals
Appendix G

Outliers and Influential Diagnostics

Influential observation diagnostics were conducted. Cook’s D measures the influence of the “ith” observation on the model as a whole, rather than a specific coefficient or predicted value. In other words, Cook’s D reflects the “ith” case’s influence on all the coefficients and all the predicted values of y. The Cook’s D was plotted against the observation number and based on a cut off of 4/n or 0.16 [99], there were many strongly influential observations (Figure 19).

Figure 19: Cook’s D Plot Versus Observation Number

Leverage of an individual x observation measures the potential for influence resulting from an unusual x value. In multiple regression, leverage reflects how unusual the combination of x values is and does not consider value of y. Observations with leverage greater than 2(k+1)/n or 0.1234 with a studentized residual greater than 2 required further inspection [99]. Two observations have a high
leverage and student residuals (Figure 20), which were also highly influential based on the Cook’s D (Figure 19).

![Outlier and Leverage Diagnostics for metscore_diff](image)

**Figure 20: Studentized Residual Versus Leverage**

DFFIT measures the effect of deleting the \(i^{th}\) observation on the predicted values of \(y\) (difference in fit). DFFIT is also standardized and the DFFIT cut off is \(2\sqrt{(k/n)}\) or 0.513 [99]. The same observations were identified as influential (Figure 21) as in the Cook’s D plot (Figure 19) and the Leverage plot (Figure 20).
Figure 21: DFFITS Versus Observation

The influential observations were identified and the sites were contacted to confirm the accuracy of all the values used in the regression analysis for those observations. The sites confirmed the variable were correct.
Appendix H

Linear Regression: Collinearity Diagnostics

It was suspected a priori that kinesiologist contacts and dietitian contacts may have been collinear. Variance inflation factor describes how much the variance of the estimation is inflated by collinearity. A variance inflation factor exceeding 10 may indicate that collinearity is a concern in the model. The kinesiologist visits and dietitian contacts both had a tolerance of 1.8 (Table 8). Collinearity was not considered a concern in the model for any of the predictors.

Table 8: Collinearity Diagnostics of The Fully Adjusted Model

| Variable                   | DF | Parameter Estimate | Standard Error | t Value | Pr > |t| | Tolerance | Variance Inflation |
|----------------------------|----|--------------------|----------------|---------|------|----|----------------|-------------------|
| Intercept                  | 1  | -1.50              | 0.67           | -2.25   | 0.03 | .  |                 | 0.00              |
| Kinesiologist Contacts     | 1  | 0.001              | 0.02           | 0.32    | 0.75 | 0.67| 1.50           |                   |
| Dietitian Contacts         | 1  | -0.05              | 0.02           | -2.35   | 0.02 | 0.65| 1.53           |                   |
| Site: Toronto†             | 1  | 0.19               | 0.13           | 1.49    | 0.14 | 0.48| 2.06           |                   |
| Site: Laval‡               | 1  | -0.26              | 0.13           | -1.98   | 0.05 | 0.44| 2.27           |                   |
| Age                        | 1  | 0.01               | 0.01           | 2.01    | 0.05 | 0.59| 1.69           |                   |
| Sex                        | 1  | -0.03              | 0.09           | -0.29   | 0.77 | 0.84| 1.19           |                   |
| BMI                        | 1  | 0.06               | 0.02           | 3.74    | 0.00 | 0.66| 1.52           |                   |
| Depression                 | 1  | 0.33               | 0.18           | 1.85    | 0.07 | 0.83| 1.21           |                   |
| Diabetes                   | 1  | 0.01               | 0.15           | 0.04    | 0.97 | 0.35| 2.82           |                   |
| Work: Unemployed‡          | 1  | -0.06              | 0.11           | -0.61   | 0.54 | 0.69| 1.46           |                   |
| Work: Other‡               | 1  | 0.31               | 0.50           | 0.61    | 0.54 | 0.90| 1.12           |                   |
| Glucose Medication         | 1  | 0.20               | 0.14           | 1.42    | 0.16 | 0.38| 2.60           |                   |
| Antihypertensive Medication| 1  | -0.15              | 0.11           | -1.40   | 0.16 | 0.77| 1.30           |                   |
| Triglyceride Medication    | 1  | -0.08              | 0.28           | -0.29   | 0.77 | 0.87| 1.15           |                   |
| MetSyn Baseline Score      | 1  | -0.38              | 0.05           | -7.41   | <.0001| 0.66| 1.51           |                   |

† Reference site was Edmonton
‡ Reference working status was employed
Appendix I

Patient Characteristics by Complete Case, Incomplete Case and Dropped Out

Table 9: Patient Characteristics at Baseline by Complete Case, Incomplete Case and Dropped Out

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Overall mean±SD or n (%)</th>
<th>Complete Case mean±SD or n (%)</th>
<th>Incomplete Case mean±SD or n (%)</th>
<th>Dropped Out mean±SD or n (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>305 (100%)</td>
<td>175 (57.4%)</td>
<td>95 (21.1%)</td>
<td>35 (11.5%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Female</td>
<td>156 (51.1%)</td>
<td>90 (51.4%)</td>
<td>47 (49.5%)</td>
<td>19 (54.3%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Age (Range 35-76 years)</td>
<td>59.0±9.7</td>
<td>58.9±10.0</td>
<td>60.2±8.4</td>
<td>56.8±11.4</td>
<td>0.18</td>
</tr>
<tr>
<td>Ethnicity†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europids, Whites, sub-Saharan Africans, Mediterranean, middle east/Arab*</td>
<td>52 (17.0%)</td>
<td>35 (20.0%)</td>
<td>7 (7.4%)</td>
<td>10 (28.6%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Asian and South Central Americans</td>
<td>15 (4.9%)</td>
<td>10 (5.7%)</td>
<td>4 (4.2%)</td>
<td>1 (2.9%)</td>
<td></td>
</tr>
<tr>
<td>US and Canadian Whites</td>
<td>233 (76.4%)</td>
<td>128 (73.1%)</td>
<td>82 (86.3%)</td>
<td>23 (65.7%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity unclear</td>
<td>5 (1.6%)</td>
<td>2 (1.1%)</td>
<td>2 (2.1%)</td>
<td>1 (2.9%)</td>
<td></td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edmonton</td>
<td>152 (49.8%)</td>
<td>95 (62.5%)</td>
<td>36 (23.7%)</td>
<td>21 (13.8%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Toronto</td>
<td>60 (19.7%)</td>
<td>38 (63.3%)</td>
<td>11 (18.3%)</td>
<td>11 (18.3%)</td>
<td></td>
</tr>
<tr>
<td>Laval</td>
<td>93 (30.5%)</td>
<td>42 (45.2%)</td>
<td>48 (51.6%)</td>
<td>3 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>90.6 ± 14.9</td>
<td>89.5 ± 14.1</td>
<td>92.1 ± 14.9</td>
<td>94.0 ± 18.5</td>
<td>0.24</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>31.8± 3.4</td>
<td>31.5± 3.5</td>
<td>32.0±3.5</td>
<td>32.8±2.6</td>
<td>0.08</td>
</tr>
<tr>
<td>Charlson Co-morbidity Score</td>
<td>0.8± 0.9</td>
<td>0.9± 0.9</td>
<td>0.7±0.8</td>
<td>0.8±0.7</td>
<td>0.27</td>
</tr>
<tr>
<td>Diabetes (Type 2)</td>
<td>158 (51.8%)</td>
<td>94 (53.7%)</td>
<td>45 (47.4%)</td>
<td>19 (54.3%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Active Depression</td>
<td>29 (9.5%)</td>
<td>14 (8.0%)</td>
<td>7 (7.4%)</td>
<td>8 (22.9%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Metabolic Syndrome Score</td>
<td>2.2 ± 1.0</td>
<td>2.2 ± 1.0</td>
<td>2.2±1.1</td>
<td>2.3±1.0</td>
<td>0.66</td>
</tr>
<tr>
<td>Working Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>181 (59.3%)</td>
<td>109 (62.3%)</td>
<td>50 (52.6%)</td>
<td>22 (62.9%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Retired</td>
<td>102 (33.4%)</td>
<td>53 (0.3%)</td>
<td>40 (42.1%)</td>
<td>9 (25.7%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>22 (7.2%)</td>
<td>13 (7.4%)</td>
<td>5 (5.3%)</td>
<td>4 (11.4%)</td>
<td></td>
</tr>
<tr>
<td>Stage of Readiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-contemplative</td>
<td>10 (3.3%)</td>
<td>5 (2.9%)</td>
<td>4 (4.2%)</td>
<td>1 (2.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Contemplative</td>
<td>135 (44.3%)</td>
<td>72 (41.1%)</td>
<td>54 (56.8%)</td>
<td>9 (25.7%)</td>
<td></td>
</tr>
<tr>
<td>Action/Maintenance</td>
<td>160 (52.5%)</td>
<td>98 (56.0%)</td>
<td>37 (38.9%)</td>
<td>25 (71.4%)</td>
<td></td>
</tr>
</tbody>
</table>

† Ethnicity categories were based on the groupings used to determine the appropriate abdominal circumference ranges to diagnose Metabolic Syndrome. Specific ethnic categories were not available

*”Whites” in this category referred to Caucasians not from the US or Canada.
Appendix J

Baseline Metabolic Syndrome Criteria by Complete Case, Incomplete Case and Dropped Out

Table 10: Baseline Metabolic Syndrome Criteria by Complete Case, Incomplete Case and Dropped Out

<table>
<thead>
<tr>
<th>Metabolic Syndrome Criteria</th>
<th>Overall mean±SD or n/N (%)</th>
<th>Complete Case mean±SD or n (%)</th>
<th>Incomplete Case mean±SD or n (%)</th>
<th>Dropped Out mean±SD or n (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure ≥ 130/85 mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>92 (30.2%)</td>
<td>61 (34.9%)</td>
<td>21 (22.1%)</td>
<td>10 (28.6%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Mean Systolic Pressure (mmHg)</td>
<td>133.5± 14.5</td>
<td>134.3± 14.7</td>
<td>133.7±14.9</td>
<td>129.6±12.4</td>
<td>0.22</td>
</tr>
<tr>
<td>Mean Diastolic Pressure (mmHg)</td>
<td>80.6± 9.1</td>
<td>80.9± 9.2</td>
<td>79.9±8.5</td>
<td>80.6±10.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Receiving Pharmacotherapy for elevated blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>223 (73.1%)</td>
<td>128 (73.1%)</td>
<td>71 (74.7%)</td>
<td>24 (68.6%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Fasting Blood Glucose &gt; 5.6 mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>236 (77.4%)</td>
<td>132 (75.4%)</td>
<td>75 (78.9%)</td>
<td>29 (82.9%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Mean Fasting Blood Glucose (mmol/L)</td>
<td>6.6± 1.5</td>
<td>6.5±1.4</td>
<td>6.6±1.6</td>
<td>6.8±1.5</td>
<td>0.49</td>
</tr>
<tr>
<td>Receiving pharmacotherapy for elevated blood glucose levels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>124 (40.7%)</td>
<td>69 (39.4%)</td>
<td>38 (40.0%)</td>
<td>17 (48.6%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Triglyceride of &gt; 1.7 mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>188 (61.6%)</td>
<td>106 (60.6%)</td>
<td>60 (63.2%)</td>
<td>22 (62.9%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Mean triglycerides (mmol/L)</td>
<td>2.2± 1.7</td>
<td>2.2±1.9</td>
<td>2.2±1.4</td>
<td>2.0±0.9</td>
<td>0.83</td>
</tr>
<tr>
<td>Receiving pharmacotherapy for elevated triglycerides</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>11 (3.6%)</td>
<td>7 (4.0%)</td>
<td>3 (3.2%)</td>
<td>1 (2.8%)</td>
<td>0.99</td>
</tr>
<tr>
<td>HDL-C &lt; 1.0 mmol/L Males and &lt;1.3 mmol/L females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>143 (46.9%)</td>
<td>84 (48.0%)</td>
<td>44 (46.3%)</td>
<td>15 (42.9%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Mean HDL-C (mmol/L)</td>
<td>1.2± 0.3</td>
<td>1.2±0.3</td>
<td>1.1±0.3</td>
<td>1.2±0.3</td>
<td>0.81</td>
</tr>
<tr>
<td>High Abdominal Circumference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n with criteria (%)</td>
<td>292 (95.7%)</td>
<td>166 (94.9%)</td>
<td>92 (96.8%)</td>
<td>34 (97.1%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Mean abdominal circumference (cm)</td>
<td>108.1± 9.7</td>
<td>107.7±9.9</td>
<td>108.4±8.8</td>
<td>110.2±10.4</td>
<td>0.24</td>
</tr>
</tbody>
</table>
Appendix K

Cardiac Risk History

Table 11: Cardiac Risk History

<table>
<thead>
<tr>
<th>Cardiac Risk History</th>
<th>Overall n/305 (%)</th>
<th>Complete Cases n/175 (%)</th>
<th>Incomplete Cases n/90 (%)</th>
<th>Dropped Out n/35 (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angina</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>7 (2.3%)</td>
<td>0 (0.0%)</td>
<td>6 (6.3%)</td>
<td>1 (2.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Resolved</td>
<td>10 (3.3%)</td>
<td>7 (4.0%)</td>
<td>0 (0.0%)</td>
<td>3 (8.6%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (1.0%)</td>
<td>3 (1.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Arrhythmia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>8 (2.6%)</td>
<td>4 (2.3%)</td>
<td>4 (4.2%)</td>
<td>0 (0.0%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Resolved</td>
<td>4 (1.3%)</td>
<td>1 (0.6%)</td>
<td>3 (3.2%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (1.0%)</td>
<td>2 (1.1%)</td>
<td>1 (1.1%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Heart Failure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>9 (3.0%)</td>
<td>5 (2.9%)</td>
<td>3 (3.2%)</td>
<td>1 (2.9%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Resolved</td>
<td>2 (0.7%)</td>
<td>1 (0.6%)</td>
<td>1 (1.1%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Hyperlipidemia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>214 (70.2%)</td>
<td>129 (73.7%)</td>
<td>63 (66.3%)</td>
<td>22 (62.9%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Resolved</td>
<td>1 (0.3%)</td>
<td>0 (0.0%)</td>
<td>1 (1.1%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.3%)</td>
<td>1 (0.6%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>232 (76.1%)</td>
<td>136 (77.7%)</td>
<td>69 (72.6%)</td>
<td>27 (77.1%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Resolved</td>
<td>1 (0.3%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (2.9%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Myocardial Infarction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>2 (0.7%)</td>
<td>0 (0.0%)</td>
<td>2 (2.1%)</td>
<td>0 (0.0%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Resolved</td>
<td>9 (3.0%)</td>
<td>7 (4.0%)</td>
<td>1 (1.1%)</td>
<td>1 (2.9%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.3%)</td>
<td>1 (0.6%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>31 (10.2%)</td>
<td>17 (9.7%)</td>
<td>6 (6.3%)</td>
<td>8 (22.9%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Resolved</td>
<td>30 (9.8%)</td>
<td>20 (11.4%)</td>
<td>6 (6.3%)</td>
<td>4 (11.4%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix L

Sensitivity Analysis: Dietitian Visits

Figure 22: Kinesiologist Visits Versus Dietitian Visits by Patient

Figure 23: Change in MetSyn Score Versus Dietitian Visits
Table 12: Comparing the Exposure Definition of Dietitian Contacts and Dietitian Visits

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter [95% CI]</th>
<th>p</th>
<th>Parameter [95% CI]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-1.67 [-2.86, -0.49]</td>
<td>0.01</td>
<td>-1.92 [-3.21, -0.63]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dietitian Contacts</td>
<td>-0.05 [-0.09, -0.01]</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietitian Visits (Face-to-face)</td>
<td></td>
<td></td>
<td>-0.08 [-0.14, -0.02]</td>
<td>0.01</td>
</tr>
<tr>
<td>Kinesiologist Contacts</td>
<td>0.02 [-0.02, 0.05]</td>
<td>0.39</td>
<td>0.03 [-0.02, 0.08]</td>
<td>0.32</td>
</tr>
<tr>
<td>Site: Toronto</td>
<td>0.17 [-0.07, 0.4]</td>
<td>0.16</td>
<td>0.47 [0.19, 0.76]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Site: Laval</td>
<td>-0.34 [-0.57, -0.1]</td>
<td>0.01</td>
<td>0.01 [-0.3, 0.32]</td>
<td>0.94</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.01 [0, 0.02]</td>
<td>0.09</td>
<td>0.01 [0, 0.02]</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.01 [-0.18, 0.15]</td>
<td>0.87</td>
<td>-0.05 [-0.24, 0.14]</td>
<td>0.6</td>
</tr>
<tr>
<td>BMI (per unit)</td>
<td>0.06 [0.04, 0.09]</td>
<td>&lt;0.01</td>
<td>0.07 [0.04, 0.1]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Depression</td>
<td>0.25 [-0.07, 0.57]</td>
<td>0.13</td>
<td>0.24 [-0.11, 0.58]</td>
<td>0.18</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.15 [-0.1, 0.39]</td>
<td>0.24</td>
<td>0.03 [-0.24, 0.31]</td>
<td>0.8</td>
</tr>
<tr>
<td>Work: Unemployed</td>
<td>-0.05 [-0.24, 0.14]</td>
<td>0.63</td>
<td>-0.06 [-0.27, 0.15]</td>
<td>0.58</td>
</tr>
<tr>
<td>Work: Other</td>
<td>0.25 [-0.66, 1.16]</td>
<td>0.59</td>
<td>0.27 [-0.75, 1.29]</td>
<td>0.6</td>
</tr>
<tr>
<td>Glucose Medication</td>
<td>0.08 [-0.17, 0.33]</td>
<td>0.51</td>
<td>0.21 [-0.06, 0.49]</td>
<td>0.13</td>
</tr>
<tr>
<td>Antihypertensive Medication</td>
<td>-0.12 [-0.32, 0.08]</td>
<td>0.22</td>
<td>-0.15 [-0.37, 0.07]</td>
<td>0.18</td>
</tr>
<tr>
<td>Triglyceride Medication</td>
<td>-0.15 [-0.6, 0.31]</td>
<td>0.53</td>
<td>0.03 [-0.47, 0.54]</td>
<td>0.9</td>
</tr>
<tr>
<td>MetSyn Baseline Score</td>
<td>-0.43 [-0.52, -0.34]</td>
<td>&lt;0.01</td>
<td>-0.4 [-0.5, -0.3]</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

1 Reference site was Edmonton  
2 Reference was male  
3 Reference was no diagnosis of depression at baseline  
4 Reference was no diagnosis of diabetes at baseline  
5 Reference working status was employed  
6 Reference was no medication use  
7 MetSyn Score is standardized to have a mean of zero and a standard deviation of one
## Appendix M

**Comparison of Regression Modelling Methods**

Table 13: Comparison of Regression Modelling Methods

<table>
<thead>
<tr>
<th></th>
<th>Crude Unadjusted&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Partially Adjusted&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Fully Adjusted B&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parameter [95% CI]</td>
<td>Parameter [95% CI]</td>
<td>Parameter [95% CI]</td>
</tr>
<tr>
<td><strong>Ordinary Least Squares</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(OLS) Model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kinesiologist Visits</td>
<td>-0.037 [-0.08, -0.00]</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>Dietitian Contacts</td>
<td>-0.067 [-0.11, -0.02]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>OLS Model</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Outliers Removed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kinesiologist Visits</td>
<td>-0.029 [-0.06, 0.01]</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Dietitian Contacts</td>
<td>-0.068 [-0.10, -0.03]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Robust Model with</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisquare Weight (n=243)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kinesiologist Visits</td>
<td>0.037 [-0.07, 0.00]</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Dietitian Contacts</td>
<td>-0.060 [-0.10, -0.02]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Robust Model After</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Imputation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=305)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kinesiologist Visits</td>
<td>-0.031 [-0.07, 0.00]</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Dietitian Contacts</td>
<td>-0.060 [-0.10, -0.02]</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

<sup>1</sup> The crude model is unadjusted.

<sup>2</sup> This model is adjusted for either kinesiologist visits or dietitian contacts.

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Appendix N
Comparing Parameter Estimates Between the Complete Cases Model (n=245) and the Imputed Model (n=305)

Table 14: Comparing Parameter Estimates between the Complete Cases Model (n=245) and the Imputed Model (n=305)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Complete Case Model (n=243)</th>
<th>Multiple Imputation Model (n=305)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parameter [95% CI]</td>
<td>p</td>
</tr>
<tr>
<td>Intercept</td>
<td>-1.49 [-2.6, -0.36]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Kinesiologist Visits</td>
<td>0.02 [-0.01, 0.05]</td>
<td>0.27</td>
</tr>
<tr>
<td>Dietitian Contacts</td>
<td>-0.05 [-0.08, -0.01]</td>
<td>0.02</td>
</tr>
<tr>
<td>Site: Toronto¹</td>
<td>0.12 [-0.08, 0.33]</td>
<td>0.23</td>
</tr>
<tr>
<td>Site: Laval¹</td>
<td>-0.34 [-0.55, -0.14]</td>
<td>0.02</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.01 [-0.00, 0.02]</td>
<td>0.17</td>
</tr>
<tr>
<td>Sex²</td>
<td>0.03 [-0.12, 0.18]</td>
<td>0.70</td>
</tr>
<tr>
<td>BMI (per unit)</td>
<td>0.06 [0.03, 0.08]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Depression³</td>
<td>0.41 [0.11, 0.71]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes⁴</td>
<td>0.07 [-0.16, 0.29]</td>
<td>0.54</td>
</tr>
<tr>
<td>Work: Unemployed⁵</td>
<td>-0.03 [-0.20, 0.14]</td>
<td>0.73</td>
</tr>
<tr>
<td>Work: Other⁵</td>
<td>0.18 [-0.59, 0.95]</td>
<td>0.65</td>
</tr>
<tr>
<td>Glucose Medication⁶</td>
<td>0.16 [-0.07, 0.38]</td>
<td>0.17</td>
</tr>
<tr>
<td>Antihypertensive Medication⁶</td>
<td>-0.10 [-0.27, 0.07]</td>
<td>0.26</td>
</tr>
<tr>
<td>Triglyceride Medication⁶</td>
<td>-0.36 [-0.86, 0.14]</td>
<td>0.16</td>
</tr>
<tr>
<td>MetSyn Baseline Score⁷</td>
<td>-0.40 [-0.50, -0.31]</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

¹ Reference site was Edmonton
² Reference was male
³ Reference was no diagnosis of depression at baseline
⁴ Reference was no diagnosis of diabetes at baseline
⁵ Reference working status was employed
⁶ Reference was no medication use
⁷ MetSyn Score is standardized to have a mean of zero and a standard deviation of one
⁸ CI stands for Confidence Interval
Appendix O

Healthy Eating Index Mediation Analysis without Multiple Imputation (n=190)

Figure 24: Mediation Analysis of Healthy Eating Index In The Relationship Between Dietitian Contacts and Change in MetSyn Score (Without Multiple Imputation) (n=190)
Appendix P

Power

The full model used 15 degrees after considering the categorical and continuous variables (15 confounder and precision variables). The primary exposure of interest for Objective 1 was kinesiologist visits, and the primary exposure for objective 2 was dietitian contacts. Three hundred and five participants were enrolled into the study. A dropout rate of 20% was assumed a priori such that it was determined that a model with 15 covariates and a sample size of 250 evaluable subjects would achieve 93% power at alpha=0.05 if the exposure explained at least 10% of the variance in the outcome (continuous metabolic syndrome which is scaled to have a SD of 1) \([121, \ 122]\). Given the sample size of 243 pre-imputation, I had sufficient power to conduct the primary analysis.