The Effect of Non-exercise Activity Thermogenesis on subjects with Metabolic Syndrome

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THE EFFECT OF NON-EXERCISE ACTIVITY THERMOGENESIS ON
SUBJECTS WITH METABOLIC SYNDROME

By
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Each person whose signature appears below certifies that this dissertation, in his/her opinion, is adequate in the scope and quality as a dissertation for the degree of Doctor of Public Health.

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ABSTRACT OF THE PROPOSAL

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Metabolic syndrome is a cluster of metabolic abnormalities that increases the risk of cardiovascular disease and type 2 diabetes. Several criteria establish the diagnosis of metabolic syndrome, including high waist circumference, low HDL cholesterol, high triglycerides and glucose and above normal blood pressure. The prevalence of metabolic syndrome is on the rise following the rise in obesity across the globe. Qatar, a country in the Arabian Peninsula shares the burden of obesity with recent studies showing prevalences of ~61% among women and ~39% among men. These studies found that metabolic syndrome is more common among women. Physical activity helps reduce visceral obesity, controls glucose levels, and improves blood pressure, triglyceride, and HDL cholesterol levels. One way of increasing physical activity is by promoting non-exercise activity thermogenesis (NEAT). NEAT represents 10% of daily human energy expenditure and is expended during daily life activities like mowing the lawn or climbing stairs. A lifestyle intervention study was conducted with 200 Qatari subjects identified
with metabolic syndrome. The study was approved by the research committee at Hamad Medical Hospital in Doha, Qatar. The study aimed to reduce the number of components of metabolic syndrome in men and women with metabolic syndrome treated at the diabetes and endocrinology department by promoting increased NEAT. In a randomized clinical trial lasting one year the intervention group received general exercise and dietary guidelines in addition to information on how to increase their daily NEAT, while the control group received solely the general exercise and dietary guidelines. Subjects in the intervention group were asked to incorporate NEAT by modifying their work environment, and daily habits such as going shopping, standing instead of sitting, and walking instead of using the car. Text message reminders were sent to the intervention group at two, four, eight, and 10 months. Body weight, waist circumference as a measure of visceral obesity, blood pressure, glucose level and lipid profile were assessed at baseline, 6 months, and 1 year in both groups. Archival data obtained through this study were analyzed after gaining permission from the Loma Linda University Institutional Review Board. After 1 year 52 intervention and 55 control subjects completed the study. The results revealed no statistically significant differences in metabolic syndrome components between the two randomized groups. Additionally analysis of subgroups including those on anti-diabetic medication versus those not taking such medication revealed no differences between the intervention and control groups. The amount of recommended NEAT activity appears to have been too small to influence study outcomes. Future studies in similar populations may need to consider the high dropout rate, and use of incentives or culturally appropriate interventions to increase compliance and retention.
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A. Statement of the Problem

1. High Prevalence of Metabolic Syndrome

Metabolic syndrome is a combination of several abnormalities that increase the risk of cardiovascular disease (CVD). Each abnormality is associated with cardiovascular disease cases (Bener et al., 2009), such as stroke, myocardial infarction, and heart failure (Musallam et al., 2008). These abnormalities may include, but are not limited to the following items, high blood pressure (hypertension), elevated levels of fasting glucose, insulin resistance (Bener et al., 2009), obesity, especially central obesity characterized by accumulation of fat in the abdomen, dyslipidemia characterized by low levels of HDL cholesterol, also known as “good cholesterol”, and high levels of triglycerides (Meigs, 2003). The constellation of the above items increases the risk of developing diabetes, or impaired fasting glucose (Bener et al., 2009), and ultimately increases the risk of premature mortality (International Diabetes Federation (IDF), 2006). Meigs (2004) reports that obese patients with metabolic syndrome have a 10 fold increased risk of developing diabetes and a twofold increased risk for CVD, in comparison to individuals with normal weight and without metabolic syndrome. Meigs recommends aggressive lifestyle intervention in order to reduce the associated risk. Grundy et al. (2005) indicate that the primary goal in the clinical management of patients with this syndrome is focused around reducing risk of atherosclerosis by modifying risk factors like obesity, physical inactivity, and diet which may occur through appropriate lifestyle changes.
Metabolic syndrome can be identified according to different criteria. For the National Cholesterol Education Program/Adult Treatment Panel III criteria, the person must have three or more of the following five abnormalities; (a) Fasting plasma glucose over or equal to 100 mg/dL (5.6 mmol/L), or drug treatment for elevated blood glucose; (b) HDL cholesterol less than 40 mg/dL (1.0 mmol/L) for men, and 50 mg/dL (1.3 mmol/L) for women, or treatment for low HDL cholesterol; (c) Triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or treatment for elevated triglycerides; (d) High blood pressure over or equal to 130/85 mmHg, or treatment for hypertension; (e) Obesity characterized by a waist circumference over or equal to 102 cm (40.15 inch) for men, and over or equal to 88 cm (34.64 inch) for women (Meigs, 2004).

For the International Diabetes Federation, central obesity is the primary criteria with different cutoff scores for different ethnicities, with elevated waist circumference of over or equal to 94 cm for men, and 80 cm for women. Additionally, the patient must have two or more abnormalities out of four of the following: (a) Fasting plasma glucose over or equal to 100 mg/dL (5.6 mmol/L), or diagnosed type 2 diabetes; (b) High blood pressure over or equal to 130/85 mmHg, or treatment for hypertension; (c) Triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or treatment for elevated triglycerides; (d) HDL cholesterol less than 40 mg/dL (1.0 mmol/L) for men, and 50mg/dL (1.3 mmol/L) for women, or treatment for low HDL cholesterol (IDF, 2006).

In order to have a single definition, several organizations, including the above two, agreed on a harmonized definition in 2009. For the harmonized definition of metabolic syndrome, the person must have three or more of the following five abnormalities; (a) Elevated waist circumference which is population and country specific;
(b) Elevated triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or drug treatment for elevated triglycerides; (c) Reduced HDL cholesterol less than 40 mg/dL for males and less than 50 mg/dL for females, or drug treatment for reduced HDL cholesterol; (d) Elevated blood pressure over or equal to 130 mm Hg for systolic and/or over or equal to 85 mm Hg for diastolic, or drug treatment for hypertension; (e) Elevated fasting glucose above or equal to 100 mg/dL, or drug treatment for elevated glucose (Alberti et al., 2009).

Worldwide, approximately 25% of the population suffers the burden of symptoms related to metabolic syndrome. Novak and Levine (2007), report that approximately one billion people worldwide are overweight or obese. After conducting a thorough literature review on metabolic syndrome in the Middle East, no comprehensive peer reviewed literature studies were found to provide accurate numbers of the prevalence in the area in general. Most studies focus on specific countries, such as Iran and Emirates. Both of these studies showed increased prevalence of metabolic syndrome among their populations. The burden is shared among the Qatari population, which suffer from high prevalence rates of obesity and type 2 diabetes. The metabolic syndrome prevalence rates in this population are about 26.4% according to the Adult Treatment Panel III (ATP) criteria, and 34% according to the International Diabetes Federation (IDF) criteria (Musallam et al., 2008). In regard to gender, females had higher prevalence rates. According to the ATP criteria the prevalences are 56.3% for females, and 43.3% for males with higher rates using IDF criteria (Bener et al., 2009).
2. Metabolic Syndrome Risk Factors

Some of the common risk factors include age, menopause, race, sex hormone disturbances, hyperandrogenism in pre and post menopausal women, high caloric intake, physical inactivity, family history, obstructive sleep apnea syndrome, and psychosocial and personality factors (Fan, 2007). The risk for metabolic syndrome increases with age; reports show that metabolic syndrome affects about 10% of those in their twenties in comparison to 40% of those that are in their sixties, while signs and symptoms can appear as early as childhood. For type 2 diabetes, risk is increased in people with a family history of type 2 diabetes, or with gestational diabetes during pregnancy. In regard to race, some ethnicities seem to have higher risk of developing this syndrome, such as Hispanics or Middle Easterners. For obesity, a body mass index (BMI) above 25 increases the risk of developing the metabolic syndrome. Abdominal obesity increases the risk; due to the effects of visceral fat accumulation and its several clinical implications which are discussed in more detail later (Mayo Clinic, 2009).

Risk factors associated with metabolic syndrome in the Qatari population include age, ethnicity, obesity and family history of diabetes (Musallam et al., 2008). Musallam et al.'s study showed that abdominal obesity is the most common metabolic syndrome abnormality in the Qatari population. The authors attribute this to the general economic growth witnessed in that geographic area, for example increased levels of urbanization and lifestyle leading to increases in diabetes mellitus. Additionally, the hot weather environment seems to be a factor that limits physical activity. In regard to age, the study showed a nine fold increase in age specific prevalence of metabolic syndrome for the age group 20-30, who had a prevalence rate of 7.9%, and to above 60 years of age, a group
that had a prevalence rate of 70.3%. As for gender, women had higher prevalence rates than men, as 61.4% in comparison to 38.6% in men. The authors attribute this partially to cultural factors that restrict women engagement in outdoor activities. More individuals with family history of diabetes had metabolic syndrome in comparison to those not having a family history of diabetes in this population.

3. Metabolic Syndrome Etiology

Factors that play an important role in the development of this condition include genetics, sedentary lifestyle, cigarette smoking, progressive weight gain, and a Western diet high in carbohydrates, saturated fat, and low in fiber (Pitsavos et al., 2007; Schiltz et al., 2009). As for diet, an atherogenic one, which is rich in saturated fat and cholesterol, may increase the risk of developing CVD in individuals with metabolic syndrome, although it is not listed as a risk factor for the syndrome (Grundy et al., 2005). It is clear that excess consumption of energy, regardless of the macronutrient composition, is associated with visceral accumulation of excess fat (Levine, 2007).

Meigs (2002) reports that certain genes may contribute to metabolic syndrome, as family studies show that specific metabolic risk factors may be transmitted from the parents to the offspring. These studies also show that certain gene abnormalities are associated with the fasting insulin levels, lipids and obesity of the metabolic syndrome.

Kushner and Bessesen (2007) indicate that physical inactivity contributes to the risk of developing obesity related diseases, like metabolic syndrome. They give an example of the Harvard alumni study which reports that individuals participating in regular moderate intensity exercise activity have lower body weight in comparison to those reporting less physical activity. They highlight the importance of establishing
public health programs and interventions that address these issues and in turn help curb the obesity epidemic. The role of lifestyle is emphasized in the current study.

Novak and Levine (2007) show that sedentary behaviors increase as physical activity decreases which leads to increased obesity and decreased health at the population level. They report that weight gain comes as a result of lower energy expenditure when compared to caloric intake. "Indeed increasing physical activity levels may be the missing link needed to reverse the current obesity trends" (p. 923).

In most studies, physical activity is associated with a decreased risk of metabolic syndrome. Structured physical activity may help prevent metabolic syndrome (Ford et al., 2005). Laaksonen et al. (2002) conducted a study on 612 individuals without metabolic syndrome to assess the role of physical activity in predicting metabolic syndrome development. Their results show that individuals practicing 3 or more hours of structured physical activity per week have decreased risk of developing metabolic syndrome by 50%. Their results also showed that among high risk individuals, moderate to vigorous exercise was effective in reducing their risk of developing metabolic syndrome.

In another study by Ford et al. (2005), individuals not participating in any moderate or vigorous exercise during their leisure time showed twice the risk of developing metabolic syndrome, outlining the fact that "excess weight and lack of physical activity are two important determinants of the metabolic syndrome" p. 608).

"Increasing physical activity at the population level not only has potential to help tackle the obesity problem, but would also address many of the other key health problems" (Fox & Hillsdon, 2007, p. 116). The authors recommend that promoting physical activity is needed now more than ever before. For example, fewer current jobs
require physical activity; labor saving equipment is being used in the home, work and even in retail establishments, changes in shopping patterns with the emergence of the internet, and increased self sufficiency in the home. Collectively these reasons have led to a reduction in energy expenditure, which in turn played a role in increasing related health problems. In regard to sedentariness, authors indicate that sitting and obesity are related in a dose response manner, as obesity risk increases with the increase in time spent sitting during leisure time. Additionally, this risk increases with the increase in time spent in the car while travelling. They conclude by recommending that reduction in this sedentary time should be a target for interventions and health policy (Fox & Hillsdon, 2007).

One way to increase physical activity both on an individual and population level is through increasing non-exercise activity thermogenesis (NEAT), which is the energy used when conducting different life activities. James Levine (2007) describes it as “NEAT includes all those activities that render us vibrant, unique, and independent beings such as dancing, going to work or school, shoveling snow, playing the guitar, swimming, or walking in the modern mall” (p. 275). This includes movement of muscle groups that is not performed for the purpose of exercise, but for the purpose of fulfilling the requirements of daily life.

Levine and Miller (2007) indicate that during the last 20 years the work environment shifted mainly to be a computer based one which contributed to a major reduction in energy expenditure and physical activity levels, whether at the individual or population level. They conducted a study assessing the effectiveness of NEAT in increasing energy expenditure during work time. They recruited 15 individuals and asked them to work on a vertical station composed of a treadmill with a computer on top of it,
instead of the typical work station or desk. Their results showed a significant increase in energy expenditure during walking. Additionally, it showed a linear relationship between walking speed and energy expenditure in these individuals. Lanningham, Nysse, and Levine (2003) studied the difference in energy expenditure between using the elevator, dishwasher, and driving in compare to walking, taking the stairs, and washing dishes manually. The results showed that using the former three options increases ones energy expenditure by 120 calories per day. They conclude that this adds up to 12 pounds of fat per year.

Levine and Kotz (2005) indicate that obesity is associated with a predisposition to be seated for a longer period of time in comparison to more lean individuals. The authors conclude that if obese individuals used this time to stand or ambulate they would enhance their energy expenditure by 350 kcal/day. Novak and Levine (2007) report that NEAT has an important influence on energy expenditure, that even small changes in NEAT overtime may have an influence on body weight. Wilson indicates that “NEAT may explain the majority of the difference between individuals in terms of their energy expended in a given day. In fact, it ranges from 15-50% of total calories expended in a given day depending on whether an individual is sedentary or active” (Wilson, 2004, p. 2).

According to Kate Trainor (2009) “the beauty of NEAT is that you can start anytime, anywhere. No need to wait for a gym membership to kick in or a new year to turn over, it’s easy to incorporate” (p. 2). For an ideal NEAT office environment, Trainor recommends several NEAT enhancing activities such as replacing the chair with a treadmill or an exercise ball, or standing when on the phone while using a mini-sized
stepper. Also, Wilson suggests several items on how to enhance ones daily NEAT at work, for an example, to ignore the elevator and use the stairs, or to ambulate when reading instead of sitting (Wilson, 2004).

Levine (2007) recommends two approaches to make people more active during their day. The first is an ‘individualized approach’ where NEAT enhancing activities are personalized according to ones daily life activities. The second is ‘environmental re-engineering’ and involves changing the surrounding environment, whether at the house or at work. While other factors play a role in overall energy expenditure balance, the current study will be an attempt to increase NEAT specifically through certain lifestyle modifications associated with an individual’s environment, or daily habits, by using NEAT enhancing activities.

Novak and Levine (2007) suggest that NEAT may have an important contribution to overall energy expenditure, as small changes in physical activity overtime may have influence on body weight. For many, maintaining a healthy diet and regular exercise may be difficult goals to achieve which is why the authors recommend NEAT as an easy and accessible way to increase energy expenditure.

B. Purpose of the Study

The goal of this study was to determine whether NEAT can be used to reduce the burden associated with metabolic syndrome in Qatari patients. This was planned to be achieved by increasing the amount of energy used or calories burned throughout the day utilizing NEAT. The specific objectives of this study were: (a) to examine the effect of NEAT on the number of components of metabolic syndrome, and (b) to examine the
effect of NEAT on the number of subjects meeting the IDF definition of metabolic syndrome.

C. Research Questions

- Among men and women with metabolic syndrome, does advice to increase NEAT reduce the number of components of metabolic syndrome after 1 year?
  - Among men and women with metabolic syndrome, does advice to increase NEAT improve their waist circumference after 1 year?
  - Among men and women with metabolic syndrome, does advice to increase NEAT improve their glucose level after 1 year?
  - Among men and women with metabolic syndrome, does advice to increase NEAT improve their HDL levels after 1 year?
  - Among men and women with metabolic syndrome, does advice to increase NEAT improve their triglycerides levels after 1 year?
  - Among men and women with metabolic syndrome, does advice to increase NEAT improve their blood pressure after 1 year?
  - Among men and women with metabolic syndrome, does advice to increase NEAT improve their weight after 1 year?

- Among men and women with metabolic syndrome, does advice to increase NEAT reduce the proportion of subjects meeting the IDF definition of metabolic syndrome?
D. Theoretical Justification

1. Components of Human Energy Balance

Human energy expenditure is divided into three major components: first, resting metabolic rate (RMR), which is the energy used at rest, and accounts for approximately 60% of energy expenditure in humans (Wilson, 2004). This is the energy needed for body functions like respiration, ion transport, blood flow, and maintaining cellular integrity. For men, the RMR is approximately equivalent to 1800 kcal, for a 70 kg adult. For women, the associated RMR for a 50 kg adult is 1300 kcal. For sedentary individuals RMR may account for 50-70% of daily energy expenditure (Harvey & Ferrier, 2008). A study by Huang et al. (2004) showed higher RMR among severely obese individuals with type 2 diabetes in comparison to those without diabetes. Another study compared the RMR in obese, moderately obese and control individuals, and found that obese individuals have significantly higher RMR in comparison to those with normal weight (Ravussin et al., 1982). Thus, RMR is not a factor that is amenable to intervention in people with metabolic syndrome.

The second component is the thermic effect of food. This is energy used during eating, digesting, and processing food (Wilson, 2004). During these processes heat production by the body increases as much as 30% above the normal resting level (Harvey & Ferrier, 2008). This accounts for approximately 10-15% of overall energy expenditure (Wilson, 2004).

The third component is activity thermogenesis which may be divided into exercise and NEAT. This accounts for the remaining human energy expenditure (Wilson, 2004). This component of human energy expenditure usually accounts for the majority of
variation in overall energy expenditure between different individuals and is most
amenable to intervention of the components of energy expenditure. For an example, a
sedentary individual may require 30-50% above resting caloric need, while a highly
active individual may need up to 100% or more calories above resting caloric need
(Harvey & Ferrier, 2008). While studies generally focus on increasing exercise,
increasing NEAT may be an effective way of increasing energy expenditure.

2. Non-exercise Activity Thermogenesis

NEAT is the energy expended while people conduct life activities other
than exercise, such as fidgeting and maintaining posture (NICHD, 2008). Levine defines
NEAT “as those activities that render us vibrant, unique and independent beings, such as
dancing, going to work or school, shoveling snow, playing the guitar, swimming, or
walking in the modern mall” (Levine, 2007, p. 275). Levine et al. identify four
environmental factors that have an influence on NEAT. First, the concrete urban
environment and mechanization, as comparing the energy cost of mechanization to
manual work shows that approximately 111 kcal per day is lost to mechanization.
Second, gender, as women may have more duties than men in some societies. Third,
education, as reports show that educated individuals report more leisure time in
comparison to those with less education. Fourth, seasonal variations in physical activity
(Levine et al., 2006) as reports from agricultural societies show that NEAT doubles in the
summer as compared to the winter time (Wilson, 2004).

Levine et al. (2006) show that NEAT plays an important role in overall energy
balance because it may vary as much as 2000 kcal/day between individuals. Moreover,
they indicate that highly active people may expend as much as three times more than
inactive people. In 2006, a study conducted at the Mayo Clinic, one of the prominent research institutes on the topic, found that the mean energy expenditure while seated was approximately 70 kcal/h, in contrast to walking and working which was about 190 kcal/h, with the mean increase of energy expenditure at approximately 120 kcal/h. The study concluded that replacing time sitting at the desk by time walking and working, individuals would lose 20-30 kg per year, if other components of energy expenditure remained the same (Levine & Miller, 2007).

In another study by Levine, the author indicates that when a person walks at 1 mile per hour, instead of sitting, the energy expenditure of a 70 kg person is approximately 100 kcal/h (Levine, 2007). Levine and Kotz (2005), in a third study, indicate that obesity is associated with a predisposition to be seated for a longer period of time in comparison to more lean individuals (about 160 min/day), and if these individuals used this time to stand or ambulate they would spend up to 350 kcal/day (Levine & Kotz, 2005).

3. Non-exercise Activity Thermogenesis Mechanisms in Reducing Components of Metabolic Syndrome

As identified by the harmonized definition of metabolic syndrome, the main components are elevated waist circumference, elevated triglycerides or drug treatment for elevated triglycerides, reduced HDL cholesterol or drug treatment for reduced HDL cholesterol, elevated blood pressure or drug treatment for hypertension, and elevated fasting glucose or drug treatment for elevated glucose.

a. Elevated Waist Circumference. Fan (2007) indicates that adipose tissue is a metabolic and endocrine organ that is highly active, as it is responsible for releasing
fatty acids, cytokines, and inflammatory mediators. This may contribute to the cardiovascular and metabolic risk associated with metabolic syndrome. Ford et al. (2005) indicate that physical activity and metabolic syndrome are inversely associated, as sedentary behaviors contribute to different components of the syndrome. In the previously mentioned study by Levine and Miller who compared the energy expenditure of persons sitting in front of a computer screen to those using a 'walk and work' desk station, the results show that there was a mean increase in energy expenditure for using the station over sitting of 119 kcal/h. The authors conclude that if obese individuals replace their sitting time with walking, an annual weight loss of 20-30 kg may occur (Levine & Miller, 2007).

In a study by Levine et al. (1999), NEAT was found to be a significant predictor of resistance to fat gain with overfeeding (r = 0.77, p < 0.001), as participants with higher levels of NEAT had lower fat available for storage, in compare to those with lower levels of NEAT and higher predisposition for obesity. The authors conclude that enhancing NEAT through behavior modification may be useful in preventing obesity.

Levine and Yeager (2009) show that choosing a more active option during daily activities increases energy expenditure. For an example a person would spend approximately 15 calories when parking the car next to work and using the elevator, while the amount of calories burnt increases to approximately 80-120 if parking was further away and the stairs were used instead. The table below provides further examples of more active options.
### Typical day at the office

| Activity                                      | Calories burned | Picking up the pace                      | Calories burned |
|-----------------------------------------------|-----------------|------------------------------------------|-----------------|
| Park by building, take elevator               | 15              | Park 5 blocks from office, take stairs   | 80-120          |
| Make phone calls for an hour at desk          | 15              | Take calls standing up and pacing        | 100-130         |
| Seated 45 minute lunch                        | 25              | Walk 30 minutes to lunch, sit and eat 15 minutes | 100-130         |
| Seated 1 hour lunch                          | 15              | 1 hour walking meeting                   | 150-200         |
| Take elevator to ground floor, walk to car, drive home | 15              | Take stairs out of the building, walk back to car | 80-100         |
| Total                                         | 85              | Total                                    | 510-680         |

### Lipids

Marrugat et al. conducted a study on 537 individuals to assess the role of physical activity in modifying the different components of their lipid profile. Their results show that individuals participating in leisure physical activity greater than 7 kcal/minute had a significant increase in their HDL cholesterol and reduction in their atherogenic index, independent from other confounding variables. Additionally, it showed that participating in physical activity with intensity higher than 9 kcal/minute was associated with decrease in total cholesterol and non HDL cholesterol (Marrugat et al., 2015).
Gutierrez recommends physical activity and exercise as an adjunctive intervention because of its positive impact on abnormal lipids. Exercise improves HDL cholesterol levels through altering composition and maturation of the particles, as it increases the size of HDL particles and the maturation of the nascent HDL particle. Additionally it improves total cholesterol levels (Gutierrez, 2007). The improvement in HDL cholesterol levels is due to increase in lipoprotein lipase activity which is responsible for breaking down triglycerides (Kravitz & Hayward, 2011).

Kraus and Slentz (2009) indicate that moderate intensity exercise is significantly more effective in improving triglyceride levels and insulin sensitivity than vigorous intensity exercise. Additionally, it significantly improved a composite score for metabolic syndrome. They suggest that regular walking is an effective method in reducing health risk including the risk of developing cardiovascular disease, which comes through favorable changes in fasting lipids and atherogenic dyslipidemia.

c. Glucose. Reaven (2002) indicates that resistance to insulin mediated glucose disposal increases a person’s risk of developing abnormalities associated with the metabolic syndrome. He shows that physical activity enhances insulin sensitivity which in turn reduces the risk of CVD. Grundy et al. (2005) indicates that insulin resistance is an essential cause of metabolic syndrome, as it contributes to hyperglycemia of type 2 diabetes. Additionally, insulin resistant individuals usually have abnormal fat distribution which is characterized by upper body fat. The authors show that the high release of fatty acids contributes to the accumulation of lipids in other sites than adipose tissue such as liver and muscles which contributes to worsening insulin resistance in the muscles for an example. Furthermore, they show that in patients with metabolic syndrome, physical
activity may delay or prevent the development of type 2 diabetes. They further conclude by indicating that glycemic control reduces both associated microvascular and macrovascular complications.

Healy et al. (2007) showed a significant association between the effect of light intensity physical activity and glucose levels among 173 participants. They concluded the substitution of light intensity activity for other sedentary time may be a successful prevention method that contributes to the reduction of both type 2 diabetes and CVD risk.

In another study, Gordon et al. (2008) looked into the effects of yoga and exercise combined in comparison to a control group on lipids among 77 patients with type 2 diabetes. This 6-month study showed significant reductions in fasting blood glucose and both total cholesterol and VLDL cholesterol levels. They concluded that yoga and exercise can be used as a preventive therapeutic measure for type 2 diabetes patients.

Another study looked into the effect of aerobic exercise and impaired fasting glucose and type 2 diabetes. This was a prospective study, with an average follow up of 6 years, which was conducted on 8633 individuals without diabetes. These were divided into three groups with low, moderate, and high fitness. The results showed that those in the low fitness level have a 3.7 fold greater risk of developing diabetes in comparison to those in the high fitness group. Additionally it showed a dose response gradient between the assigned fitness level and incidence of both impaired fasting glucose and diabetes. They concluded that a sedentary lifestyle is a contributor to the progression from normal fasting glucose to impaired fasting glucose and diabetes (Wei et al., 1999).

d. High Blood Pressure. Reaven (2002) indicates that patients with hypertension are at higher risk of developing cardiovascular disease. Grundy et al. (2005)
show that lifestyle changes are crucial in hypertensive individuals with metabolic syndrome. They recommend physical activity as a tool to help control elevations in blood pressure. The Mayo Clinic on their website indicates that not getting enough exercise and having high blood pressure are closely related. For some, participating in regular physical activity lowers the need for anti hypertensive medication. They show that physical activity helps in strengthening the heart so that it requires less effort to pump blood through the arteries which helps lower blood pressure (Mayo Clinic, 2011).

Arroll and Beaglehole (1992) show that physical activity reduces blood pressure in both hypertensive and non hypertensive individuals, with an average reduction of 6-7 mmHg for both systolic and diastolic blood pressure, indicating that this is comparable to drug treatment for hypertension, and concluding that this effect is independent from other factors. The results of another study by Padilla et al. (2005) shows that physical activity is effective in reducing systolic blood pressure in hypertensive and prehypertensive individuals, suggesting that physical activity may be used to treat both hypertension and prehypertension. Another study by Kerrie et al. (2001) showed that walking for 30 minutes over a 24 week period reduced systolic blood pressure in women with borderline to stage 1 hypertension.

In this study, NEAT is used to increase the energy expenditure among participants in the intervention group, which reflects positively on the waist circumference, glucose level, blood pressure, and lipid profile, which in turn reflects on the number of metabolic syndrome components along with the number of patients. The theoretical framework of this study is outlined in Figure 1.1.
Figure 1.1 NEAT contributes to energy expenditure by causing more calories to be burned, which may reduce the number of metabolic syndrome components and the number of subjects with metabolic syndrome.

E. Significance to Preventive Care

The results of this study may provide preventive care specialists with another tool that may aid in improving the health of subjects with metabolic syndrome, through reduction in the number of metabolic syndrome components. A tool that may be used as part of overall lifestyle recommendations given by preventive care specialists to improve the life quality of subjects with metabolic syndrome. It may also have an impact for recommendations given to individuals who feel they cannot exercise or are not motivated
to do so. In the long run, increasing the amount of energy used throughout the day utilizing NEAT, may be further reflected in a lowering of certain metabolic syndrome markers, and or decreasing risk of developing metabolic syndrome, and decreased risk for developing cardiovascular disease and or type 2 diabetes.
A. Overview

The increasing prevalence of metabolic syndrome in Qatar is just one indication among many that this population is suffering as a result of major lifestyle changes that have occurred in the past four decades. This literature review should serve to (a) identify factors behind the rise of metabolic syndrome prevalence, (b) evaluate current efforts to curb the prevalence, and (c) explore possibilities of improving the overall quality of life among metabolic syndrome patients.

This literature review is divided into two main sections. The first covers an overview of metabolic syndrome along with its different definitions, the prevalence globally and in Qatar, risk factors, and implications. The second part discusses NEAT, how it has been used previously, how it has been used in the current study, how it influences energy expenditure, and recent studies on the topic.

After conducting my research over the past few months, it was found that Dr. James Levine at The Mayo Clinic has provided the foundation of work done on NEAT. Several of his studies on the topic will be covered here.

B. Metabolic Syndrome Overview

Metabolic syndrome is a health condition which involves a combination of abnormalities in one person, this may include but not limited to the following items; high blood pressure (hypertension), elevated levels of fasting glucose, insulin resistance (Bener et al., 2009), obesity especially central obesity characterized by accumulation of fat in the abdomen, dyslipidemia characterized by low levels of HDL cholesterol, also
known as “good cholesterol”, and high levels of triglycerides (Meigs, 2003). The constellation of the above items increases the risk of developing diabetes, or cardiovascular disease (CVD) (Bener et al., 2009) and ultimately increasing the risk of mortality (International Diabetes Federation (IDF), 2006). For an example, Grundy et al. (2005) showed that adipose tissue among obese individuals is usually insulin resistant which increases fatty acid levels, thus increasing insulin resistance in muscle tissue. Furthermore, this adipose tissue produces abnormal adipokines which also alters insulin resistance and increases risk for CVD. The health risk associated with metabolic syndrome is discussed in more detail under the clinical implications section.

Factors that play an important role in the development of this disease include genetics, sedentary lifestyle, cigarette smoking, progressive weight gain, and a Western diet (Pitsavos et al., 2007; Schiltz et al., 2009). Lifestyle plays a major role in the etiology of metabolic syndrome either through low physical activity or excess caloric intake or both. The most common risk factor seems to be abdominal obesity which majorly justifies lifestyle modification. The American Heart Association states that “in the long run, the greatest benefit for those with metabolic syndrome will be derived from effective lifestyle intervention” (Minich & Bland, 2008).

C. Different Criteria for Metabolic Syndrome

Several criteria establish the diagnosis of metabolic syndrome, these vary by geographical region or by the organization that issues the definition. Currently, five definitions of metabolic syndrome exist, these were established by the World Health Organization (WHO) in 1999, the American Association of Clinical Endocrinologists (AACE) in 2003, the European Group for the Study of Insulin Resistance (EGIR) in
1999, the International Diabetes Federation (IDF) in 2004, and the National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ ATP III) in 2001 (Meigs, 2004). The most popular and widely used are the definitions by the National Cholesterol Education Program and the International Diabetes Federation and more recently the harmonized definition; these are discussed in detail below.

1. **Harmonized Definition of Metabolic Syndrome**

   The patient must have three or more of the following five abnormalities:

   (a) Elevated waist circumference which is population and country specific; (b) Elevated triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or drug treatment for elevated triglycerides; (c) Reduced HDL cholesterol less than 40 mg/dL for males and less than 50 mg/dL for females, or drug treatment for reduced HDL cholesterol; (d) Elevated blood pressure over or equal to 130 mm Hg for systolic and/or over or equal to 85 mm Hg for diastolic, or drug treatment for hypertension; (e) Elevated fasting glucose above or equal to 100 mg/dL, or drug treatment for elevated glucose (Alberti et al., 2009).

2. **International Diabetes Federation**

   Central obesity is the primary criteria with different cutoff scores for different ethnicities, with elevated waist circumference of over or equal to 94 cm for men, and 80 cm for women. Additionally, the patient must have two or more abnormalities out of four of the following: (a) Triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or treatment for elevated triglycerides; (b) HDL cholesterol less than 40 mg/dL (1.0 mmol/L) for men, and 50 mg/dL (1.3 mmol/L) for women, or treatment for low HDL cholesterol; (c) High blood pressure over or equal to 130/85 mmHg, or treatment for
hypertension; (d) Fasting plasma glucose over or equal to 100 mg/dL (5.6 mmol/L), or diagnosed type 2 diabetes (IDF, 2006).

3. **National Cholesterol Education Program/Adult Treatment Panel III**

   The patient must have three or more of the following five abnormalities; (a) Obesity characterized by waist circumference over or equal to 102 cm (40.15 inch) for men, and over or equal to 88 cm (34.64 inch) for women; (b) Triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or treatment for elevated triglycerides; (c) HDL cholesterol less than 40 mg/dL (1.0 mmol/L) for men, and 50 mg/dL (1.3 mmol/L) for women, or treatment for low HDL; (d) High blood pressure over or equal to 130/85 mmHg, or treatment for hypertension; (e) Fasting plasma glucose over or equal to 100 mg/dL (5.6 mmol/L), or drug treatment for elevated blood glucose (Meigs, 2004).

D. **Metabolic Syndrome Prevalence Worldwide**

   “The metabolic syndrome is very common and will become even more common as populations age and become more obese” states Meigs in a report in 2002 (p. 283). Estimates by the International Diabetes Federation in 2005 in regard to the worldwide prevalence of metabolic syndrome indicate that approximately 25% of the population suffers the burden of symptoms related to metabolic syndrome (IDF, 2006). Other studies show that up to 30% of middle aged individuals in developed nations have several features of this disease, with prevalence increasing up to 60% of individuals in their 70’s, with a minimal 30% of all adults living without any features (Haslam, 2005).

   In the United States, according to the National Center for Health Statistics in a report published in 2009, approximately 34% of adults meet the criteria set by the National Cholesterol Education Program/Adult Treatment Panel III (Ervin, 2009). For the
age category under 40 years, 20% of males and 16% of females meet the criteria. For the age category 40-59 years, 41% of males and 37% of females meet the criteria. And finally, for the age category 60 years and over, 52% of males and 54% of females meet the criteria. Ethnicity wise, 25% of non Hispanic Black males meet the criteria in comparison to 37% of non Hispanic White males (Ervin, 2009). In a different study, Meigs indicates that about 24% of the US population between ages 20-70 have the syndrome, which is more common in older and Mexican American individuals (Meigs, 2002). A third study estimates that 69 million American meet the criteria set by the International Diabetes Federation (Schiltz et al., 2009).

E. Metabolic Syndrome Prevalence in Qatar

In a recent study by Musalam et al., the Qatari population was found to have high prevalence rates of obesity, diabetes, and further with metabolic syndrome prevalence rates of 27.6% (ATP III criteria) and 35.4% (IDF criteria) (Musalam et al., 2008). Bener et al. (2009) attribute this to the general economic growth witnessed in that geographic area. Bener, Zirie, and Al-Rikabi, (2005) find that this influences levels of urbanizations and lifestyle leading to increases in diabetes mellitus to the point where many consider it a main public health concern in the country. Additionally, the hot weather environment seems to be a factor that limits or restricts physical activity opportunities (Musalam et al., 2008). Al-Sarraj reports similar results from the neighboring United Arab Emirates (UAE), where prevalence rates indicate that 39% and 40% of the population has metabolic syndrome, according to ATP and IDF respectively (Al-Sarraj 2010).

The socio-demographic characteristics breakdown of metabolic syndrome patients in Qatar, show age and body mass index (BMI) as significant contributors to the
prevalence of the disease in Qatar. It also shows a significant relationship with gender, and educational status. In regard to gender, females had higher prevalence rates. According to the IDF criteria, 61% of females have metabolic syndrome in comparison to 38.6% of men, the ATP criteria showed lower rates with 56.3% for females, and 43.3% for males (Bener et al., 2009). These results are similar to prevalence studies conducted in different geographic regions of the world, like the United Kingdom where females had a higher prevalence rate of metabolic syndrome 24.9%, in comparison to 17.4% for men (Santos et al., 2008). Or like Slovakia, where females report 23.9% in comparison to 15.9% males (Mokan et al., 2008).

F. Metabolic Syndrome Risk Factors

The Mayo clinic on their website lists the following items as risk factors for metabolic syndrome. The first factor is age, as the risk of developing metabolic syndrome increases with age. Reports show that metabolic syndrome affects about 10% of those in their twenties in comparison to 40% of those that are in their sixties. The second factor is diabetes, as the risk of developing metabolic syndrome increases with family history of type 2 diabetes, or gestational diabetes. The third factor is race, as some ethnicities seem to have higher risk of developing this syndrome, such as Hispanics or Asians. The fourth factor is obesity, as a body mass index (BMI) above 25 increases the risk of developing the metabolic syndrome. The fifth factor is other diseases, such as high blood pressure, cardiovascular disease, or polycystic ovary syndrome may increase risk of developing metabolic syndrome (Mayo Clinic, 2009). Meigs indicates that age, weight, and race are common risk factors for metabolic syndrome. Additionally, postmenopausal status,
smoking, low household income, high carbohydrate diet, and physical inactivity may also increase the risk of developing metabolic syndrome (Meigs, 2004).

Two researchers have studied these risk factors in metabolic syndrome patients in Qatar. Mussalam et al. (2008) found abdominal obesity to be the most common factor among Qatari patients, which also seems to be more prevalent among females, as abdominal obesity prevalence for Qatari females was estimated at 74% in comparison to 56% for males. Other contributing risk factors reported in the study were genetics, environmental factors leading to physical inactivity, and high illiteracy rate (11.8%). In a different study, Bener et al. (2009) found that gender, age, and educational status, are significant contributors to metabolic syndrome in this population. This study also showed a nine fold increase in age specific prevalence, when comparing the age group 20-30 (7.9%) with the age group 60 and above (70.3%).

G. Metabolic Syndrome Clinical Implications

Metabolic syndrome is a medical condition associated with modern western civilizations, with many risk factors that come with the name; along comes higher susceptibility to a long list of crucial and serious illnesses. Many sources consider this disease a major global public health issue that requires a multi factorial effort to curb the increasing prevalence. For example, Meigs indicates that patients with metabolic syndrome have double the risk of developing CVD, and have four times the risk of developing type 2 diabetes in comparison to individuals not classified under metabolic syndrome (Meigs, 2002).

The Metabolic Syndrome Institute associates metabolic syndrome with an increased risk of coronary heart disease, myocardial infarction, and stroke in both
genders. Furthermore, the institute indicates that metabolic syndrome patients are three times more likely to suffer a cardiovascular event as compared to non-metabolic syndrome individuals (Metabolic Syndrome Institute, 2010). These associations are similar to ones reported in a study conducted by Isomaa et al. (2001), where 3606 metabolic syndrome patients were followed for 6.9 years. Individuals with metabolic syndrome were found to have three times the risk of coronary heart disease, myocardial infarction, and stroke in comparison to those without it. Metabolic syndrome patients also had a 1.8 times the risk of cardiovascular morbidity.

II. Components of Human Energy Balance

Total human energy expenditure is divided into three major components; these are basal metabolic rate, thermic effect of food, and activity thermogenesis (Levine, 2007). Basal metabolic rate (BMR), or resting metabolic rate (RMR), is the energy used for core body functions and is measured during rest while fasting. This contributes to 60-70% of all energy utilized, and usually varies by size, the bigger the person the higher the basal metabolic rate. Thermic effect of food accounts for about 10-15% of all energy utilized and represents the energy needed for digestion, absorption, and storage. For example, proteins have the highest thermic effect of all macronutrients, which is followed by carbohydrates and then fats (Wilson, 2004).

Activity thermogenesis accounts for the rest of the energy utilized throughout the day, and divides into two components, exercise activity and non-exercise activity thermogenesis (NEAT). The former is the energy used when exercising, and the latter is the energy used throughout the day for all non-exercise activities, such as shopping, mowing the lawn, or fidgeting. This part plays an important role in overall energy
balance, and may vary as much as 2000 kcal/day between individuals, which makes it an important tool in weight loss or in preventing weight gain (Levine, 2007).

I. Non-exercise Activity Thermogenesis (NEAT)

James Levine (2007) describes it as “NEAT includes all those activities that render us vibrant, unique, and independent beings such as dancing, going to work or school, shoveling snow, playing the guitar, swimming, or walking in the modern mall” (p. 275). Some of the activities that classify under NEAT—listed in ascending order of energy expenditure—include standing, gum chewing, fidgeting, stair climbing, and walking.

J. Non-exercise Activity Thermogenesis and Obesity

It is estimated that 1 billion individuals across the globe are overweight or obese; this comes as a result of the increased sedentary lifestyle behaviors (Novak & Levine, 2007). A study conducted at Mayo clinic in 2006, one of the prominent research institutes on the topic, found that the mean energy expenditure while seated was approximately 70 kcal/h, in comparison to walking and working which was about 190 kcal/h, with the mean increase of energy expenditure at approximately 120 kcal/h. The study concluded that replacing time sitting at the desk by time walking and working, individuals would lose 20-30 kg annually if remaining energy components remained the same (Levine & Miller, 2007).

In another study by Levine, the author indicates that when a person walks at 1 mile per hour, instead of sitting, the energy expenditure of a 70 kg person is approximately 100 kcal/h (Levine, 2007). Levine and Kotz (2005) in a third study indicate that obesity is associated with a predisposition to be seated for a longer period of
time in compare to more lean individuals (about 160 min/day), and if these individuals used this time to stand or ambulate they would spend up to 350 kcal/day.

**K. Non-exercise Activity Thermogenesis Strategies**

Examples of activities classified under NEAT—listed in ascending order of energy expenditure—include; standing, gum chewing, and fidgeting (Levine, 2007). A comparison of the energy expenditure associated with each item is shown in Figure 2.1. For example, when a person stands instead of sitting, energy expenditure is increased by 10% above rest. When a person chews gum, energy expenditure is increased by 20% above rest. When fidgeting, energy expenditure is increased by 50%, and when a person walks at one mile per hour energy expenditure is doubled (Increasing the rate to three miles per hour increases expenditure by 250%) (Wilson, 2004).

![Figure 2.1](image.png)  
*Figure 2.1 Energy expenditure during different activities in comparison to rest (Levine, 2007).*
NEAT can be divided into NEAT associated with leisure activities, and NEAT associated with occupation or work (Levine, 2007). To promote individual NEAT strategies, Levine recommends the following steps: (a) self monitoring and feedback, (b) modify specific seated behaviors so that they can be performed while standing, (c) use sedentary behaviors to reinforce physically active choices, (d) identify substitutes of sedentary behaviors, (e) stimulus control, both at work and home, and (f) presence of a motivated team (Levine et al., 2006).

Kate Trainor states “the beauty of NEAT is that you can start anytime, anywhere.” Simple items like using the stairs instead if the elevator may burn 12 calories. Or like walking the dog which burns 200 calories per hour or up to the 300 calories if it was a one hour jog, may increase ones daily NEAT (Trainor, 2009). Strategies that increase NEAT at the office or work environment include (a) replacing the chair with a treadmill or exercise ball; (b) keeping exercise equipment handy, like mini sized steppers; (c) using a pedometer to measure the amount of steps per day with a goal of 10,000 steps; (d) keeping walking or running shoes accessible, near the desk; (e) walking while using the phone (Trainor, 2009).

To help ease NEAT into individuals life, Levine recommends the following steps, represented by the acronym STRIPE: (a) Select a NEAT activity that is enjoyable to start with, (b) Targeted, goals must be well defined, (c) Reward must be per goal, (d) Identify barriers and work on overcoming them, (e) Plan NEAT activity sessions, (f) Evaluate adherence (Levine, 2007).
L. Non-exercise Activity Thermogenesis Measurement

Several methods that measure NEAT are currently available. For example, Levine and Miller used a vertical work station—instead of the typical horizontal one—to assess energy expenditure in one of his many studies on the topic. The new work station, which he called “walk and work desk” was designed so that participants can walk on a treadmill while conducting normal office work on their personal computer which was placed on top of the treadmill. The study reports a mean increase in energy expenditure of 119 kcal/h when using the walk and work desk compared to sitting (Levine & Miller, 2007).

In a clinical trial conducted by the United States government in 2006, which was sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), participants wore a timed device that vibrates at pre-set intervals and measures the amount of NEAT, the results have not been published yet (Non-exercise Activity Thermogenesis, 2008). Other options that measure energy expenditure include pedometers and accelerometers. Some high tech accelerometers can save data for days and allows easy transfer to a computer data base for analysis (Kushner & Bessesen, 2007).

M. Conclusions

The Metabolic Syndrome Institute associates metabolic syndrome with an increased risk of coronary heart disease, myocardial infarction, and stroke in both genders. Furthermore, the institute indicates that metabolic syndrome patients are three times more likely to suffer a cardiovascular event in compare to non metabolic syndrome individuals (Metabolic Syndrome Institute, 2010). Many studies cover the morbidity and mortality of the metabolic syndrome; a lesser number covers it in relation to the Qatari
population. From the little research done, it appears necessary to conduct more experimental studies on this topic in this population, as the majority of information comes from observational studies and personal reviews. In regard to NEAT, the unknown seems to outweigh the known. Much more experimental research needs to be conducted in relation to the mechanisms of how NEAT works, how it influences obesity, and how to convince people to incorporate NEAT into their lives. The results of this study may be of use for future preventive care specialists when counseling patients with metabolic syndrome, as it adds another method that may be utilized for calorie burning on daily basis.
A. Design

The study is a randomized experiment, with a pretest and posttest control group. There are 200 metabolic syndrome patients, ages 18 and above from Qatar. NEAT enhancing activities were used as a lifestyle intervention over a one year period. Following the outline shown in Table 1, subjects were followed up twice after baseline measurements were taken. Figure 3.1 shows the overall design of the study according to Shadish, Cook, and Campbell (2002) notation.

|        | Baseline | 6 months | 1 year |
|--------|----------|----------|--------|
| Experimental group |
| R      | O        | x        | O      | x      | O      | Experimental group |
| Control group |
| R      | O        | O        | O      | O      | Control group |

*Figure 3.1* The design using Shadish, Cook, & Campbell notation, where X = treatment, O = observation, R = randomized.

B. Participants

A total of 200 subjects with metabolic syndrome were recruited from the endocrinology and diabetes department clinics at Hamad Medical Corporation in Doha, Qatar. The endocrinologist introduced the study to his patients; the ones who decided to participate later met with the nurse for a health assessment, and to sign the consent form. Finally, subjects met with the research assistant for educational material and further
details. Participants were asked to provide demographic data during the initial health assessment visit. A designed questionnaire was used to collect patient information such as age, gender, and marital status. Additional information collected includes the reason for referral, other co-morbidities and medications at the start and end of study, along with changes.

The IDF definition for metabolic syndrome was used to establish diagnosis (IDF, 2006). The inclusion criteria is: patients over the age of 18, who have elevated waist circumference (over or equal to 94 cm for men, over or equal to 80 cm for women), and two or more abnormalities out of four, of the following: (a) glucose levels over or equal to 5.6 mmol/L, or diagnosed diabetes (b) blood pressure over or equal to 130/85 mmHg, or drug treatment for hypertension (c) triglycerides levels over or equal to 1.7 mmol/L, or drug treatment for high triglycerides) (d) HDL levels less than 1.0 mmol/L for men and less than 1.3 mmol/L for women, or drug treatment for low HDL.

The exclusion criteria excluded subjects (a) diagnosed with major illnesses, (b) taking any type of medication that may affect weight, and (c) cannot tolerate study procedures (NICHD, 2008).

C. Procedures

The research assistant randomized subjects to an intervention \( (n = 100) \) and a control group \( (n = 100) \). The randomization list was produced using random allocation software. The control group received general dietary and physical activity guidelines. The intervention group additionally received information on how to increase their daily NEAT. Subjects were followed for one year, during which the waist circumference and lipid profile were assessed at baseline, 6, and 12 months. During each of these visits
subjects met with the nurse for a weight assessment and to draw blood samples. Subjects then met with the research assistant to report their NEAT activity and get educational material.

A contracted marketing company sent a reminder of participation to subjects in the intervention group via text messages at 2, 4, 8, and 10 months. The reminder included the title of the study, along with instructions on NEAT enhancing activities. For follow up visits at 6 and 12 months, participants received a reminder call of their appointment date, one week and one day before their arranged appointments. These calls were carried out by the nurse or the research assistant according to availability. The above procedures were mentioned in detail in the informed consent and were described to subjects before they decided whether or not to join.

D. Measurements

A Seca digital medical weighing scale was used to obtain weight information, which was measured in kilograms. Waist circumference was assessed using a measure tape at the level of the superior iliac crest with the person lightly clothed. The fasting glucose and lipid profile were assessed by drawing blood samples, and submitting them to the facility lab for a report. This includes information on the blood levels of (a) LDL cholesterol, (b) HDL cholesterol, (c) total cholesterol, and (d) triglycerides. These were measured in millimole per liter. The blood pressure was measured using an electronic sphygmomanometer after the patient was seated for 10 minutes.

E. Intervention

Subjects were asked to practice the following NEAT enhancing activities recommended by Levine et al. (2006); standing instead of sitting, gum chewing,
fidgeting, using the stairs instead of the elevator, walking instead of using the car. This information along with the frequency was reported by the subjects on weekly report sheets. These were turned in to the research assistant at the 6 and 12 month visit. A copy of the report sheet is shown in Table 3.

F. Data Analysis

The analysis was based on the results of a repeated measure ANOVA test with two groups, with data collected at baseline, 6 months, and 1 year. Results of both groups were compared, then, results of the amount of NEAT were compared among the intervention group. The independent variable was being in the intervention or the control group. The dependent variables were (a) the change in the number of metabolic syndrome components at baseline, 6 months, and 1 year; and (b) the change in the number of subjects meeting criteria for metabolic syndrome, and were measured on a continuous scale.

G. Power Analysis

Based on Cohen’s (1992) estimation of a medium effect size \( f=25 \), power = 80%, and \( \alpha = 0.05 \), 64 subjects were needed in each group for a total of 128. To allow for any dropouts, the goal was to recruit 200 subjects, 100 per group, which allowed for a good dropout rate.

H. Limitations

Randomization controls for some threats to validity such as maturation, history, regression, instrumentation and selection. However, the design fails to control for other sources of threats to internal validity: (a) It is possible that subjects interacted with each other at the hospital due to the small size of the waiting room, which may have lead some
from the control group to try the intervention on their own. (b) Self-report was used during follow up visits where subjects may tend to over report, or simply forget. (c) Under attrition, a high dropout rate was experienced.

The study also fails to control for sources of threats to construct validity: (a) Compensatory equalization, it is possible that subjects from the control group may have gotten access to information related to the intervention from the hospital personal and decided to try it on their own. (b) Compensatory rivalry, it is possible that subjects from the control group tried to show that they can do as well as the other group. (c) Resentful demoralization, it is possible that subjects from the control group may have become resentful because they didn’t receive the intervention, and decided to drop out of the trial. Finally, under external validity, because the study was conducted in a certain geographic area and the patients were of a certain disease, the results of the study cannot be generalized to other geographical areas or patients with other types of diseases.

I. Research Ethics

Under autonomy, subjects had the right to decide whether to join the study or not. Those with diminished autonomy had the right to be protected from harm. Furthermore, subjects were asked to sign a consent form, which is a ten page document that covers the following items: (a) A description of the study and its purpose. (b) The information the participant was asked to give. (c) A description of what the participant was asked to do and for how long. (d) A description of potential risks and benefits. (e) A statement indicating that participation is voluntary. (f) Reassurance that all data will be confidential. (g) The name and number of a person the participant may call to get further information. (h) The name and number of a person the participant may call if he has a complaint.
(i) Information regarding compensation provided. (j) A description of alternatives to the research. (k) Explanation that a summary of the results will be available if wanted. (l) Places for signatures (Cone & Foster, 2006). Subjects were asked to sign the consent form during the recruitment visit and before receiving any instructions.

For the sake of protecting patient confidentiality, these documents were kept in a designated folder, placed in a locked filing cabinet, located in the assigned research room, where the principal investigator was the only person who had access. Additionally, each subject was assigned a tracking number, where the list of names and tracking numbers were kept separately from the data and the tracking number. Under justice, subjects had equal opportunity in participating and benefiting from the research, this was carried out by excluding only those that meet the exclusion criteria, and not for any irrelevant factor like age or gender. Participants were recruited fairly using randomization which allowed each participant a 50% chance of being in either group. Also, subjects were informed of alternative treatments. Under beneficence, harm was minimized and benefits were maximized, any risks or advantages were revealed to subjects during the initial visit with the research assistant.
CHAPTER 4

PUBLISHABLE PAPER

The Effect of Non-Exercise Activity Thermogenesis on Subjects With Metabolic Syndrome—A Proof of Concept Study in Qatar

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Abstract

Qatar shares the burden of much of the rest of the world with high prevalence of metabolic syndrome. In a recent study, gender, age, and educational status were significant contributors to metabolic syndrome in this population. Other studies associate metabolic syndrome with an increased risk of coronary heart disease, myocardial infarction, and stroke in both genders\(^{(1)}\).

Total human energy expenditure is divided into three major components; resting metabolic rate, thermic effect of food, and activity thermogenesis which is divided into exercise and non exercise activity thermogenesis (NEAT). In this study NEAT was used as a lifestyle intervention on subjects with metabolic syndrome. 200 eligible patients from the Diabetes and Endocrinology Department at Hamad Medical Hospital in Doha, Qatar were assigned to an intervention \((n=100)\) or control \((n=100)\) group and followed for one year. The intervention group was advised to practice NEAT enhancing activities, while the control group was not advised about NEAT. Measurements of waist circumference, weight, BMI, blood pressure, glucose and lipid profile were assessed at baseline, 6 months, and 1 year. After one year 52 intervention and 55 control subjects completed the study. The results revealed no statistically significant differences in metabolic syndrome components between the two randomized groups. The amount of recommended NEAT activity appears to have been too small to influence study outcomes. Future studies in similar populations may need to consider the high dropout rate, and use of incentives or other interventions to increase compliance and retention.
Introduction

Metabolic syndrome is a combination of several abnormalities that increase the risk of cardiovascular disease (CVD) such as increased waist circumference, lipids, or blood pressure. Each abnormality is associated with cardiovascular disease cases (1), such as stroke, myocardial infarction, and heart failure (2). Worldwide, approximately 20-25% of the population suffers the burden of symptoms related to metabolic syndrome (3). The burden is shared among the Qatari population, which suffers from high prevalence rates of obesity and type 2 diabetes (1). A recent study indicates that the crude prevalence of metabolic syndrome in Qatar is 34% according to the International Diabetes Federation (IDF) criteria (2). Risk factors associated with metabolic syndrome in the Qatari population include age, ethnicity, obesity, and family history of diabetes (2).

Total human energy expenditure divides into basal metabolic rate, thermic effect of food, and activity thermogenesis. Activity thermogenesis is further divided into exercise, and non exercise activity thermogenesis (NEAT); NEAT is defined as the energy used throughout the day for all non exercise activities (4). Novak and Levine (5) show an inverse relationship between sedentary behaviors and physical activity; which leads to increased obesity and decreased health at the population level. Structured physical activity may help prevent metabolic syndrome (6). One way to increase physical activity both on an individual and population level is through increasing NEAT, such as walking instead of driving, or taking the stairs instead of using the elevator.

Gutierrez recommends physical activity as an adjunctive intervention because of its positive impact on abnormal lipids. Exercise improves HDL cholesterol levels through altering composition and maturation of the particles, as it increases the size of HDL
particles and the maturation of the nascent HDL particle. Additionally, it improves total cholesterol levels\(^{(7)}\). Grundy et al. show that lifestyle changes are crucial in hypertensive individuals with metabolic syndrome. They recommend physical activity as a tool to help control elevations in blood pressure. Additionally, insulin resistant individuals usually have abnormal fat distribution which is characterized by upper body fat. The authors show that the high release of fatty acids contributes to the accumulation of lipids in other sites than adipose tissue such as liver and muscles which contributes to worsening insulin resistance in the muscles. Furthermore, they show that patients with metabolic syndrome who are physically active may delay or prevent the development of type 2 diabetes\(^{(8)}\).

A lifestyle intervention study was conducted with 200 Qatari subjects identified with metabolic syndrome. This proof of concept study aims to understand whether it is feasible to attempt to reduce the burden of metabolic syndrome in Qatari outpatients by promoting increased NEAT.

**Methods**

The study is a one year randomized experiment, with a pretest and posttest intervention and control group. The study was conducted between March 2010 and August 2011. NEAT enhancing activities were used as a lifestyle intervention. Subjects were recruited from the endocrinology and diabetes department clinics at Hamad Medical Corporation in Doha, Qatar. Subjects were asked to sign a written consent form before enrollment. The study was approved by the research ethics committee at Hamad Medical Hospital in Doha, Qatar (research protocol number 9181/09). Permission for use of the data for the first author’s dissertation was given by the Institutional Review Board at Loma Linda University.
The IDF definition for metabolic syndrome was used to establish diagnosis\(^9\). The inclusion criteria included subjects over the age of 18, who have elevated waist circumference (over or equal to 94 cm for men, over or equal to 80 cm for women), and two or more abnormalities out of four, of the following: (a) elevated triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or drug treatment for elevated triglycerides; (b) reduced HDL cholesterol less than 40 mg/dL (1.0 mmol/L) for males and less than 50 mg/dL (1.3 mmol/L) for females, or drug treatment for reduced HDL cholesterol; (c) elevated blood pressure over or equal to 130 mm Hg for systolic and/or over or equal to 85 mm Hg for diastolic, or diagnosed hypertension; and (d) elevated fasting glucose above or equal to 100 mg/dL (5.6 mmol/L), or diagnosed diabetes. The exclusion criteria excluded subjects: (a) diagnosed with major illnesses; (b) taking any type of medication that may affect weight; (c) cannot tolerate study procedures\(^{10}\).

Subjects were divided to an intervention \((n = 100)\) and a control group \((n = 100)\). The randomized list was produced using random allocation software. The control group received general dietary and physical activity guidelines. The intervention group received additional information on how to increase their daily NEAT. This information was given by the nurse, on a one to one basis, over a 10 minute period of time. Participants also received a one page handout explaining different NEAT options and how it works. Subjects were asked to practice the following NEAT enhancing activities recommended by Levine et al.\(^4\) standing instead of sitting, gum chewing, fidgeting, using the stairs instead of the elevator, walking instead of using the car. This information along with the frequency was reported by subjects on weekly report sheets that were turned in at their 6- and 12-month visit.
Subjects were followed for 1 year, during which the waist circumference, blood pressure, weight, glucose and lipid profile were assessed at baseline, 6, and 12 months. Subjects in the intervention group received reminders, via text messages, to practice NEAT at 2, 4, 8, and 10 months.

Measurements

A Seca digital medical weighing scale was used to obtain body weight. Waist circumference was assessed using a measure tape at the level of the superior iliac crest with the person lightly clothed. The fasting glucose and lipid profile were assessed by drawing blood samples. This included information on the blood levels of total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and glucose (Roche/Hitachi modular p chemistry analyzer using enzymatic in vitro assay) at the facility laboratory. LDL cholesterol was calculated unless triglycerides were > 4.5 mmol/L, when it was measured directly. The blood pressure was measured using an electronic sphygmomanometer after the patient was seated for 10 minutes.

Statistical Analysis

Power analysis revealed that based on Cohen’s estimation of a medium effect size ($f=25$), power = 80%, and $\alpha = 0.05$, 64 subjects were needed for each group, for a total of 128$^{(11)}$. Categorical and continuous data were expressed as frequency (percentage) and mean ± SD. Descriptive statistics were used to summarize all demographic and clinical characteristics of the participants. Baseline participant characteristics in the two independent groups were compared using an unpaired $t$-test for continuous variables and a chi-square test for categorical variables. For the primary outcome variable i.e., average number of components of metabolic syndrome, data from the baseline, 6 months, and
12 months were compared using repeated measure analysis of variance (ANOVA). The results were presented with the associated 95% confidence interval. Where an overall group difference was found statistically significant, pair-wise comparisons were made using the appropriate post-hoc test. All statistical tests were two-sided and the p value smaller than 0.05 was considered to be statistically significant. All statistical analyses were done using statistical packages SPSS 19.0 (SPSS Inc. Chicago, IL).

**Study Progress**

A total of 200 individuals were recruited between March and August of 2010. These were randomized using random allocation software into two groups, an intervention and control group. At the 6-month visit, 62 were lost at follow up; 32 of the intervention and 29 of the control group. Additionally one person died from the latter group. At the 12-month visit, 31 additional subjects were lost at follow up, 16 and 15 of the intervention and control group respectively. The following flow chart shows the overall study progress.

[Insert Figure 4.1 here]

**Results**

Among those recruited 120 (60%) were men, and 80 (40%) were women. The number of males was higher in both groups, 58 in the intervention and 62 in the control groups. All subjects were of the same ethnicity as they were all Qatari nationals. The mean height for the intervention group was 162.7cm ±8.71 (range: 139-182), and for the control group 162.5cm ±9.29 (range: 143-185). Patient demographics, metabolic syndrome components and anthropometrics are listed in Table 1 below.

[Insert Table 4.1 here]
Information regarding the number of components of metabolic syndrome among each group is summarized in table 2 below.

[Insert Table 4.2 here]

The results showed no significant difference over time between the groups in regard to weight, BMI, waist circumference, glucose, HDL cholesterol, triglycerides, diastolic, and systolic blood pressure, and the number of metabolic syndrome components as well as total and LDL cholesterol. The detailed results are presented in Table 3.

[Insert Table 4.3 here]

**NEAT Activity**

In regard to the frequency of NEAT practiced, among the 40 participants that did report their activity, 24 (60%) were found to have practiced NEAT enhancing activities 1-2 times a week, 10 (25%) practiced it 3-4 times a week, and 3 (7.5%) did it more than 4 times a week, while 3 (7.5%) reported no activity.

**Discussion**

The increasing prevalence of metabolic syndrome in Qatar is just one indication among many that this population is suffering as a result of major lifestyle changes that have occurred in the past four decades. In this study on 200 subjects, there was no significant difference between the groups on the measures of metabolic syndrome after a 1-year intervention study. We are unaware of previous studies using NEAT as an intervention in patients with metabolic syndrome. Most of the patients were middle aged or older, and already had established type 2 diabetes. Such interventions may be effective in younger patients, and work better for prevention rather than cure.
Factors that play an important role in the development of metabolic syndrome include genetics, sedentary lifestyle, cigarette smoking, progressive weight gain, and a Western diet\(^{(12,13)}\). Lifestyle plays a major role in the etiology of metabolic syndrome either through low physical activity or excess caloric intake or both. The most common risk factor seems to be abdominal obesity which majorly justifies lifestyle modification. The American Heart Association states that “in the long run, the greatest benefit for those with metabolic syndrome will be derived from effective lifestyle intervention”\(^{(14)}\).

Levine et al.\(^{(4)}\) show that NEAT plays an important role in overall energy balance because it may vary as much as 2000 kcal/day between individuals. Moreover, they indicate that highly active people may expend as much as three times more than inactive people. In 2006 a study conducted at the Mayo Clinic found that the mean energy expenditure while seated was approximately 70 kcal/h, in contrast to walking and working which was about 190 kcal/h, with the mean increase of energy expenditure at approximately 120 kcal/h. The study concluded that replacing time sitting at the desk by time walking and working, individuals would lose 20-30 kg per year, if other components of energy expenditure remained the same\(^{(15)}\).

In another study by Levine, the author indicates that when a person walks at 1 mile per hour, instead of sitting, the energy expenditure of a 70 kg person is approximately 100 kcal/h\(^{(16)}\). Levine and Kotz in a third study indicate that obesity is associated with a predisposition to be seated for a longer period of time in comparison to more lean individuals (about 160 min/day), and if these individuals used this time to stand or ambulate they would burn up to 350 kcal/day\(^{(17)}\).
Despite the previously mentioned studies that highlighted the importance and effectiveness of NEAT in increasing energy expenditure, components of metabolic syndrome showed no significant difference between the groups in this study. This can be due to many reasons. Non compliance is one of the major influencing factors, which can be due to social norms, or lack of local convincing evidence on the effectiveness of NEAT, or lack of awareness. It appears that not enough NEAT was accomplished per week to influence the results. It is possible that NEAT should be carried out and practiced on a daily basis to the point where it becomes a personal habit or part of one’s lifestyle before one might expect to see significant results.

While the results were disappointing they provide a basis for future studies. To increase NEAT, more significant activities that expend more energy than others may be emphasized like walking. Furthermore, specific goals to be attained in regard to frequency and duration of activity should be promoted. Another suggestion would be to use pedometers or other physical activity sensors as an incentive to increase NEAT as Gardner and Campagna show that such devices help increase motivation and aid in raising awareness to different activity patterns\(^{(18)}\). Also, self-report was used as a reporting method, where subjects may tend to over report, or simply forget. Only 40% of participants in the intervention group filled out the report forms.

Other factors may include the high dropout rate and missing data. To improve the dropout rate, one may consider shortening the time between follow up visits or by providing incentives at each visit. Other possible options include increasing the frequency and type of reminders, such as using phone follow ups on regular basis. Additionally the quality of training of personnel who gave the advice may be improved, as well as the
quality of advice given. Additionally, many other factors may have influenced participants of this study, such as the limited physical activity outlets considering the overall hot weather, which also contributes to the common sedentary lifestyle, which is quite prevalent in the area, as well as the occurrence of the month of fasting during the final evaluation of some participants.

Due to the high rate of metabolic syndrome locally, it would be beneficial to conduct similar studies as the one here but on a larger scale, to help curb the epidemic of metabolic syndrome and its hazardous outcome. Such studies should take into consideration the high dropout rate which occurred in this study, and should be constructed to minimize such occurrences.

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200 started

100 intervention group

32 lost to follow up

6 months: 68

16 lost to follow up

12 months: 52

100 control group

29 lost to follow up
1 died

6 months: 70

15 lost to follow up

12 months: 55

Figure 4.1 Flow chart showing study progress
| Variable                          | Intervention (n=100) | Control (n=100) | p-value* |
|----------------------------------|----------------------|-----------------|----------|
| **Gender**                       |                      |                 |          |
| Male                             | 58 (58%)             | 62 (67%)        | 0.564    |
| Female                           | 42 (42%)             | 38 (38%)        |          |
| **Age (years)**                  | Mean ± SD 57.1±13.44 | Mean ± SD 55.9±12.32 | 0.490    |
| **Marital Status**               |                      |                 |          |
| Married                          | 83 (83.0%)           | 88 (88.0%)      | 0.195    |
| Single                           | 9 (9.0%)             | 10 (10.0%)      |          |
| Widowed                          | 7 (7.0%)             | 1 (1.0%)        |          |
| Divorced                         | 1 (1.0%)             | 1 (1.0%)        |          |
| **Height (cm)**                  | Mean ± SD 162.7±8.71 | Mean ± SD 162.3±9.29 | 0.772    |
| **Weight (kg)**                  | Mean ± SD 86.9±18.48 | Mean ± SD 87.9±19.25 | 0.952    |
| **BMI (kg/m²)**                  | Mean ± SD 33.0±7.04  | Mean ± SD 33.1±7.66 | 0.935    |
| **Waist circumference (cm)**     | Mean ± SD 108.2±12.26| Mean ± SD 108.4±14.13 | 0.902    |
| **Glucose (mmol/L)**             | Mean ± SD 8.4±3.15   | Mean ± SD 8.5±3.5 | 0.762    |
| **High-density lipoprotein cholesterol (mmol/L)** | Mean ± SD 1.1±0.28 | Mean ± SD 1.1±0.35 | 0.595    |
| **Low-density lipoprotein cholesterol (mmol/L)** | Mean ± SD 2.7±0.94 | Mean ± SD 2.7±0.89 | 0.872    |
| **Triglyceride (mmol/L)**        | Mean ± SD 1.6±0.94   | Mean ± SD 1.6±1.1 |          |
| **Cholesterol (mmol/L)**         | Mean ± SD 4.6±1.1    | Mean ± SD 4.6±1.0 | 0.965    |
| **Systolic blood pressure (mmHg)**| Mean ± SD 145.1±18.31| Mean ± SD 140.5±20.18 | 0.096    |
| **Diastolic blood pressure (mmHg)**| Mean ± SD 76.8±10.65 | Mean ± SD 76.3±10.77 | 0.744    |
| **Medications**                  |                      |                 |          |
| Anti-diabetic                     |                      |                 |          |
| Yes                              | 65 (72.2%)           | 64 (72.7%)      | 0.940    |
| No                               | 25 (27.8%)           | 24 (27.3%)      |          |
| Lipid-lowering                   |                      |                 |          |
| Yes                              | 62 (68.9%)           | 62 (70.5%)      | 0.820    |
| No                               | 28 (31.1%)           | 26 (29.5%)      |          |
| Anti-hypertensive                |                      |                 |          |
| Yes                              | 69 (76.7%)           | 66 (75.0%)      | 0.795    |
| No                               | 21 (23.3%)           | 22 (25.0%)      |          |

Table 4.1 Patient demographics, metabolic syndrome components, and anthropometrics (Quantitative values expressed as mean ± SD/ p-value derived using independent t-test, qualitative values expressed as number (percentage)/ p-value derived using chi square test).
| Components of metabolic syndrome          | Intervention  | Control   | P value |
|-----------------------------------------|---------------|-----------|---------|
| Elevated waist circumference            | (n=100)       | (n=100)   | 0.390   |
| Yes                                     | 95 (95.0%)    | 92 (92.0%)|         |
| No                                      | 5 (5.0%)      | 8 (8.0%)  |         |
| Elevated triglycerides                  | (n=94)        | (n=98)    | 0.690   |
| Yes                                     | 63 (67.0%)    | 63 (64.3%)|         |
| No                                      | 31 (33.0%)    | 35 (35.7%)|         |
| Elevated blood pressure                 | (n=100)       | (n=99)    | 0.620   |
| Yes                                     | 91 (91.0%)    | 88 (88.9%)|         |
| No                                      | 9 (9.0%)      | 11 (11.1%)|         |
| Reduced HDL cholesterol                 | (n=94)        | (n=96)    | 0.134   |
| Yes                                     | 70 (74.5%)    | 80 (83.3%)|         |
| No                                      | 24 (25.5%)    | 16 (16.7%)|         |
| Elevated glucose                        | (n=97)        | (n=96)    | 0.502   |
| Yes                                     | 86 (88.7%)    | 82 (85.4%)|         |
| No                                      | 11 (11.3%)    | 14 (14.6%)|         |

Table 4.2 Patients' metabolic syndrome components (p-value derived using chi square test).
| Variable                                      | Time Points |   |   |   |
|-----------------------------------------------|-------------|---|---|---|
|                                               | Baseline (Mean ± SD) | 6 months (Mean ± SD) | 12 months (Mean ± SD) | p-value* |
| Weight (kg)                                   |             |   |   |   |
| Intervention (n=48)                          | 84.2±18.51  | 84.6±18.46  | 84.9±19.16  | 0.677    |
| Control (n=49)                                | 86.5±20.19  | 85.9±20.34  | 86.3±21.23  |           |
| Body mass index (kg/m²)                       |             |   |   |   |
| Intervention (n=47)                          | 32.15±7.62  | 32.26±7.42  | 32.38±7.74  | 0.611    |
| Control (n=49)                                | 33.21±8.32  | 32.99±8.37  | 33.12±8.77  |           |
| Waist circumference (cm)                      |             |   |   |   |
| Intervention (n=40)                          | 104.5±13.21 | 104.6±11.38 | 104.6±11.44 | 0.159    |
| Control (n=47)                                | 108.5±13.21 | 108.1±13.24 | 108.4±13.38 |           |
| Glucose (mmol/L)                              |             |   |   |   |
| Intervention (n=45)                          | 8.78±3.54   | 8.86±3.83   | 8.62±3.47   | 0.501    |
| Control (n=39)                                | 9.42±3.93   | 9.29±4.42   | 9.09±4.33   |           |
| High-density lipoprotein cholesterol (mmol/L) |             |   |   |   |
| Intervention (n=43)                          | 1.14±0.29   | 1.10±0.25   | 1.15±0.28   | 0.396    |
| Control (n=38)                                | 1.05±0.31   | 1.03±0.28   | 1.15±0.51   |           |
| Low-density lipoprotein cholesterol (mmol/L)  |             |   |   |   |
| Intervention (n=43)                          | 2.57±0.81   | 2.63±0.71   | 2.58±0.68   | 0.789    |
| Control (n=39)                                | 2.53±0.79   | 2.56±0.70   | 2.58±1.05   |           |
| Triglyceride (mmol/L)                         |             |   |   |   |
| Intervention (n=43)                          | 1.64±0.93   | 1.47±0.68   | 1.51±0.65   | 0.124    |
| Control (n=39)                                | 1.79±1.45   | 2.02±1.66   | 1.87±1.35   |           |
| Cholesterol (mmol/L)                          |             |   |   |   |
| Intervention (n=43)                          | 4.55±0.90   | 4.40±0.73   | 4.38±0.82   | 0.889    |
| Control (n=39)                                | 4.41±1.09   | 4.45±0.82   | 4.54±1.42   |           |
| Systolic blood pressure (mmHg)                |             |   |   |   |
| Intervention (n=43)                          | 144.77±19.60| 137.49±18.76| 137.21±16.64| 0.456    |
| Control (n=46)                                | 142.07±19.94| 143.59±18.82| 141.24±19.19|           |
| Diastolic blood pressure (mmHg)               |             |   |   |   |
| Intervention (n=43)                          | 75.79±9.03  | 75.12±9.39  | 72.72±9.46  | 0.218    |
| Control (n=46)                                | 75.70±11.76 | 78.22±10.81 | 76.15±10.43 |           |
| Number of components of metabolic syndrome    |             |   |   |   |
| Intervention (n=50)                          | 3.64±0.77   | 3.68±0.79   | 3.78±0.76   | 0.059    |
| Control (n=45)                                | 3.98±0.78   | 3.96±0.85   | 4.02±0.86   |           |

Table 4.3 Comparison of anthropometric and metabolic parameters at baseline, 6 months, and 12 months in completers in the intervention and control group (p-value derived using repeated measures ANOVA test).
CHAPTER 5
ADDITIONAL DATA

A. Background

In this proof of concept study, there were no differences in metabolic syndrome components between groups randomized to the NEAT or control interventions. In order to clarify whether certain subgroups showed changes in parameters following the intervention, we compared results in the intervention and control groups among individuals with diagnosed diabetes, among males and females separately, and among subjects that reported the amount of NEAT performed. Finally we looked at baseline characteristics of completers versus non-completers of the study to better understand characteristics associated with compliance.

B. Results in Individuals Using Anti-Diabetic Medications

Physical activity in general and NEAT in specific benefit diabetic individuals through improving their sensitivity to insulin therefore reducing their risk for CVD. Sigal (2006) indicates that exercise for two months or more is significantly effective in reducing HbA1c in patients with type 2 diabetes. This section had two goals, (a) to look at the risk level of those using anti-diabetic medications versus their counterparts not taking medications, and (b) to examine if results in those on anti-diabetics differed from the whole group (because of their higher risk level).

In this study, 72.2% of the intervention groups were using anti-diabetic medication, while 27.8% were not. For the control group 72.7% were using anti-diabetic medication, while 27.3% were not. To compare risk factors among those on anti diabetic medications and those not on medications, we ran a chi square test on the 5 components of
metabolic syndrome. Not surprisingly, as shown in the table below almost all those on anti-diabetic medication fulfilled the high glucose criterion of metabolic syndrome. In addition subjects on anti-diabetic medication were more likely to meet the low HDL cholesterol criterion of metabolic syndrome than their counterparts.

**Table 5.1** Percentages of Risk Factors Among Those Using and Not Using Anti Diabetic Medications (*p*-value derived using chi square test)

| Components of metabolic syndrome | On anti diabetic medications | Not on anti diabetic medications | *p*-value |
|---------------------------------|-----------------------------|----------------------------------|-----------|
| Elevated waist circumference    |                             |                                  |           |
| (n=178)                         |                             |                                  |           |
| Yes                             | 120 (93.0%)                 | 47 (95.9%)                       | 0.474     |
| No                              | 9 (7.0%)                    | 2 (4.1%)                         |           |
| Elevated triglycerides (n=175)  |                             |                                  |           |
| Yes                             | 91 (72.0%)                  | 29 (59.3%)                       | 0.950     |
| No                              | 35 (27.8%)                  | 20 (40.8%)                       |           |
| Elevated blood pressure (n=177) |                             |                                  |           |
| Yes                             | 116 (90.6%)                 | 45 (91.8%)                       | 0.801     |
| No                              | 12 (9.4%)                   | 4 (8.2%)                         |           |
| Reduced HDL cholesterol (n=173) |                             |                                  |           |
| Yes                             | 108 (85.0%)                 | 33 (71.7%)                       | 0.047     |
| No                              | 19 (15.0%)                  | 13 (28.3%)                       |           |
| Elevated glucose (n=175)        |                             |                                  |           |
| Yes                             | 128 (99.2%)                 | 29 (63%)                         | 0.000     |
| No                              | 1 (8.0%)                    | 17 (37%)                         |           |

**C. Comparison Between Groups**

When looking at those participants that were treated with anti diabetic medications alone in the NEAT intervention versus the control group, upon analyzing the results using a repeated measures ANOVA test; there was no significant difference over time between the groups in regard to weight, BMI, waist circumference, glucose, HDL cholesterol, triglycerides, diastolic and systolic blood pressure, as well as total and LDL cholesterol.
cholesterol and the number of metabolic syndrome components. The table below summarizes the results.

**Table 5.2** Comparison of Anthropometric and Metabolic Parameters at Baseline, 6 Months, and 12 Months in Completers in the Intervention and Control Group Among Those on Anti-diabetic Medication (*p*-value derived using repeated measure ANOVA test)

| Variable                          | Baseline (Mean ± SD) | 6 months (Mean ± SD) | 12 months (Mean ± SD) | *p*-value* |
|-----------------------------------|----------------------|----------------------|-----------------------|------------|
| Weight (kg)                       |                      |                      |                       |            |
| Intervention (n=37)               | 82.0±15.79           | 82.4±15.65           | 82.5±15.98            | 0.888      |
| Control (n=33)                    | 82.3±16.38           | 81.5±16.81           | 81.5±16.98            |            |
| Body mass index (kg/m²)           |                      |                      |                       |            |
| Intervention (n=37)               | 31.0±6.34            | 31.2±6.09            | 31.2±6.27             | 0.933      |
| Control (n=33)                    | 33.2±6.03            | 30.9±6.31            | 30.9±6.46             |            |
| Waist circumference (cm)          |                      |                      |                       |            |
| Intervention (n=32)               | 103.3±11.86          | 103.4±11.81          | 103.4±11.92           | 0.291      |
| Control (n=31)                    | 106.9±12.90          | 106.6±12.87          | 106.7±12.98           |            |
| Glucose (mmol/L)                  |                      |                      |                       |            |
| Intervention (n=35)               | 9.6±4.52             | 9.5±4.84             | 9.4±4.42              | 0.489      |
| Control (n=31)                    | 10.37±3.85           | 10.23±4.46           | 9.79±4.58             |            |
| High-density lipoprotein cholesterol (mmol/L) |       |                      |                       |            |
| Intervention (n=35)               | 1.12±0.26            | 1.09±0.22            | 1.14±0.27             | 0.709      |
| Control (n=30)                    | 1.05±0.33            | 1.03±0.28            | 1.19±0.56             |            |
| Low-density lipoprotein cholesterol (mmol/L) |       |                      |                       |            |
| Intervention (n=35)               | 2.54±0.87            | 2.61±0.73            | 2.49±0.67             | 0.627      |
| Control (n=30)                    | 2.37±0.76            | 2.48±0.71            | 2.55±1.15             |            |
| Triglyceride (mmol/L)             |                      |                      |                       |            |
| Intervention (n=35)               | 1.69±1.00            | 1.48±0.67            | 1.49±0.65             | 0.166      |
| Control (n=30)                    | 1.85±1.64            | 2.05±1.84            | 1.93±1.51             |            |
| Cholesterol (mmol/L)              |                      |                      |                       |            |
| Intervention (n=35)               | 4.53±0.96            | 4.36±0.75            | 4.26±0.81             | 0.835      |
| Control (n=31)                    | 4.31±1.15            | 4.39±0.86            | 4.59±1.55             |            |
| Systolic blood pressure (mmHg)    |                      |                      |                       |            |
| Intervention (n=36)               | 146.00±20.83         | 138.83±19.61         | 138.89±17.23          | 0.978      |
| Control (n=32)                    | 141.50±21.84         | 142.88±20.51         | 139.69±19.91          |            |
| Diastolic blood pressure (mmHg)   |                      |                      |                       |            |
| Intervention (n=36)               | 75.25±9.19           | 75.42±9.88           | 72.64±9.69            | 0.603      |
| Control (n=32)                    | 75.44±10.14          | 76.69±10.86          | 74.25±10.05           |            |
| Number of components of MS         |                      |                      |                       |            |
| Intervention (n=39)               | 3.69±0.83            | 3.79±0.80            | 3.82±0.75             | 0.143      |
| Control (n=36)                    | 4.00±0.75            | 4.00±0.86            | 4.06±0.86             |            |
D. Results by Gender

The results of comparing the groups over time, for males only, showed no difference for all variables except for the number of metabolic syndrome components which shows a significant increase in the intervention group while there is a tendency toward lowering of triglycerides in males in the intervention group. None of the risk factors were numerically worsened in the males in the intervention group, but as the definition of metabolic syndrome is based on medications used, not only on blood test values, that may be the explanation of this result. The results of an analysis using a repeated measure ANOVA test, on males alone, is listed in Table 5.3.

Table 5.3 Comparison of Anthropometric and Metabolic Parameters at Baseline, 6 Months, and 12 Months in Completers in the Intervention and Control Group Among Males (p-value derived using repeated measure ANOVA test)

| Variable                          | Baseline (Mean ± SD) | 6 months (Mean ± SD) | 12 months (Mean ± SD) | p-value |
|----------------------------------|---------------------|---------------------|----------------------|---------|
| Weight (kg)                      |                     |                     |                      |         |
| Intervention (n=26)              | 83.04±14.69         | 83.90±14.78         | 83.92±15.23          | 0.746   |
| Control (n=29)                   | 85.31±18.30         | 84.78±18.89         | 85.28±19.31          |         |
| Body mass index (kg/m²)          |                     |                     |                      |         |
| Intervention (n=25)              | 28.98±4.72          | 29.32±4.79          | 29.31±4.98           | 0.467   |
| Control (n=29)                   | 30.29±5.19          | 30.09±5.47          | 30.33±5.80           |         |
| Waist circumference (cm)         |                     |                     |                      |         |
| Intervention (n=24)              | 104.17±9.70         | 104.42±9.82         | 104.37±9.87          | 0.645   |
| Control (n=27)                   | 105.85±12.51        | 105.69±12.62        | 105.85±12.66         |         |
| Glucose (mmol/L)                 |                     |                     |                      |         |
| Intervention (n=24)              | 9.69±4.12           | 8.8±3.94            | 9.14±3.87            | 0.892   |
| Control (n=26)                   | 9.05±3.51           | 9.4±4.84            | 9.62±4.88            |         |
| High-density lipoprotein cholesterol (mmol/L) |               |                     |                      |         |
| Intervention (n=25)              | 1.08±0.25           | 1.05±0.24           | 1.09±0.24            | 0.599   |
| Control (n=27)                   | 0.99±0.30           | 0.99±0.28           | 1.12±0.58            |         |
| Low-density lipoprotein cholesterol (mmol/L) |          |                     |                      |         |
| Intervention (n=25)              | 2.71±0.87           | 2.78±0.81           | 2.74±0.68            | 0.298   |
| Control (n=27)                   | 2.56±0.85           | 2.54±0.68           | 2.53±1.10            |         |
| Triglyceride (mmol/L)            |                     |                     |                      |         |
| Intervention (n=25)              | 1.56±1.04           | 1.35±0.71           | 1.43±0.58            | 0.060   |
| Control (n=27)                   | 1.96±1.71           | 2.28±1.93           | 2.02±1.58            |         |
| Cholesterol (mmol/L)             |                     |                     |                      |         |
| Intervention (n=25)              | 4.63±0.97           | 4.46±0.81           | 4.49±0.89            | 0.977   |
| Control (n=28)                   | 4.50±1.21           | 4.50±0.80           | 4.56±1.51            |         |
Table 5.3—Continued.

| Variable                              | Baseline (Mean ± SD) | 6 months (Mean ± SD) | 12 months (Mean ± SD) | p-value |
|----------------------------------------|----------------------|----------------------|-----------------------|---------|
|                                       |                      |                      |                       |         |
| Systolic blood pressure (mmHg)         |                      |                      |                       |         |
| Intervention (n=23)                    | 142.78±18            | 136.61±19.22         | 140.26±18.23          | 0.666   |
| Control (n=27)                         | 142±19.75            | 142.44±19.79         | 141.11±19.20          |         |
| Diastolic blood pressure (mmHg)        |                      |                      |                       |         |
| Intervention (n=23)                    | 75.74±9.21           | 76.57±9.57           | 75.52±10.19           | 0.491   |
| Control (n=27)                         | 76.44±10.60          | 79.22±11.34          | 76.96±9.52            |         |
| Number of components of MS             |                      |                      |                       |         |
| Intervention (n=30)                    | 3.57±0.77            | 3.63±0.76            | 3.80±0.76             | 0.007   |
| Control (n=28)                         | 4.14±0.75            | 4.18±0.77            | 4.18±0.72             |         |

As for females, the results of comparing the groups over time, show no difference for all variables between the intervention and control groups. The results of an analysis using a repeated measure ANOVA test, on females alone, is listed in Table 5.4 below.

Table 5.4 Comparison of Anthropometric and Metabolic Parameters at Baseline, 6 Months, and 12 Months in Completers in the Intervention and Control Among Males (p-value derived using repeated measure ANOVA test)

| Variable                              | Baseline (Mean ± SD) | 6 months (Mean ± SD) | 12 months (Mean ± SD) | p-value |
|----------------------------------------|----------------------|----------------------|-----------------------|---------|
|                                       |                      |                      |                       |         |
| Weight (kg)                            |                     |                      |                       |         |
| Intervention (n=22)                    | 85.73±22.50          | 85.44±22.38          | 86.5±23.29            | 0.762   |
| Control (n=20)                         | 88.25±23.04          | 87.65±22.68          | 87.8±24.18            |         |
| Body mass index (kg/m²)                |                     |                      |                       |         |
| Intervention (n=22)                    | 35.76±8.72           | 35.61±8.51           | 35.88±8.87            | 0.608   |
| Control (n=20)                         | 37.44±10.18          | 37.20±10.07          | 37.17±10.75           |         |
| Waist circumference (cm)               |                     |                      |                       |         |
| Intervention (n=16)                    | 105.06±13.91         | 104.94±13.74         | 104.94±13.81          | 0.143   |
| Control (n=20)                         | 112.20±13.56         | 111.57±13.62         | 111.90±13.85          |         |
| Glucose (mmol/L)                       |                     |                      |                       |         |
| Intervention (n=21)                    | 7.74±2.41            | 8.94±3.8             | 8.04±2.95             | 0.402   |
| Control (n=13)                         | 10.16±4.74           | 9.07±3.6             | 8.01±2.83             |         |
| High-density lipoprotein cholesterol (mmol/L) |     |                      |                       |         |
| Intervention (n=18)                    | 1.23±0.34            | 1.17±0.25            | 1.24±0.32             | 0.819   |
| Control (n=11)                         | 1.21±0.29            | 1.13±0.24            | 1.23±0.30             |         |
| Low-density lipoprotein cholesterol (mmol/L) |  |                      |                       |         |
| Intervention (n=18)                    | 2.39±0.77            | 2.43±0.47            | 2.35±0.53             | 0.388   |
| Control (n=12)                         | 2.46±0.67            | 2.61±0.79            | 2.69±0.98             |         |
Table 5.4—Continued.

| Variable                  | Baseline (Mean ± SD) | 6 months (Mean ± SD) | 12 months (Mean ± SD) | p-value |
|---------------------------|----------------------|-----------------------|-----------------------|---------|
| **Triglyceride (mmol/L)** |                      |                       |                       |         |
| Intervention (n=18)       | 1.75±0.76            | 1.64±0.61             | 1.61±0.75             | 0.319   |
| Control (n=12)            | 1.42±0.40            | 1.43±0.45             | 1.52±0.47             |         |
| **Cholesterol (mmol/L)**  |                      |                       |                       |         |
| Intervention (n=18)       | 4.43±0.79            | 4.31±0.62             | 4.23±0.70             | 0.972   |
| Control (n=11)            | 4.19±0.71            | 4.30±0.90             | 4.51±1.20             |         |
| **Systolic blood pressure (mmHg)** |          |                       |                       |         |
| Intervention (n=20)       | 147.05±21.52         | 138.50±18.67          | 133.70±14.26          | 0.526   |
| Control (n=19)            | 142.16±20.75         | 145.21±17.75          | 141.48±19.71          |         |
| **Diastolic blood pressure (mmHg)** |        |                       |                       |         |
| Intervention (n=20)       | 75.85±9.06           | 73.45±9.13            | 69.5±7.55             | 0.337   |
| Control (n=19)            | 74.63±13.47          | 76.79±10.13           | 75.0±11.78            |         |
| **Number of components of MS** |            |                       |                       |         |
| Intervention (n=20)       | 3.75±0.78            | 3.75±0.85             | 3.75±0.78             | 0.803   |
| Control (n=17)            | 3.71±0.77            | 3.59±0.87             | 3.76±1.03             |         |

E. Subjects Reporting NEAT Versus Not Reporting NEAT in the Intervention Group

As for those that did report their NEAT activity; we ran a separate analysis comparing these participants alone, on the different variables used previously using a paired t test comparing baseline and 6 months, and baseline and 12 months, to examine whether or not their NEAT activity modified their metabolic syndrome components. The results showed no difference for all variables between baseline and 6 months and baseline and 12 months. The results are shown in Table 5.5.

Table 5.5 Comparison of Anthropometric and Metabolic Parameters Among Those That Did Report Their NEAT (p-value derived using a paired t-test)

| Variable                  | Mean | p-value |
|---------------------------|------|---------|
| **Weight (kg)**           |      |         |
| baseline vs. 6 months (n=29) | 89.90 | 90.28   | .312   |
| baseline vs. 12 months (n=22) | 86.41 | 87.18   | .209   |
| **Body mass index (kg/m²)** |      |         |
| baseline vs. 6 months (n=29) | 33.42 | 33.56   | .306   |
| baseline vs. 12 months (n=22) | 32.66 | 32.93   | .286   |
| **Waist circumference (cm)** |      |         |
| baseline vs. 6 months (n=28) | 108.93 | 109.00  | .663   |
| baseline vs. 12 months (n=19) | 107.47 | 107.63  | .506   |
Table 5.5—Continued.

| Glucose (mmol/L) | baseline vs. 6 months (n=30) | baseline vs. 12 months (n=23) |
|------------------|-------------------------------|-------------------------------|
|                  | 9.07                          | 9.09                          |
|                  | 8.36                          | 9.03                          |
|                  | .148                          | .918                          |

| High density lipoprotein cholesterol (mmol/L) | baseline vs. 6 months (n=29) | baseline vs. 12 months (n=20) |
|----------------------------------------------|-------------------------------|-------------------------------|
|                                              | 1.140                         | 1.250                         |
|                                              | 1.06                          | 1.20                          |
|                                              | .333                          | .278                          |

| Low density lipoprotein cholesterol (mmol/L) | baseline vs. 6 months (n=29) | baseline vs. 12 months (n=20) |
|---------------------------------------------|-------------------------------|-------------------------------|
|                                             | 2.68                          | 2.73                          |
|                                             | 2.56                          | 2.54                          |
|                                             | .399                          | .267                          |

| Triglycerides (mmol/L) | baseline vs. 6 months (n=29) | baseline vs. 12 months (n=20) |
|------------------------|-------------------------------|-------------------------------|
|                        | 1.84                          | 1.66                          |
|                        | 1.61                          | 1.50                          |
|                        | .158                          | .474                          |

| Cholesterol (mmol/L) | baseline vs. 6 months (n=29) | baseline vs. 12 months (n=20) |
|----------------------|-------------------------------|-------------------------------|
|                      | 4.50                          | 4.75                          |
|                      | 4.35                          | 4.42                          |
|                      | .469                          | .063                          |

| Systolic blood pressure (mmHg) | baseline vs. 6 months (n=28) | baseline vs. 12 months (n=22) |
|-------------------------------|-------------------------------|-------------------------------|
|                               | 148.75                        | 146.00                        |
|                               | 140.93                        | 139.09                        |
|                               | .062                          | .142                          |

| Diastolic blood pressure (mmHg) | baseline vs. 6 months (n=28) | baseline vs. 12 months (n=22) |
|--------------------------------|-------------------------------|-------------------------------|
|                                | 78.43                         | 76.86                         |
|                                | 76.18                         | 75.45                         |
|                                | .275                          | .595                          |

| Number of components on metabolic syndrome | baseline vs. 6 months (n=32) | baseline vs. 12 months (n=22) |
|--------------------------------------------|-------------------------------|-------------------------------|
|                                            | 3.63                          | 3.55                          |
|                                            | 3.75                          | 3.59                          |
|                                            | .255                          | .576                          |

F. Characteristics of Completers Versus Non-completers

Since the characteristics of completers might be different than non-completers, we ran a separate analysis using an independent t test to explore baseline metabolic parameters and other anthropometric measurements between the two groups. The analysis revealed that mean LDL cholesterol and total cholesterol levels were statistically significantly different between groups. It was observed that mean LDL cholesterol and total cholesterol levels were significantly higher among non-completers than completers. Additionally, the results indicate that more men than women were non-completers (66% of non-completers versus 54.2% of completers). These results may
become useful to future researchers when deciding on their study populations. The results are summarized in Table 5.6.

Table 5.6 Comparison of Anthropometric and Metabolic Parameters Among Completers and Non-completers (p-value derived using independent t-test)

| Variable                          | Completers      | Non-completers | p-value |
|-----------------------------------|-----------------|----------------|---------|
| Gender                           | (n=107)         | (n=93)         | 0.073   |
| Male                             | 58 (54.2%)      | 62 (66.7%)     |         |
| Female                           | 49 (45.8%)      | 31 (33.3%)     |         |
| Height (cm)                      | (n=107)         | (n=93)         | 0.349   |
| Mean ± SD                        | 162.0±9.19      | 163.2±8.74     |         |
| Weight (kg)                      | (n=107)         | (n=93)         | 0.263   |
| Mean ± SD                        | 85.6±18.70      | 88.5±18.93     |         |
| BMI (kg/m²)                      | (n=107)         | (n=93)         | 0.649   |
| Mean ± SD                        | 32.8±7.74       | 33.3±6.89      |         |
| Waist circumference (cm)         | (n=107)         | (n=93)         | 0.219   |
| Mean ± SD                        | 107.2±11.89     | 109.5±14.53    |         |
| Glucose (mmol/L)                 | (n=106)         | (n=81)         | 0.541   |
| Mean ± SD                        | 8.6±3.56        | 8.3±3.08       |         |
| High-density lipoprotein cholesterol (mmol/L) | (n=105) | (n=81) | 0.971 |
| Mean ± SD                        | 1.1±0.31        | 1.1±0.33       |         |
| Low-density lipoprotein cholesterol (mmol/L) | (n=105) | (n=81) | 0.002 |
| Mean ± SD                        | 2.5±0.83        | 2.9±0.96       |         |
| Triglyceride (mmol/L)            | (n=105)         | (n=81)         | 0.576   |
| Mean ± SD                        | 1.6±1.19        | 1.6±0.83       |         |
| Cholesterol (mmol/L)             | (n=105)         | (n=80)         | 0.008   |
| Mean ± SD                        | 4.4±0.99        | 4.8±1.10       |         |
| Systolic blood pressure (mmHg)   | (n=107)         | (n=92)         | 0.496   |
| Mean ± SD                        | 141.9±19.32     | 143.8±19.66    |         |
| Diastolic blood pressure (mmHg)  | (n=107)         | (n=92)         | 0.070   |
| Mean ± SD                        | 75.3±10.45      | 78.0±10.83     |         |
| Components of metabolic syndrome | (n=105)         | (n=89)         | 0.796   |
| Mean ± SD                        | 3.72±0.83       | 3.75±0.69      |         |
| Medications                      | (n=102)         | (n=76)         |         |
| Anti-diabetic                    |                 |                |         |
| Yes                               | 76 (74.5%)      | 53 (69.7%)     | 0.481   |
| No                                | 26 (25.5%)      | 23 (30.3%)     |         |
| Lipid-lowering                   |                 |                |         |
| Yes                               | 68 (66.7%)      | 56 (73.7%)     | 0.314   |
| No                                | 34 (33.3%)      | 20 (26.3%)     |         |
| Anti-hypertensive                |                 |                |         |
| Yes                               | 77 (75.5%)      | 58 (76.3%)     | 0.899   |
| No                                | 25 (24.5%)      | 18 (23.7%)     |         |
G. Conclusion

This study looked into whether or not giving advice to increase daily NEAT would influence metabolic markers in participants. The theoretical framework suggested that since NEAT is part of human energy expenditure, then increasing NEAT throughout the day would increase energy expenditure among metabolic syndrome patients, thus improving their metabolic markers, and in turn positively adjusting their risk of CVD.

Giving advice to increase daily NEAT showed no significant effects on metabolic syndrome components in this study. These additional analyses looking at subgroups of study individuals also found no significant differences between groups according to use of anti-diabetic medication or gender (with the exception that the number of metabolic syndrome components seemed to increase in men in the intervention group). In addition, subjects that reported NEAT did not differ in their results from subjects that did not report NEAT. Finally, non-completers tended to be males, and had higher total and LDL cholesterol levels than completers. Future researchers might build on this study by conducting studies in a shorter period of time, using more efficient follow up methods; like increasing the frequency of follow up visits, or by providing incentives to participants at each visit. Additionally, the main concept of the study may be studied using a higher level and better controlled intervention.
CHAPTER 6
CONCLUSIONS

The results of the study show no significant difference in metabolic syndrome parameters between the group that received advice to practice NEAT and the control group. These results also apply to comparisons made between those on anti diabetic medications and those that are not on anti diabetic medications. Additionally, they also apply for comparisons made between genders.

The concept of the study originated during one of Dr. Tonstad’s classes which was titled “Obesity and Disordered Eating,” during which the concept of NEAT was covered as a method of increasing energy expenditure among obese individuals. I further researched the topic to find it used in several of Levine’s studies. After deciding on doing this study in Qatar, I looked into what disease should be chosen and realized that the country had high numbers of obesity and diabetes. Therefore I decided to go with metabolic syndrome as it includes both an overweight and increased glucose aspect.

Conducting this study in all its steps and stages was a good learning experience, as I had the chance to be exposed to the different aspects of a study, starting from the process of planning the different steps of it, obtaining IRB approval, collecting the data, analyzing, and interpreting it. All these were the principles that I learned theoretically in the classroom through classes taken during the course of my studies. But doing it in person brought things into perspective, and a lot of information learned took place in reality.

One of the more pleasurable parts of the study was interaction with patients which was a rich learning experience. Reflecting on some of the conversations I had with some
of the participants, I learned that people in Qatar have certain restrictions prohibiting them from exercising in what can be considered as conclusive reasons that exist in such a culture. During one conversation with one of the participants, she indicated that the major factor behind her failure to exercise was the presence of non-family members in their house yard, such as the driver or other house help that commonly work in homes of Qataris, in many cases not out of necessity but rather as a cultural norm.

On the other hand, another participant expressed that she was pleased with this method of increasing energy expenditure, referring to NEAT, and said she finds it to be an easy and accessible method to do so. She now used the stairs whenever visiting her doctor, occasionally asks her driver to park further down the parking lot, when weather permits so. Additionally she tries to walk around the house for a few minutes each day, and takes the longer route to things that are within house limits, like when going to the kitchen or trying to reach the living room.

On a different aspect I find several areas of the study that are worth improving or changing. First example is the setting of the study, had it allowed us to include younger participants, rather than older participants with established disease - about three-fourths of the subjects were treated with anti-diabetic medication. Furthermore, all of the participants were of the same ethnicity, limiting generalizability.

Another item is related to health education and raising awareness to the negative aspect of metabolic syndrome and the positive aspects of the concept of NEAT. Had the participants been scheduled for monthly visits with a health educator to highlight the previously mentioned points, it would have possibly helped some participants in realizing
the risks associated with the disease along with the benefits of NEAT and increased their motivation for change.

In all, the concept of NEAT as shown in literature through Levine’s studies was a feasible approach to recruitment of subjects. 200 subjects were recruited and followed up within a short period of time. Thanks to my advisors and staff at the hospital for facilitating this study. Though the results were disappointing, future efforts should probably be focused on creating new approaches to increasing NEAT among high risk patients.
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## APPENDIX A: GANTT CHART SHOWING STUDY TIMELINE

|                          | Mar / Apr | May / Jun | Jul / Aug | Sep / Oct | Nov / Dec | Jan / Feb | Mar / Apr | May / Jun | Jul / Aug | Sep / Oct |
|--------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Final approval           | X         |           |           |           |           |           |           |           |           |           |
| Quest. design            | X         |           |           |           |           |           |           |           |           |           |
| Data collection          | X         | X         | X         | X         | X         | X         | X         | X         | X         |           |
| Data analysis            |           |           |           |           |           |           |           |           | X         |           |
| Write up                 |           |           |           |           |           |           |           |           | X         |           |
| Progress report          | X         |           |           |           |           |           |           |           | X         |           |
| Final report             |           |           |           |           |           |           |           |           |           | X         |
# APPENDIX B: BUDGET BREAKDOWN

| BUDGET CATEGORY TOTALS | INITIAL BUDGET PERIOD (from Form Page 4) | 2nd ADDITIONAL YEAR OF SUPPORT REQUESTED | 3rd ADDITIONAL YEAR OF SUPPORT REQUESTED | 4th YEAR | 5th YEAR |
|-------------------------|------------------------------------------|------------------------------------------|------------------------------------------|-----------|----------|
| PERSONNEL: Salary and fringe benefits. Applicant organization only. | 1500 | 800 | 50 | 50 | |
| CONSULTANT COSTS | 800 | 50 | 50 | 50 | |
| EQUIPMENT | 50 | | | | |
| SUPPLIES | 50 | | | | |
| TRAVEL | | | | | |
| INPATIENT CARE COSTS | | | | | |
| OUTPATIENT CARE COSTS | | | | | |
| ALTERATIONS AND RENOVATIONS | | | | | |
| COMMUNICATION EXPENSES | | 100 | | | |
| DIRECT CONSORTIUM/CONTRACTUAL COSTS | | | | | |
| SUBTOTAL DIRECT COSTS (Sum = Item 8a, Face Page) | | 2500 | | | |
| F&A CONSORTIUM/CONTRACTUAL COSTS | | | | | |
| TOTAL DIRECT COSTS | 2500 | | | | |
| TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD | $ 2500 | | | | |
Budget Justification

The budget has five major categories; these are personnel, consultant costs, equipment, supplies, and communication expenses. Under personnel, a nurse charges $500; a total of three nurses will participate for a total of $1500. Under consultant costs, a research assistant charges $800 per study. Under equipment, the educational material to be given to participants will be purchased in bulk from the health education department at Hamad General Hospital. The cost for a total of 200 booklets is $50. Under supplies, office supplies and paper copies cost approximately $50. Under other expenses, the contracted marketing company charges 25 cents for each text message including a reminder message of participation. A total of 400 reminders will be sent over a one year period for the cost of $100. This brings the grand total to $2500.
APPENDIX C: REPORT SHEET USED IN CURRENT STUDY

| Week 1 | NEAT Weekly Report Sheet |
|--------|--------------------------|
| Day/Date | Stair climbing instead of using the elevator | Gum chewing/others | Fidgeting voluntarily | Walking instead of driving | Standing instead of sitting | Notes |
| Sunday |  |
| Monday |  |
| Tuesday |  |
| Wednesday |  |
| Thursday |  |
| Friday |  |
| Saturday |  |
APPENDIX D: CONSENT FORM IN ENGLISH

| MEDICAL RESEARCH CENTRE |
|-------------------------|
| HGH □ WH □ RH □ AAH □ AKH □ |
| Others □ |

| MR #: |
| PATIENT NAME: |
| DOB: |
| GENDER: |
| NATIONALITY: |

Patient Label

GENERIC SIGNED CONSENT FORM

You are invited to participate in this study entitled “The effect of non-exercise activity thermogenesis (NEAT) on weight among Qatari patients with metabolic syndrome, a randomized controlled study”. You are free to ask as many questions as you like before, during or after in this research, you decide to give consent to participate in this research study. The information in this form is only meant to better inform you of all possible risks or benefits. Your participation in this study is voluntary. You do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of rights or other benefits to which you are entitled. The investigator(s) may stop your participation in this study without your consent for reasons such as: it will be in your best interest; you do not follow the study plan; or you experience a study-related injury. Randomization will be carried out by asking patients to randomly choose from two envelopes that contain the type of group.

Project title: The effect Non Exercise Activity Thermogenesis (NEAT) on weight among Qatari subjects with metabolic syndrome; a randomized controlled study.

Name of Principal Investigator:
Dr. Samer Hammoudeh

Location and phone numbers:
Outpatient Department/Endocrinology and Diabetes clinic, Hamad Medical Corporation
-7007642
-5546316
Dr. Mahmoud Zirie
Dr. Abdullah Al-Hamaq
**Introduction to the research**
Metabolic syndrome is a combination of medical conditions in one person that increase the risk of that person to develop diabetes as well as diseases of the heart and blood vessels. Metabolic syndrome is very common that it affects one in five people, and the chance of getting it increases with age. Persons who suffer from the metabolic syndrome are usually overweight, stressed, have high blood pressure, and high fat levels in their blood. In addition, their body cannot use its insulin, the hormone that is supposed to regulate blood sugar, in a proper way. Many treatments have been proposed to prevent the development of metabolic syndrome. These include increased physical activity (such as walking 30 minutes every day), and eating healthy food that is low in fat. There are many researches that support the value of a healthy lifestyle as above. But keeping up with such lifestyle is difficult for many people, that is why we decided to do research in one of the life style modifications that does not require physical activity. This is called non exercise activity thermogenesis (NEAT). We will use this lifestyle intervention on high risk Qatari individuals with components of metabolic syndrome.

1- **Purpose of the research:**
The purpose of this study is to examine the effect of non exercise activity thermogenesis (NEAT) in reducing the following metabolic syndrome markers; 1- weight 2- waist circumference 3- hip circumference 4- triglycerides level. These markers will also be used to establish high risk criteria.

2- **Selection of research subjects:**
You will be invited to participate in this research if you are over 18 years old and you have A and 2 out of 5 of the following criteria:
A) Elevated waist circumference of 102 cm or above (men) and 88 cm or above (women)
B) Fasting blood sugar over 5.6 mmol/L
C) Blood pressure over or equal 130/85 mmHg
D) Triglycerides above or equal 1.7 mmol/L
E) HDL cholesterol lower than 1.03 mmol/L (men) and 1.29 mmol/L (women)

3- **Distinction between routine care and research activities:**
Your participation in this research is completely voluntary; you will continue your treatment with your doctor as usual. Should you choose to participate in this research; you will be advised on ways to modify your diet and life style. For example, you will be advised to do some activities that you were not doing before like parking your car away instead of close to the entrance, standing instead of sitting for long time, moving your legs and arms as much as you can during the day and other such non-exercise activities. You may or may not benefit from this life style modification, but previous research have shown benefit from these changes.

4- **Explanation of the procedures:**
The tool "NEAT" that we will use in this research is defined as all other movements outside of exercise such as walking, talking, toe tapping, guitar playing, dancing or shopping. Researchers found that obese move 2.5 hours less per day than lean people. This equates to 350 calories expended per day. What all this means is that society as a whole needs to be moving move and spend less
time sitting around at the office, watching TV etc. If you watch TV you only burn 5 calories an hour above your metabolic rate. After 4 hours of sitting and watching TV you have only burned 20 calories.

5-The risks and discomfort involved:
You will spend more time in doing more of the Non Exercise Activities than sitting. There is no risk for you and no discomfort. You may feel better.

6-The Safety precautions in this research:
There are no safety precautions

7-The benefits of the study:
You may or may not benefit from this research. If you benefited from this research, you may be able to lose weight, which may result in better control of blood sugar, high blood pressure, and blood fat levels.

8-The alternative procedures or treatments for this research:
If you decide not to participate in this research, you can continue the same treatment that you are already on.

9-The options to remain on the research treatment after termination of the research:
Your participation in this research is expected to last for one year. After one year, we encourage that you continue these activities on your own.

10-Details of the person to contact in case of Injury or enquiry during the research:
Dr. Samer Hammoudeh 7007642 -5546316

11-Details of the financial or other compensator which might be provided to the research participants if any:
We will not provide money for your participation in this research.

12-Duration of the research:
If you participate in this research, you will be asked to come for a hospital visit at 6 and at 12 months after your enrollment. You will receive by mail reminders to these NEAT exercises and visits.

13-Where the research is going to be conducted:
The research will be conducted at your home. You will be assessed in the outpatient clinic on the day of your appointment.

14-Assurance of anonymity and confidentiality:
Total privacy cannot be guaranteed. We will protect your privacy to the extent permitted by law. All research data will be stored in a password protected computer. If the results from this research are published, your name will not be made public. The following may look at your research and medical records: The research team or persons authorized by the research team; the research committee member’s if/when they choose to.

15-Non-coercive disclaimer:
There is no pressure on you to participate in the study; you are free to choose any of the treatment modalities offered and that there will be no pressure on you to continue in the study even after enrollment. You are free to withdraw from this research at any time, and this decision will not and in any way affect the medical care you are entitled to.
16-Option to withdraw from the study without penalty:
You can withdraw at any time from the study even after enrollment in the research without any penalty.

17-Details about termination of the study:
The study will continue for one year for the participant. At the end of the study you may continue these activities as part of your learned life style modification activities.

18-Instances in which there might be incomplete disclosure of information: None

**Consent:** You (the participant) have read or have had read to you all of the above; **Dr. Samer Hammoudeh** or his/her authorized representative has provided you with a description of the study, including an explanation of what this study is about, why it is being done, and the procedures involved. The risks, discomforts, and possible benefits of this research study, as well as alternative treatment choices, have been explained to you. You have the right to ask questions related to this study or your participation in this study at any time. Your rights as a research subject have been explained to you, and you voluntarily consent to participate in this research study. By signing this form, you willingly agree to participate in the research study described to you. You will receive a copy of this signed consent form. As long as the study is renewed as required by the IRB, your signature on this document is valid for the duration of the entire research study. Should any changes occur during the course of the study that may affect your willingness to participate, you will be notified.

| Participant / Parent(s)/ Guardian’s Name | Signature & Date signed |
|----------------------------------------|-------------------------|
|                                        |                         |

| Child's Name | Signature & Date signed |
|--------------|-------------------------|
|              |                         |

| Witness Name | Signature & Date signed |
|--------------|-------------------------|
|              |                         |

| Principal Investigator’s Name | Signature & Date signed |
|-----------------------------|-------------------------|
| Dr. Samer Hammoudeh |                         |

For use of Medical Research Centre only
**APPENDIX E: CONSENT FORM IN ARABIC**

| **MEDICAL RESEARCH CENTRE** | **مركز البحوث الطبية** |
|-----------------------------|-----------------------|
| HGH □ | م. حمد العام |
| WH □ | م. النساء |
| RH □ | م. الرملة |
| AAH □ | م. الخور |
| AKH □ | م. الأمل |
| □ Others | أ. أ. أخرى |

| **Label** |
|------------------------------|
| رقم السجل: |
| إسم المشارك: |
| تاريخ الميلاد: |
| النوع (ذكر | أنثى) : |
| الجنسية: |

**موافقة مستبينة للمشاركة بدراسة بحث طبي**

بمؤسسة حمد الطبية

لقد طلب منك ان تشارك في هذه الدراسة والتي تمثل:

**أثر حرق الطاقة بالنشاطات الاعتيادية اليومية بدون تمرين رياضية على مرضى المتلازمة الاستقلابية الفترتين**

وكمشارك في هذا البحث العلمي فإن لك مطلق الحرية في طرح أي سؤال أو استفسار عن هذا البحث وذلك قبل أثناء إجراء أ و بعد إكمال إجراء البحث. الهدف الرئيسي من المعلومات الواردة في هذا النموذج هو أن تقم تسمية الشرح الوافي والمستفيد عن كل الأخطار والفوائد التي يمكن أن تتمخض عن إجراء هذا البحث. المشاركة في هذا البحث عمل طوعي خالص وبالتالي لم تطلق الحرية بعدم المشاركة. قرارك بعدم المشاركة في هذا البحث العلمي لا يترتب عليه أي تبعات أو حرمان من حقوقكم المستحقة. أيضا يمكنك الانسحاب وعدم مواصلة المشاركة في هذا البحث في أي وقت أو مرحلة دون أن يؤثر ذلك في حقوقكم أو فوائدكم المستحقة والمشرعة. لأعضاء فريق البحث العلمي الخاص بهذه الدراسة الحق في إيقاف أو إلغاء مشاركتكم في هذه الدراسة إذا رأوا مصلحة لكم في هذا الإيقاف أو الإلغاء أو في حالة عدم التزامكم بخطة البحث الموضوعة أو إذا تبين لهم ضرر أو إصابة نتيجة إجراء الدراسة وذلك دون أخذ موافقتكم. سيتم اختيار المرضى لطريقة عشوائية بنختاروا واحدا من الطرقين الذين يمثلان مجموعتي الدراسة.

1- عنوان البحث:

**أثر حرق الطاقة بالنشاطات الاعتيادية اليومية بدون تمرين رياضية على مرضى المتلازمة الاستقلابية الفترتين**

2- اسم الباحث: د. س. حمودة

3- موقع إجراء البحث وأوقات الدراسة (أثناء أيام الدراسة، بعد الدوام و/or العطلات).

في البيت وخارج المستشفى

يتم إجراء هذا البحث بقيادة الخبرة لأمراض الغدد والسكري

82
梅西مة على البحث:
an
الدراسات في انتشار التنانز (المتلازمة) الاستقلابية قد أزداد في الأونة الأخيرة والمتلازمة الاستقلابية تعني
نواجت الأعراض التالية في الشخص.

- ارتفاع الضغط
- ارتفاع دهون الدم
- مقارنة النسخة للإنسولين
- وعلى الرغم من أن عوامل أخرى تساهم في ارتفاع الضغط في الجسم فإن زيادة الطاقة المحرقة بالنشاطات اليومية
وذلك يتغير نمط المعيشة والتي لها علاقة ببيئة العمل والفعاليات اليومية التقليدية أو حتى بالإعلان التي لها طابع
دبي على تغذية بعض المؤسات التي لها علاقة بمتلازمة الاستقلاب وذلك بحرق سعرات حرارية وذلك بممارسة
نشاطات اليومية الاستقلابية

وفي الغرض من إجراء دراسة البحث:

1- أن هذه الدراسة مرتبطة بفحص الإفراد الطريين الذين يعانون من متلازمة الاستقلاب الاستقلابية.
2- زيادة النشاط اليومية الاستقلابية بدون تمارين رياضية وذلك بقياس بعض مؤشرات الاستجابة ومنها:
3- الوزن
4- قياس محيط الخصر
5- قياس مستوى الفخذ
6- قياس مستوى الدهن الثلاثية

وهذه المؤشرات سوف يتم استخدامها لتحديد عوامل الخطورة لمتلازمة الاستقلاب

- اختيار المشاركين بالدراسة

يمكن أن تشارك في هذه الدراسة إذا

1- عمره أكثر من 18 سنة وكان عندهم 1 واثناء من المواليد السلالة التالية:
2- زيادة محيط الخصر عن 102 سلم للرجال و88 للنساء
3- مستوى سكر الدم على الريق أكثر من 6 مليمونات ليلتر
4- ضغط الدم معايير أو أكثر من 130/85 مليمونات ليلتر
5- الدهن الثلاثية أكثر من 1.7 مليمونات ليلتر
6- معدل الكوليسترول بالعالم

ومن 1.03 مليمولليتر في الرجال و1.29 مليمولليتر للنساء
7- الغير من حمية الرعاية الصحية وبحث الطبي

- سوف يطلب منك الاستمرار بالعملية التي تتناولها ومتاحة طبيب المشرف وبالإضافة إلى ذلك فإنه سيطلب منك أن

قم بهذه النشاطات غير البيلية.

فقط إذا وجد أن الأشخاص الذين يقومون بزيادة النشاطات اليومية الاستقلابية دون تمارين رياضية لإزداد أوزانهم حتى
ونما بعد أن يزيد تناول الطعام عندهم بينما أولاً أفراد الذين لم يستطيعوا زيادة النشاطات اليومية زاد عندهم
الوزن لحوالي 5 كيلو لذا فإن حرق الطاقة هذه النشاطات اليومية يساعد على تخفيف الوزن.

-وضح الآثار التي يمكن استخدامها في الدراسة

إن حرق الطاقة بالنشاطات اليومية الاستقلابية دون تمارين رياضية تعزز بأنه كل الحركات والنشاطات التي تجريها
الإنسان بشكل اعتيادي بدون أن يقوم بتمارين رياضية ومن هذه النشاطات هو الكلام والمشي وحركة أصابع الرجلين

83
12-

19-

81-

15-

11-

10-

6-
أيضاً شرح وايضاح فرص العلاج البديل والمتاح لي. وفهمت محتوائهما. كما تم إخطارًا بأن المشاركة في هذه البحث عمل طوعي خالص وبالتالي لي مطلق الحرية بالمشاركة أو عدم المشاركة. في حالة إتخاذ القرار بعدم المشاركة في هذا البحث، يقوم بالإنسحاب وعدم مواصلة المشاركة في هذا البحث في أي وقت أو مرحلة أثناء دون أي تبعات أو تأثيرات في حقوق أو قواعد المستحقة والمربعة والمشرعة. أقر بأن لأعضاء فريق البحث العلمي الخاص بهذه الدراسة الحق في إيقاف أو إلغاء مشاركتي في هذه الدراسة إذا رأى مصلحة لي في هذا الإيقاف أو الإلغاء أو في حالة عدم التزامي بخطة البحث الموضوعة أو إذا تبين لهم ضرر أو إصابه نتيجة إجراء الدراسة وذلك دون أخذ موافقتى أو أنه قد أجبت كل أسئلتي والتي طرحتها، ويعتبر أدق اتفاق على المشاركة في البحث.

| التوقيع وتاريخه | اسم: المشارك (والد أو الوالدين) أو الوصي |
|----------------|--------------------------------------|
|                | اسم الطفل المشارك                   |
|                | التوقيع وتاريخه                       |
|                | اسم الشاهد                           |
|                | التوقيع وتاريخه                       |
|                | اسم الباحث الرئيسي                   |
|                | د. سامر حمودة                       |

لاستخدام مركز البحوث الطبية فقط
APPENDIX F: APPROVAL LETTER FROM HAMAD HOSPITAL

HAMAD MEDICAL CORPORATION

Ref. No: RC/1092/2010
Date: 31 January 2010

Prof. Abdulbari Bener
Consultant & Head
Department of Epidemiology & Medical Statistics

Dear Prof. Bener,

Research Protocol #9181/09: The effect of “Non exercise activity thermogenesis (NEAT)” on weight loss among Qatari subjects with metabolic syndrome in a randomized clinical trial.

Reference is made to the above Research Protocol submitted for review and approval from the Research Committee.

On behalf of the Research Committee, it is to inform you that the above Research Proposal meets up with the ethical requirements of the Hamad Medical Corporation and approval is granted for one year from 31st January 2010.

Signed Informed Consent should be taken from each participant. One copy of the consent should be handed over to the participant and the second copy should be kept with Principal Investigator whereas the third copy of the same should be kept in subject’s Medical Record.

Progress report of the study should be submitted bi-annually and final report upon completion to Medical Research Centre.

We wish you all success and await the result in due course.

Yours sincerely,

Dr. Rajvir Singh
Coordinator, Research Committee

Cc:
1) Dr. Samer Hammoudeh, DDS, MPH, Dr. PH Student, Loma Linda University, USA
2) Dr. Mahmoud Zirie, Head of the Department of Endocrinology
3) Dr. Abdullah Al-Hamaq, President of Diabetes Association, Qatar Foundation
APPENDIX G: APPROVAL LETTER FROM LLU IRB

INSTITUTIONAL REVIEW BOARD
LOMA LINDA UNIVERSITY
SPONSORED RESEARCH • 1188 Anderson Street • Loma Linda, CA 92350
(909) 558-4351 (voice) • (909) 558-0131 (fax)

Initial Approval Notice - Expedited

To: Tonstad, Serena
Department: Health Promotion & Education
Protocol: The effect of non-exercise activity thermogenesis on subjects with metabolic syndrome

This study was reviewed and approved administratively on behalf of the IRB. This decision includes the following determinations:

- Risk to research subjects: Minimal
- Approval period begins: 01-Mar-2012 and ends 28-Feb-2013
- Stipulations of approval: Research intervention is under IRB approved by Hamad Medical Corp.

Consent Form

Unless IRB has given a specific waiver of informed consent (as documented in the approval stipulations above) the IRB-approved and stamped consent form accompanies this letter. This now becomes the official master consent form for making copies to provide to study participants.

Adverse Events / Protocol Changes

The IRB should be notified in writing of any modifications to the approved research protocol. Adverse effects must be reported to the IRB in accordance with institutional policy. If sponsor or contractual adverse event reporting requirements differ from requirements for reporting to IRB, all reporting requirements must still be met.

Protocol Review

Your protocol is tentatively scheduled for review and renewal at least two weeks prior to the approval end-date indicated above. To assure uninterrupted approval of this project, you will be sent a report form to request renewal by completing and timely returning to Office of Sponsored Research. Anticipate the approval expiration so your study does not lapse; contact IRB for assistance if necessary. In addition to reporting the requested renewal status information, you may also use the form to close the study at that time, if applicable.

Records

All records relating to this project, including signed consent forms, must be kept on file for three years following completion of the study.

Please note the PI's name and the IRB number assigned to this IRB protocol (as indicated above) on any future communications with the IRB. Direct all communications to the IRB c/o the Office of Sponsored Research.

Thank you for your cooperation in LLU's shared responsibility for the ethical use of human subjects in research.

Signature of IRB Chair/Designee: R.S. Rigby
Date: 3/2/12

Loma Linda University Adventist Health Sciences Center holds Federalwide Assurance (FWA) No. 6447 with the U.S. Office for Human Research Protections, and the IRB registration No. 1600002226. This Assurance applies to the following institutions: Loma Linda University, Loma Linda University Medical Center (including Loma Linda University Children's Hospital, LLU Community Medical Center), Loma Linda University Behavioral Medicine, and affiliated medical practice groups.

IRB Chair: Rhodes L. Rigby, M.D.
Department of Medicine
(909) 558-2241, rigby@llu.edu

IRB Administrator: Linda G. Hildbrand, M.A., Director
Sponsored Research
Ext 43570, Fax 80131, lhildbrand@llu.edu

IRB Specialist: Mark Testerman
Sponsored Research
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