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Effect of a Lifestyle Modification Intervention on Perceived Stress: Associations with Weight Loss and A1c in Type 2 Diabetes

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UNIVERSITY OF MIAMI

EFFECT OF A LIFESTYLE MODIFICATION INTERVENTION ON PERCEIVED
STRESS: ASSOCIATIONS WITH WEIGHT LOSS AND A1C IN TYPE 2 DIABETES

By

Karin A. Garcia

A THESIS

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Master of Science

Coral Gables, Florida

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EFFECT OF A LIFESTYLE MODIFICATION INTERVENTION ON STRESS:
ASSOCIATIONS WITH WEIGHT LOSS AND A1C IN TYPE 2 DIABETES

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Effect of a Lifestyle Modification Intervention
On Perceived Stress: Associations with
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Stress may have an important role in the development of type 2 diabetes (T2D) and its complications (Black, 2006). Individuals with T2D who experience higher levels of stress also tend to experience poorer glycemic control and more exacerbated diabetes related complications than less stressed counterparts (Surwit & Schneider, 1993). Obesity has also been linked to T2D as those with a higher BMI are at greater risk for developing the disease and disease-related comorbidities (Astrup & Finer, 2000; Moore, Wilson, D'Agostino, Finkle & Elliso, 2000). Lifestyle modification interventions, designed for individuals with or at risk for developing T2D, have primarily focused on reducing weight via dietary and physical activity interventions (Wolf et al., 2004; Lifshitz & Hall, 2002; Tuomilehto et al., 2001; Lindström et al., 2006). Little research has been done examining effects of stress management in combination with diet and exercise modification on improved glycemic control and weight loss in individuals with T2D (Wadden, 2006). The first primary aim of this study is to determine the effect of a lifestyle modification intervention involving diet, exercise and stress management on reducing stress in patients with T2D. The second aim is to examine associations between stress reduction and weight loss and stress reduction and glycemic control in individuals with T2D. We studied 111 socio-economically disadvantaged, mostly minority (85% Hispanic, 10% African American) adults (mean age: 55 years; 58% women) with T2D

recruited for the Community Approach to Lifestyle Modification for Diabetes (CALM-D) study who were randomized to a 17 session 12 month lifestyle intervention or usual care. Participants in both groups were assessed at baseline, 6 months and 12 months post-randomization. Stress was measured using the Perceived Stress Scale (PSS). Glycemic control was assessed using glycosylated hemoglobin (HbA1c). Relative to usual care, the intervention resulted in significant decreases in PSS ($\beta = -.515$, $SE = .220$, $p < .05$), controlling for age and gender. There was no association between change in PSS and change in HbA1c in the control group ($\beta = .038$, $SE = .037$, $p = .301$) or the intervention group ($\beta = .013$, $SE = .022$, $p = .568$). Similarly, there was no association between change in PSS and change in weight in the control group ($\beta = -.117$, $SE = .09$, $p = .192$) or the intervention group ($\beta = .167$, $SE = .096$, $p = .081$). However, there was a trend in the relationship between change in stress and change in weight in the intervention group, suggesting a possible relationship between stress and weight loss in the intervention group but not in the control group. Future research is needed in a larger sample to elucidate the relationships between decreases in perceived stress and changes in weight and glycemic control.

TABLE OF CONTENTS

	Page
LIST OF TABLES AND FIGURES.....	iv
Chapters	
1 INTRODUCTION	1
2 METHODS	25
3 RESULTS	34
4 DISCUSSION.....	37
5 CONCLUSIONS.....	43
References	44
Tables	54
Figures	55

LIST OF TABLES AND FIGURES

	Page
TABLE 1: BASELINE SAMPLE CHARACTERISTICS	54
FIGURE 1 STRESS REDUCTION GROWTH MODEL.....	55
FIGURE 2: STRESS REDUCTION GROWTH MODEL WITH RANDOMIZATION VARIABLE.....	56
FIGURE 3: STRESS REDUCTION GROWTH MODEL WITH COVARIATES.....	57
FIGURE 4: INTERVENTION AND CONTROL MEANS: PERCIEVED STRESS....	58
FIGURE 5: CONSORT DIAGRAM OF STUDY PARTICIPANTS.....	59

Chapter 1

Introduction

Type 2 Diabetes: Prevalence and Lifestyle Factors

Type 2 diabetes (T2D) is a chronic illness that occurs when the pancreas fails to produce enough insulin in the body or when the body cannot effectively use the insulin it produces (World Health Organization, 2013). An estimated 347 million people worldwide have diabetes and 90% of them have T2D (World Health Organization, 2013). T2D can result in several health related complications such as cardiovascular disease (CVD), retinopathy, renal disease, and neuropathy (World Health Organization, 2013). The American Diabetes Association estimated the total direct and indirect cost of diabetes in the U.S. in 2007 was \$174 billion (Ariza, Vimalananda & Rosenzweig, 2010), a figure that has surely increased over the years.

Type 2 Diabetes has also been conceptualized as a lifestyle-dependent disease as many of its identifiable risk factors are related to behavioral factors. The World Health Organization states that a healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use can prevent or delay the onset of type 2 diabetes (World Health Organization, 2013). Research supports the idea that behavioral/lifestyle risk factors affect incidence for and progression of type 2 diabetes including diet, physical inactivity, socioeconomic status and obesity (Rewers & Hamman, 1995). Obesity has been particularly implicated as contributing to increased risk of developing Type 2 Diabetes and has been directly linked to increased morbidity of CVD, hypertension and dyslipidemia (Astrup & Finer, 2000). In fact, a moderate decrease in body weight, estimated at about a 5-7% loss, is thought to decrease risk for diabetes by

50 percent (Moore, Wilson, D'Agostino, Finkle & Elliso, 2000). A large number of studies have shown that obesity and sedentary behavior are independently related to increased chance of developing T2D (Wing et al., 2001). Manson et al (1991; 1992) found a relationship between lower levels of physical activity and increased rates of developing diabetes in both men and women. More recently, the Nurses' Health Study found that diets high in glycemic load and trans fat were associated with increased risk of developing diabetes (Hu et al., 2001).

Health outcomes, Stress, and Socio-economic Disadvantage

Similarly, socioeconomic status (SES) has been implicated in several health-related outcomes, including obesity and T2D. SES is commonly defined as the social standing or class of an individual or group and is a construct measured via several different variables including income, education level, and occupation (Cohen, Doyle, and Baum, 2006). SES has been found to be negatively associated with rates of morbidity and mortality for almost every illness and has been shown to be an important predictor of health (Cohen, Doyle, and Baum, 2006). The relationship between health and SES can be seen across countries and healthcare systems, suggesting a more environmentally-based causal mechanism involved in SES. One hypothesis is that the health- SES association results from with the association between SES and chronic stress (Baum, Garofalo, and Yali, 1999).

Several studies have examined the relationship between stress hormones and SES. A study by Cohen, Doyle, and Baum (2006) of 193 adults determined the relationship between SES and systemic stress hormones including epinephrine, norepinephrine, and

cortisol. Participants provided 24-hour urine samples to examine catecholamines on 2 different days. Subjects also provided 7 salivary cortisol samples for 3 days at several time points per day. Lower SES was shown to be associated with higher levels of all stress hormones examined, independent of race, gender, age, and BMI. The relationship between self-reported stress and SES has also been linked to health outcomes. The National Study of Daily Experiences provided data from 1031 individuals who reported daily hassles and stresses (Grzywacz, Almeida, Neupert, and Ettner, 2004). Results showed that high SES individuals reported fewer physical symptoms and less psychological distress than low SES individuals. High SES individuals also reported more daily stressors but low SES individuals reported more severe stressors in their daily lives (Grzywacz, Almeida, Neupert, and Ettner, 2004).

A theory proposed by Anderson, McNeily, and Myers (1993) indicated that the environment in which many ethnic minority individuals live was disproportionately characterized by lower SES and expose these individuals to more life stressors than that experienced by non-minority groups. Life stressors common to ethnic minorities include discrimination/ prejudice, unemployment, low education, low income, and poorer living conditions (Baum, Garofalo, and Yali, 1999). Additionally, the largest minority groups in the U.S. are on the lower end of the household income and SES brackets. Poverty among ethnic minority individuals is more than 3 times that for other groups in the U.S. (Baum, Garofalo, and Yali, 1999). Living in these low SES environments increases the likelihood of experiencing stressors that cannot be adequately coped with, leading to health related consequences. Along with physical health issues, depression and mental health problems have been shown to be more common in low SES groups when compared with middle or

high SES groups (Stronks, Van de Mheen, Looman, & Mackenbach, 1998). Gallo and Matthews' (2003) review of the literature suggested that low SES individuals have higher levels of depressive symptoms and major depressive disorder specifically. Given that ethnic minority groups experience lower education levels and higher rates of unemployment/ underemployment, poverty, and stress than non-minority groups, these individuals are also less likely to have medical insurance or seek medical care (Baum, Garofalo, and Yali, 1999), placing them at an even higher risk of developing serious health complications.

Obesity is one of the strongest predictors of T2D (Everson, Maty, Lynch, and Kaplan, 2002) and has recently been linked to lower levels of SES globally. A systematic review on obesity in the United States between the years of 1990 and 2006 examined disparities across gender, age, SES, race/ethnicity, and geographic region (Wang & Beydoun, 2007). Overall, ethnic minority and low SES groups were shown to be disproportionately affected by obesity at all ages. Analyses also showed that in the U.S., those with less than a high school education had a higher prevalence of obesity than their better educated counterparts (Wang & Beydoun, 2007). SES was also shown to be inversely related to prevalence of obesity among Whites but not among African Americans or Hispanics (Wang & Beydoun, 2007). Similarly, the U.S. Department of Health and Human Services found that between the years of 2005-2008, the obesity prevalence among White women increased as income level decreased versus the opposite among African American and Hispanic women (Ogden, Lamb, Carroll & Flegal, 2010). These findings indicate that differences in obesity across ethnic groups are not simply explained by differences in SES across groups; in fact, the opposite association between

obesity and income in white women versus African American and Hispanic women suggests that the relationship between obesity and SES may vary as a function of ethnicity. It is important to learn more about these differences to better understand and treat obesity. Further, understanding these relationships and how they relate to disease incidence is important, particularly in ethnic minority groups that may be at more risk for the development of diseases such as T2D. The present study will examine how a stress-reduction lifestyle modification intervention affects weight and glycemic control in a sample of socioeconomically disadvantaged, primarily minority, overweight or obese population with T2D.

Socio-economic Disadvantage and T2D

The prevalence of T2D has been shown to be directly related to several indicators of SES including education, occupation, and income level. Socio-economically disadvantaged individuals may also be at an increased risk for developing T2D due to a variety of unhealthy behaviors associated with their environment. Low SES individuals are more likely to live in poorer neighborhoods which have higher rates of crime and greater prevalence of smoking, alcohol use, and sedentary lifestyles than higher SES groups. Low SES neighborhoods have limited access to economical and nutritious food choices often leading these individuals to eat more poorly (Everson, Maty, Lynch, and Kaplan, 2002). Low SES individuals also experience higher levels of stress than higher SES groups due to economic uncertainties and lower levels of education which limit job-related opportunities (Everson, Maty, Lynch, and Kaplan, 2002). The combination of

high-stress living situations, poor nutrition, and sedentary behaviors can lead to a greater chance of becoming overweight/obese.

Robbins, Vaccarino, Zhang, and Kasl (2001) used data from the National Health and Nutrition Examination Survey (NHANES) to examine associations between poverty level, education, and occupation with prevalence of T2D among African American and White individuals. In this study, poverty was shown to have the strongest association with prevalent diabetes across all groups (Robbins et al., 2001). A meta-analysis conducted by Agardh, Allebeck, Hallqvist, Moradi, and Sidorchuk (2011) summarized and quantified published evidence on associations between T2D and SES measure by level of education, income, and occupation. Groups were then subdivided into high, middle, and low income countries for analyses. The results of the analyses demonstrated an increased risk of developing T2D in the lowest compared with the highest SES groups when measured by educational level, occupation, and income. Analyses by income level showed that low education level was associated with a 45% increased risk of T2D and low occupation status was associated with a 31% increased risk of T2D in high income

Racial disparities also exist in diabetes prevalence and treatment. T2D has been shown to disproportionately affect minority populations, including African-Americans, Hispanics, Native Americans and Asian-Americans. These populations have been shown to experience higher levels of obesity and sedentary behavior than Caucasian counterparts (Wing et al., 2001). The prevalence of diabetes among Hispanics is significantly higher than among Blacks, Asians, and Whites (McBean, Li, Gilbertson, & Collins, 2004). Additionally, the risk of developing diabetes is significantly higher among

Hispanics and African Americans than among whites, even after controlling for BMI (Shai et al., 2006).

More specifically, SES has been examined in relation to racial/ethnic and educational differences in T2D. The NHANES national sample of 1480 White, African American, and Hispanic adults with T2D showed that poor glycemic control was more common in African American women (50%) and Hispanic men (45%) compared with White men and women (Harris et al., 1999). Both Hispanics and African Americans had higher levels of HbA1c than Whites and impaired fasting glucose (Harris et al., 1999). A cross-sectional study of 770 individuals with T2D examined hospital records over a 7 year period for socio-economic inequalities in diabetes complications and control (Bachmann et al., 2003). Results showed that least educated patients were more likely than most education patients to have higher HbA1c levels (Bachmann et al., 2003).

Despite the evidence linking SES, stress, obesity, and T2D, few treatment interventions have been designed for or tested in primarily African American and Hispanic populations, socioeconomically disadvantaged individuals. This study aims to examine the effects of a lifestyle modification intervention on stress in T2D in this population. This study also aims to examine the links between stress reduction and weight loss and glycemic control in a low SES sample.

Type 2 Diabetes and Stress

T2D has been conceptualized as a lifestyle-related disease as many of its identifiable risk factors are related to modifiable behavior. Several behavioral factors have been linked to the development and management of diabetes (Manson et al., 1991;

Hu et al., 1999). Psychological variables have also been examined as potential risk factors for the development of T2D. Researchers have placed an emphasis in the literature examining the role of stress in the development and maintenance of T2D. Stress is defined as a state of threatened homeostasis provoked by a psychological, environmental, or physiologic stressor (Black, 2006). The level of one's perceived stress has been shown to have an effect on mood and well-being. Stress in response to an acute stressor is in fact an adaptive attempt of the body to cope with environmental stimuli and maintain body homeostasis. Therefore, in healthy populations, acute stress typically does not contain any inherent health related risks (Schneiderman et al., 2005). On the other hand, chronic stress may lead to negative health outcomes over time, even in healthy populations. For individuals with T2D, stress hormones are thought to be "counter-regulatory" and generally result in a hyperglycemic effect, whether they result from acute or chronic stressors (Surwit & Schneider, 1993). Chronic hyperglycemia can lead to vascular complications over time in individuals with T2D.

Stress is thought to result in elevated blood glucose levels via different pathways (Surwit & Schneider, 1993). Psychological stressors that are experimentally induced have been shown to induce release of hypothalamic and/or amygdala corticotrophin releasing factor which activates the HPA axis to produce cortisol and the sympathetic nervous system to produce norepinephrine and epinephrine (Black, 2006). This is primarily believed to occur through the release of cortisol from the adrenal gland (Marik & Raghavan, 2012). The cortisol pathway, which is believed to cause increased glucose production by the liver and diminished cellular glucose uptake, leads to both central obesity and an increased risk of developing diabetes. This is particularly true for those

who are chronically stressed (Bjorntorp, 1991). Activation of the HPA axis with the release of cortisol is an essential component of the general adaptation to illness and stress and contributes to the maintenance of cellular and organ homeostasis (Marik & Raghavan, 2012). However, when stress becomes chronic, the high circulating levels of cortisol within the body can become detrimental to the body and lead to hyperglycemia.

It has also been proposed that stress leads to an increase in the production of growth hormone and endorphins. This proposed stress mechanism can result in a decrease in glucose uptake, suppression of insulin secretion, and elevations in glucose levels (Guillemin, 1978). While these mechanisms can be adaptive in healthy individuals, those with diabetes may experience significant problems due to their compromised ability to metabolize glucose (Surwit & Schneider, 1993). In addition, it is hypothesized that psychological stress induces insulin resistance via the exposure to stress hormones, catecholamines and corticosteroids, proinflammatory cytokines and free fatty acids involved in the body's inflammatory reaction to stressful stimuli (Black, 2006). Insulin affects cells by binding to receptors on the surface of insulin-responsive cells. The inhibition of normal downstream signaling of the insulin receptor is a primary mechanism through which inflammatory signaling leads to insulin resistance (Wellen & Hotamisligil, 2005). Exposure of cells to TNF- α or elevated levels of free fatty acids often stimulates inhibitory processes of insulin resistance. It has also been shown that inflammatory signaling pathways can also become activated by metabolic stresses originating from inside the cell as well as by extracellular signaling molecules. Excess fat in the body or obesity overloads the functional capacity of the endoplasmic reticulum, leading to the activation of inflammatory signaling pathways and further contributing to insulin

resistance (Wellen & Hotamisligil, 2005). Excess catecholamines may not only impair insulin action but also insulin release from the beta cell. Whereas insulin resistance is an early process shown to be related to obesity, pancreas beta-cell function declines gradually over time before the onset of clinical hyperglycemia (Stumvoll, Goldstein, & van Haeften, 2005). The normal pancreatic beta cell can adapt to changes in insulin action. A dysfunctional beta cell is crucial to the process of diabetogenesis.

Insulin resistance frequently develops during repeated acute or prolonged stress. This is hypothesized to occur due to the excessive control of metabolism by the stress hormones secreted during a stressful situation which is opposed by insulin increasing oxidative stress and heightening cellular inflammation. Long term insulin resistance also entails a compensatory increase in plasma concentrations of insulin and dyslipidemia including increased plasma concentrations of triglycerides and decreased concentrations of HDL-cholesterol (Black, 2006). Although long term insulin resistance itself will not lead to the development of hyperglycemia, the additional development of beta cell dysfunction in the presence of insulin resistance leads to long term blood glucose build up in the blood due to insufficient uptake and by the cells and overproduction of glucose by the liver. This process leads to the development of T2D. Given the various pathways in which stress has been linked to detrimental outcomes in T2D, it is important to better understand the role of stress-reduction interventions in individuals with T2D.

Study-based Links between Stress and T2D

Effects of Stress on Glycemic Control

The literature on the effects of both acute and chronic stress includes several animal models showing the adverse effects of stress on glycemic control in T2D (Weekers et al., 2003; Wellen & Hotamisligil, 2005). The genetically obese mouse is often used as a genetic animal model for T2D, as it is characterized by a syndrome of obesity followed by hyperinsulemia, insulin resistance, hyperglycemia, and glucose intolerance (Surwit, Schneider, & Feinglos, 1992). One experiment in these animals by Surwit, Feinglos, Livingston, Kuhn, & McCubbin (1984) examined blood sampled from obese and lean mice after either an exposure to stress or a rest period. The stressful exposure consisted of restraint in a wire mesh apparatus and a 5 minute period of shaking. Plasma glucose levels were significantly higher in the obese rats than in the lean rats. Plasma insulin levels decreased more significantly in the obese animals as well (Surwit et al, 1984). The results of this study indicate that the mice that were obese and mimicked the T2D condition were affected by the stressful stimuli while the leaner, healthier rats' glucose and insulin levels were not affected by stress.

Human models have linked increased levels of stress to poorer glycemic control in human populations (Robertson, Harmon, Tran & Poitout, 2004; Peyrot, McMurry, & Kruger, 1999; Griffith, Field, & Lustman, 1990). For example, Inui et al. (1998) found that individuals with diabetes who experienced chronic, life-threatening stress also experienced worsening glycemic control than those individuals with diabetes who were not exposed to intense stressors. Individuals with T2D also seem to have altered adrenergic sensitivity in the pancreas, making them especially sensitive to stressful

stimuli (Surwit & Schneider, 1993). Other studies in humans have been less successful in demonstrating a direct relationship between stress and glycemic control. Peyrot, McMurry & Kruger (1999) hypothesized that stress does not affect glycemic control directly through a psychophysiological pathway but instead via the indirect relationship between stress and coping style. Another study by Mooy, Vries, Grootenhuis, Bouter & Heine (2000) examined cross-sectional data from 2,380 Dutch citizens and found that the number of stressful life events was positively associated with the probability of having undiagnosed T2D. This relationship remained significant in the highest quintile of the population after controlling for family history of diabetes, alcohol consumption, physical activity, and SES (Mooy et al., 2000). However, there is a lack of research confirming the direct role of stress in the development or treatment of T2D.

Effects of Stress on Weight

Emotionality has been associated with both increased or decreased food intake and weight (Stone and Brownell, 1994; Willenbring et al., 1986). With reference to stress specifically, an increase or decrease in dietary consumption has been related to exposure to stress and the severity of a stressor (Torres & Nowson, 2007). This finding has been confirmed in both animal and human models (Ganley, 1989; Greeno & Wing, 1994).

One of the principal paradigms for testing stress-induced eating in animals is the tail pinch. In early uncontrolled studies, results showed that in 66-100% of rats, eating, gnawing, or licking food was a direct response to having their tail pinched (Nemeroff & Garth Bissette, 1978; Antelman & Szechtman, 1975). Other animal studies using rats have indicated an increase in consumption of sweet foods as a result of experimentally

induced stress (Bertiére, Mame, Baigts, Mandenoff & Apfelbaum, 1984; Ely et al., 1997). One study of 230 rats with free access to food and water exposed half of the animals to restraint stress for 50 days for 1 hour a day, 5 days per week. Results showed that the stressed rats ate more sweet food than the non-stressed rats (Ely et al., 1997). This significant difference was maintained independent of the rats' level of hunger after being restrained from eating over a period of several days.

In humans, similar patterns relating stress and eating have been observed. The effects of stress on intake of high density foods have shown that greater levels of perceived stress are positively associated with a higher fat diet and higher consumption of calories overall (Ng & Jeffery, 2003; McCann, Warnick & Knopp, 1990). A study conducted in 59 healthy women exposed participants to a stress condition and a control condition on different days (Epel, Lapidus, McEwen & Brownell, 2001). Participants were asked to eat a snack one hour before the experiment, and to refrain from consuming anything else until the experiment began. Participants were then exposed to 45 minutes of stress (i.e. challenging tasks) and after the exposure were offered a basket of snacks containing two high fat sweet and salty snacks and two low fat sweet and salty snacks after the exposure. Salivary cortisol samples were collected at various time points throughout the sessions. Results showed that experimentally induced stress resulted in higher consumption of calories overall (Epel et al., 2001). Cortisol reactivity was also linked to greater caloric intake in this study. Individuals in the stress condition with high cortisol reactivity levels were also shown to consume more sweet foods following stressful experiences (Epel et al., 2001). The tendencies to consume high fat and high energy foods under periods of stress may lead to patterns of overeating. Long-term over-

consumption of unhealthy foods may lead to obesity in those that are chronically stressed or who experience high levels of stress over time.

Studies following healthy individuals with chronic life stress have depicted a relationship between increased levels of stress and weight gain, possibly leading to obesity over time (Torres & Nowson, 2007). A recent prospective cohort study of 7965 participants of the Whitehall II Study was assessed for work stress and BMI at baseline and again 5 months later (Kivimäki et al., 2006). Results showed that work stress increased the likelihood of weight gain among men with a higher BMI at baseline. This study also showed a significant association between work stress and increased BMI 5 years later in women (Kivimäki et al., 2006). Another longitudinal study of 5867 participants assessed stress and weight at baseline, 6 years post-baseline, and 15 years post-baseline (Korkeila, Kaprio, Rissanen, Koskenvuo & Sørensen, 1998). Univariate analyses demonstrated that elevated levels of stress at baseline predicted major weight gain in men 6 years later. For younger males in this sample, high levels of stress at baseline was a significant predictor for major weight gain, even after controlling for age, gender, and baseline BMI (Korkeila et al., 1998). These findings are important as highly stressed individuals well as obese individuals are more at risk for developing T2D.

A fewer number of longitudinal studies of stress in individuals with T2D have been conducted. Heraclides, Chandola, Witte and Brunner (2011) also used Whitehall II study data to examine the interaction between work stress and obesity in relation to T2D risk 18 years later. The association between job stress and T2D incidence was stratified by BMI and examined for gender differences. Work stress was shown to be associated with incident T2D among women but not men. Work stress was associated with a lower

risk of T2D in non-obese but not in obese men. Among women, work stress was associated with higher risk of T2D in obese but not in non-obese participants (Heraclides, Chandola, Witte & Brunner, 2011). Longitudinal studies examining the relationship between stress and weight are few and are limited due to methodological issues (i.e. small sample sizes, observational studies). These studies have also focused mainly on work related stress rather than perceived stress or other general endorsements of daily stress.

Several pilot studies have recently demonstrated the efficacy of stress-reduction interventions on weight-loss in overweight and obese populations. One study by Alert et al. (2013) evaluated the effectiveness of a comprehensive mind-body intervention for weight loss in 31 overweight and obese adults. The 20-week intervention consisted of 20 minutes of guided group relaxation exercise along with 1 hour of exercise, a small meal, and a social support/group discussion. Post-intervention, participants experienced statistically significant weight loss and reduction in BMI. The average weight lost was 4.3 kg and BMI decreased 1.54 kg/m² on average (Alert et al., 2013). Another pilot RCT randomized 44 overweight or obese African American women into a 12 week adaptation of the DPP intervention with an additional stress-management component or to DPP alone (Cox et al., 2012). Each week, those in the stress-reduction intervention group were introduced to different stress management techniques including relaxation, behavioral approaches, and cognitive strategies. Results showed that both groups weighed significantly less at the 3 month time point with a trend toward greater weight loss by the stress-reduction group (Cox et al., 2012).

One pilot RCT in 47 overweight/obese women were randomly assigned to a 4 month mindfulness intervention for stress reduction and stress eating or a wait-list control

group (Daubenmier et al., 2011). The intervention consisted of components from Mindfulness-Based Stress Reduction (MBSR), Mindfulness-Based Cognitive Therapy (MBCT), and Mindfulness-Based Eating Awareness Training (MB-EAT). The study was successful at increasing mindfulness, reducing anxiety, and reducing emotional eating but was unsuccessful in reducing abdominal fat or weight as a result of the intervention. However, obese individuals in the intervention group maintained their weight while obese control participants gained weight over time (Daubenmier et al., 2011). Another more recent pilot study of overweight and obese Greek women examined an 8 week stress-management intervention consisting of progressive muscle relaxation (PMR) and diaphragmatic breathing on weight loss in 34 women (Christaki et al, 2014). Participants randomized to the stress-management group lost a significant amount of weight (4.44 kgs) versus the control group, who lost an average of 1.38 kg., which was not statistically significant (Christaki et al, 2014). Stress-reduction interventions for weight loss in T2D

It is important to note that these interventions are pilot studies conducted in small samples and often without a methodologically strong comparison control group. Additionally, these studies were conducted in obese/overweight individuals who were otherwise healthy. Randomized control trials of stress-reduction interventions for weight loss in T2D are lacking in the literature and more needs to be done to understand the associations between these two important predictors of T2D.

Psychological Stress-reduction Interventions in T2D

Due to documentation of the negative effects of stress among T2D patients, there have been attempts at developing and testing interventions aimed at reducing stress to

improve glycemic control in this population. These individualized interventions initially focused on relaxation training or time-intensive individual therapy and typically consisted of progressive muscle relaxation (PMR) with or without biofeedback, visual imagery techniques, deep breathing, or cognitive restructuring components (Lane et al., 1993; Jablon, Nailboff, Gilmore & Rosenthal, 1997; Surwit & Feinglos, 1983). Results of these trials were mixed. Some studies showed positive effects of stress-management interventions on glycemic control (Lane et al., 1993; McGrady & Gerstenmeier, 1990; Rosenbaum, 1990; McGrady, Bailey & Good, 1991) while others failed to replicate these findings (Jablon et al., 1997; Aikens, Kiolbasa & Sobel, 1997). Coping-skills training has also been incorporated into more comprehensive diabetes education programs. Most studies testing the effects of coping-skills training have found positive effects on psychological factors but few have been able to find positive effects on glycemic control (Rubin, Peyrot & Saudek, 1991; Rubin, Peyrot & Saudek, 1989). The current study aims to examine the relationship between similar stress-management training effects and glycemic control at the 6 and 12 month time point in individuals who also received a lifestyle modification intervention aimed at reducing weight.

Group based interventions of stress management have also been shown to be effective in improving glycemic control and are more generalizable to real-world applications than individualized interventions. A metaanalysis of 25 RCTs found that the mean percentage HbA1c was lower in people assigned to psychological intervention than in the control group in only 12 trials with non-significant differences in blood glucose concentration and weight gain in the remaining studies (Ismail, Winkley, & Rabe-Hesketh, 2004). Psychological distress was significantly lower in the intervention groups

overall (Ismail, Winkley, & Rabe-Hesketh, 2004). Another study by Surwit et al. (2002) randomized 108 participants into a five session diabetes education program either with or without a stress management training component. HbA1c levels were measured at 2, 4, 6 and 12 months. Results showed a general decrease over time for those in the intervention group who received the stress management training, with effects most apparent at the 12 month time point (Surwit et al., 2002). More recently, a mindfulness-based stress reduction intervention aimed at patients with T2D has preliminary data indicating that their intervention improved subjective health status (Hartmann et al., 2012). Overall, there are not many studies examining the effects of group-based stress reduction interventions on glycemic control. Findings in studies published in this area have been mixed and not very strong methodologically (i.e. few RCTs, small sample sizes). One of the reasons for this lack of effect may be due to the use of a psychological or stress-related intervention alone, rather than as part of a multi-faceted package as in other lifestyle modification intervention studies. More research is needed to further understand the role of stress management techniques in improving T2D symptoms, particularly in more generalizable group settings.

Lifestyle Modification Interventions in T2D

Interventions focusing on lifestyle modification to prevent T2D have been a primary focus in the intervention literature over the past 2 decades. From the 1990s-2000s, lifestyle modification interventions for individuals at risk for T2D were implemented on a one-to-one individualized basis (Turner et al., 1998; Gaede, Vedel, Parving, & Pedersen, 1999; Tuomilehto et al., 2001; Ohkubo et al., 1995). While the

results of these interventions were often positive, they were sometimes viewed as being too costly and too time consuming for clinical implementation (Trento et al., 2002). Group focused interventions have more recently turned their focus to weight reduction (Tuomilehto et al., 2001; Kim et al., 2006) or improved glycemic control (Pan et al., 1997; Sone et al., 2002) as the primary outcome measures. Group based lifestyle modification interventions have focused primarily on improving diet, increasing level of physical activity, or both (Wolf et al., 2004; Lifshitz & Hall, 2002; Tuomilehto et al., 2001; Lindström et al., 2006; Knowler et al., 2009).

A landmark RCT to prevent or delay the onset of T2D was the Finnish Diabetes Prevention Study (FINNISH study). The FINNISH study consisted of 522 obese participants from 5 study centers recruited from high-risk groups with impaired glucose tolerance (Tuomilehto et al., 2001). The intervention group consisted of intensive individualized instruction on weight reduction, improving diet, and increasing physical activity. Results showed that individuals in the intervention group lost an average of 4.2 ± 5.1 kg in 1 year versus an average weight loss of 0.8 ± 3.7 kg in the control group; after 2 years, the pattern continued as those in the intervention group had loss a net of 3.5 ± 5.5 kg versus a net loss of 0.8 ± 4.4 kg in the control group (Tuomilehto et al., 2001). Results for the incidence of diabetes at the end of the follow-up period indicated a 58% relative reduction in the incidence of diabetes in the intervention group compared with the control group (Zimmet, Alberti, & Shaw, 2001).

One of the most well known RCTs for the prevention of T2D is the Diabetes Prevention Program (DPP), an RCT comparable to the FINNISH study. This trial was conducted on 3150 adults who were considered to be at risk of developing T2D (Diabetes

Prevention Program Research Group, 2002). The primary outcome of interest in the DPP was development of diabetes. Secondary outcomes were the development of microvascular complications, cardiovascular disease and CVD related risk factors (Diabetes Prevention Program Research Group, 2002). DPP results post-intervention showed that the intensive lifestyle intervention decreased risk of diabetes incidence by 58% compared to the placebo condition. The metformin medication condition was independently shown to decrease diabetes incidence by 31%. Beneficial results were maintained at the 10 year follow-up time point (Diabetes Prevention Program Research Group, 2002).

More recently, the LookAHEAD trial was developed to provide a more definitive assessment of long-term health consequences of weight loss in individuals with T2D (Wadden, 2006). The Look AHEAD trial was a multi-center RCT of over 5000 individuals with T2D who were considered to be either overweight or obese (Pi-Sunyer et al., 2007). The primary objective of this study was to determine whether cardiovascular morbidity or mortality in individuals with T2D could be reduced by long-term weight reduction. The intervention combined both diet modification and increased physical activity via weekly group sessions and monthly individual sessions with study staff for the first 6 months and bi-weekly group sessions and monthly individual sessions from the 7 to 12 month time points. The control group consisted of Diabetes Support and Education (Pi-Sunyer et al., 2007). Results of the LookAHEAD study at the 1 year time point showed that the intervention group lost an average of 8.6% of their initial body weight, compared with 0.7% in the control group (Pi-Sunyer et al., 2007). Mean fasting glucose and HbA1c also decreased more in the intervention versus the control group. At

four year follow up, these patterns persisted for weight, fitness levels, HbA1c, blood pressure, HDL-cholesterol and triglyceride levels (Wing, 2010).

These studies have been largely focused on those who are risk for T2D as a preventative measure rather than focusing on those with a diagnosis of T2D, as was the case for the FINNISH and DPP interventions. Although the previously mentioned studies were efficacious in reducing weight and decreasing the incidence of diabetes, it is important to note that they lacked a stress-reduction component entirely. The LookAHEAD trial has been the only RCT to date to examine the effects of a lifestyle modification intervention in participants with T2D. However, the LookAHEAD trial also lacked a stress-management component and relied on both group and individualized interventions. These previous lifestyle intervention studies have shown that lifestyle modification interventions can produce positive effects on the reduction of weight in individuals at risk for developing T2D as well as in those already diagnosed with T2D. However, they do not provide any information about whether stress reduction plays a role in weight loss or improvement of glycemic control.

Community based interventions targeted at low-income ethnic minority groups with higher rates of T2D (e.g. Hispanics, African Americans) are scarce and have had weaker results on improving glycemic control than those conducted in ethnic majority, higher SES individuals (Satterfield et al., 2003). A recent pilot study conducted in 75 adults with T2D in a rural area of Costa Rica randomly assigned participants to an intervention or control group (Goldhaber-Fiebert, Goldhaber-Fiebert, Tristán & Nathan, 2003). The intervention group received 11 weekly nutrition classes and participated in walking groups three times per week. All individuals received basic diabetes education.

Results showed that the intervention group lost 1.0 ± 2.2 kg compared with the control group who gained 0.4 ± 2.3 kg after 12 weeks. HbA1c was also shown to decrease $1.8 \pm 2.3\%$ in the intervention group and $0.4 \pm 2.3\%$ in the control group (Goldhaber-Fiebert et al., 2003). The Diabetes Education & Prevention with a Lifestyle Intervention Offered at the YMCA (DEPLOY) pilot study implemented and tested the results of a group-based DPP lifestyle intervention 92 individuals at risk for developing T2D at two semi-urban YMCA centers (Ackermann, Finch, Brizendine, Zhou & Marrero, 2008). The control group in this study was brief diabetes education counseling alone. Results showed that body weight decreased by 6 percent in the intervention group compared to 2 percent in the control group after 6 months. Results also showed that these significant differences between groups were sustained at the 12 month follow up time point (Ackermann et al., 2008).

Although these studies targeting minority populations have shown promising results, it is important to note that these data comes from smaller, pilot studies that have yet to be implemented or tested on a larger scale. Overall, the literature is lacking in lifestyle modification interventions aimed at reaching low-income minorities who have already been diagnosed with T2D in the community. Further, the effect of stress-reduction as a component of these interventions needs to be examined in T2D to better understand how stress reduction relates to important health outcomes such as weight and glycemic control.

The present study

The relationship between stress and T2D has been extensively investigated. The incidence of developing T2D has been examined as it related to stress as well as how this relationship is affected by SES. Glycemic control has been mainly studied as the outcome of interest in the T2D and stress literature. Little emphasis has been placed on weight as an outcome in this population as it might relate to the effects of stress despite the direct relationship between obesity and development of T2D. Lifestyle modification interventions involving changes in diet and physical activity to promote weight loss to delay the onset of T2D have also been examined at length. The results of these studies have shown that lifestyle modification interventions have been effective in preventing the onset of T2D in at-risk populations and reducing weight in one RCT conducted in participants already diagnosed with T2D. However, relatively little data on this topic have examined a stress reduction component as part of a lifestyle modification intervention for weight loss for patients already diagnosed with T2D, particularly in a socio-economically disadvantaged, minority, inner city population.

Results of the CALM-D intervention on weight and HbA1c shown significant reductions in weight, HbA1c, and depressive symptoms relative to participants assigned to usual care. Reductions in weight and HbA1C variables were shown to occur mainly within the first 6 months of the intervention and maintained from the 6 month to the 12 month time points (Moncrieft et al., 2014). The present study determined the effect of a lifestyle modification intervention on reducing stress in a sample of minority, low-income adults with T2D, while controlling for age, gender, baseline stress, and baseline depression. Latent growth modeling was used to examine change and to compare the

intervention and control groups. Additionally, the relationship between stress reduction and weight loss and stress reduction and glycemic control was explored.

Study Aims and Hypotheses

Primary Aim 1: To determine intervention effects on perceived stress among inner city ethnic minority T2D patients recruited for the Community Approach to Lifestyle Modification for Diabetes (CALM-D) study.

Hypothesis 1a. Participants in the intervention group would display reduction in stress while those in the control group would not.

Primary Aim 2: To determine whether the relationship between reductions in perceived stress and reductions in weight differs as a function of receiving a lifestyle modification intervention .

Hypothesis 2a. Change in perceived stress would be significantly related to decrease in weight in the intervention group but not in the control group.

Primary Aim 3: To determine whether the relationship between reductions in perceived stress and improvements in glycemic control differs as a function of receiving a lifestyle modification intervention.

Hypothesis 3a. Change in perceived stress would be significantly related to improved glycemic control in the intervention group but not in the control group.

Chapter 2

Methods

Participants

All participants were enrolled in the Community Approach to Lifestyle Modification for Diabetes (CALM-D) study, an RCT designed to evaluate the effectiveness of a structured lifestyle modification intervention with the goals of reducing weight, increasing physical activity, and improving stress management in overweight/obese (BMI values ≥ 27 kg/m²) individuals with T2DM who also endorsed significant depressive symptoms (Beck Depression Inventory II [BDI-II] total score that was greater than or equal to 11). The sample consisted of 111 socio-economically disadvantaged (average household income of below \$15,000, average 12 years of education), mostly minority (85% Hispanic, 10% African American) adults (mean age: 55 years; 58% women) who were randomized to a 17 session 12 month lifestyle intervention or usual care.

Inclusion/Exclusion Criteria

Participants included were men and women ages 18-70 years, who were considered to be overweight or obese (BMI values ≥ 27 kg/m²). Individuals also had to have T2D and report significant depressive symptoms (Beck Depression Inventory II [BDI-II] total score ≥ 11). Participants with evidence of poor glycemic control (HbA1c $\geq 11\%$; fasting triglycerides ≥ 600 mg/dl), elevated blood pressure ($\geq 160/100$ mmHg), evidence of CVD, COPD, or renal disease (past event or current manifestations), as well

as other physical or mental limitations preventing participation in the study were excluded.

Procedures

Participants were recruited at local community health clinics or referred by word-of-mouth. The study protocol was approved by the University of Miami Human Subjects Research Office and all participants signed informed consent forms before they were eligible to participate. Participants were randomized to a 12 month, 17 session, structured lifestyle intervention (CALM-D) or a usual care control condition using a block randomization schedule with blocks of 4 to 10 participants. The study used an intent-to-treat analysis, which included all eligible participants for whom perceived stress, weight, and HbA1c data were available.

Intervention

Participants in the intervention group received a weight goal (7% weight loss) and physical activity goal (150 minutes aerobic activity/week) at the beginning of the intervention period. Participants in the intervention group were given a Salter Cygnet bathroom scale to monitor weight, a pedometer for an activity monitor, and writing materials to monitor weight, physical activity, and a “Keeping Track” booklet to record daily food intake and daily physical activity. Intervention sessions lasted approximately 1.5 to 2 hours and covered a range of topics related to diabetes, diet, physical activity, and stress reduction. Session topics included objectives such as identifying and eating less fat, being active as a way of life, managing negative thoughts and emotions, problem

solving, medication adherence, assertiveness, and staying motivated. The first half of the intervention period focused on teaching participants how to achieve their physical activity and diet-related goals; these sessions consisted of 4 weekly and 4 bi-weekly sessions. The second half of the intervention period focused on participants learning to problem solve and maintain the new behavioral changes they acquired during the first half of the intervention; these sessions consisted of monthly sessions for a total of 9 months.

All sessions began with a 3 minute relaxation exercise after which participants were asked to rate their level of stress. At the conclusion of each session, participants completed a mastery form to assess their comprehension of the material and homework assignments to incorporate material into their daily lives, including encouragement to practice relaxation material for homework. In addition, stress reduction techniques were discussed and reviewed during weekly topics covering diet and physical activity. These topics included a variety of stress-management techniques including challenging negative thoughts, learning effective verbal and non-verbal communication and listening skills, benefits of social support, and assertiveness training. Stress management, preventing stress, and coping with stress were also weekly topics in isolation during session 5 and 14.

Participants in both groups received a short educational booklet titled “Your Guide to Diabetes” in either English or Spanish that covered several topics related to diabetes management; however, individuals assigned to the usual care condition were not instructed to make any changes to their current diet, physical activity patterns or stress management practices. All participants received compensation for completing

assessments at baseline (\$225) and 6 and 12-months (\$100 each); intervention participants were also compensated (\$10) for attendance at individual sessions.

Measures

All data were collected from participants during their baseline, 6 month post-baseline, and 12month post-baseline assessment visits. During these visits, demographic information, blood samples, self-report questionnaires, as well as anthropometric measurements such as height, weight, and waist circumference were obtained.

Perceived Stress

Perceived stress was measured using the Perceived Stress Scale (PSS). The PSS is a 14-item instruments designed to measure the degree to which situations in one's life are appraised as stressful over the past month (Cohen, Kamarck & Mermelstein, 1983). The PSS was originally developed in English but has also been translated to Spanish. Studies on the validity of the Spanish version of the PSS provide evidence of comparable reliability and validity between the English and Spanish versions (Ramírez & Hernández, 2007; Remor, 2006). Psychometric properties of the Spanish version of the PSS have also been tested in medical samples (Fliege, et al., 2005). The PSS was administered at baseline and at the 6 month and 12 month follow-up time points. The PSS uses a 5-score Likert type scale (0=never, 1= almost never, 2=sometimes, 3=fairly often, 4= very often) and participants self-report how often they have felt stress in a particular situation. The total score is obtained by calculating the total scores of all the items after reversing items 4, 5, 7, and 8.

Weight

Participants' weight along with their height was assessed during the baseline visit as well as at the 6 month and 12 month follow-up time points. Weight was measured using a Tanita Body Composition Analyzer (TBF-300A) and was calculated to the nearest 0.1 kg.

HbA1c Blood Measurement

Blood was drawn following a 12 hour fast during baseline, 6 month, and 12 month follow up visits by a staff phlebotomist. HbA1c was assessed using individual blood samples for each participant.

Statistical Analyses

SPSS version 22.0 was used for data preparation, descriptive analysis and regression analysis. Mplus version 7.0 was used to compare change over time between intervention and control groups within a structural equation modeling framework.

Data preparation

Each variable included in the proposed analyses was tested for normality. The distributions were normal and no notable extreme outliers were noted in the dataset.

Missing values

Twenty participants were missing PSS data at the 6 month time point and 24 participants were missing data at the 12 month time point. Five participants were missing

HbA1c data at baseline, 24 were missing data at the 6 month time point, and 24 participants were missing data at the 12 month time point. One participant was missing weight data at baseline, 24 were missing data at the 6 month time point, and 24 participants were missing data at the 12 month time point. Assuming missing data are missing at random (MAR), Full Information Maximum Likelihood (FIML) estimation was used to obtain parameter estimates. FIML used a likelihood function calculated at the individual level, and aggregates across individuals, by borrowing information from other variables for the estimation of parameters with missing values (Enders, 2006).

Descriptive analyses

Means and standard deviations were calculated and reported for all demographic, biological, and psychological variables included in the analyses, including the control variables of age, baseline depression, and baseline stress. Student t tests were used to examine differences between participants in the intervention group versus the control group in terms of their baseline characteristics.

Inferential analyses

Latent growth modeling (LGM) was used to evaluate intervention effects on the following three variables: weight, perceived stress, and HbA1c. Measurements of each variable were taken at baseline, 6-months post-baseline, and 12 months post-baseline. Each variable was tested independently and evaluated for intervention effects separately.

Figure 1 is a path diagram of the LGM of change in PSS scores over a 12 month time period for participants randomized to receive a lifestyle modification intervention or

usual care. PSS scores were obtained at baseline (time 0), 6 months into the study (time 6) and 12 months into the study (time 12). The latent variables in this model characterize the pattern of change. More specifically, the linear change process is characterized by the intercept latent variable, which represents the baseline, and the slope latent variable, which represents change in PSS per month. The loadings for the intercept variable in this model are not estimated (set to 1). The loadings for the slope variable are used to specify the time structure of the data in months. The loading for the slope variable at the 12 month time point was estimated in the model, indicated by an asterisk in Figure 1. This time point was estimated because we did not expect the treatment effect on stress to continue in a linear pattern from the 6 to 12 month time point. We expect a non-linear pattern of change based on the change previously modeled in weight and HbA1c (Moncrieft et al., 2014). Therefore, we estimated the loading for the 12 month time point to examine at which time point the change plateaus, or levels off.

The parameters of interest in this model are the means of the intercept and slope latent variables, indicated by paths from the mean structure at the bottom of Figure 1. The randomization observed variable is shown to predict the slope latent variable (see Figure 2). The estimate of this parameter represents the difference between the means of the two groups on the slope. In this model, we assume residual variances are equal over time. The observed control variables of age, gender, baseline depression, and baseline stress with paths connecting each variable to the slope latent variable were added to the model in order to examine if intervention effects on PSS remain above and beyond these factors (see figure 3). Intervention effects are reported as betas and can be interpreted as monthly

change in stress as units per month. Positive estimates may indicate a greater increase or smaller decrease per month in stress, while negative estimates indicate a greater decrease.

Moderation analysis

The moderating effect of randomization group on the relationship between change in stress and change in weight was tested using multiple group analysis within the context of structural equation modeling. The moderating effect of randomization was also tested for the relationship between change in stress and change in HbA1c. Multiple group analyses in SEM allow assessment of the population heterogeneity in various structure parameters such as variances, covariances and paths. Multiple group analysis requires a multi-step procedure. By examining the groups separately, the relationships between reductions in stress and changes in weight and HbA1C can be compared between those who received the intervention versus those who did not.

The initial models created to examine intervention effects on stress, weight, and HbA1c were combined to assess each association of interest; specifically, PSS change and weight change models were combined and estimated simultaneously and PSS change and HbA1c change were combined and estimated simultaneously. In the model examining intervention effects on PSS and weight together, a covariance estimating the relationship between change in PSS and change in weight was added to the model for the intervention group as well as for the control group. This association was constrained equal across groups and examined for model fit.

Subsequently, a second model was tested for model fit. In this model, the

path estimating the relationship between change in PSS and change in weight was allowed to vary freely between the intervention and control groups. A chi-square difference test was then conducted to determine whether parameters can be estimated equally between groups. A significant chi-square difference test indicated moderation. Similarly, separate models were fitted to test the relationship between change in PSS and change in HbA1c.

Chapter 3

RESULTS

Sample Characteristics

The study sample consisted of 111 participants (33 males and 78 females). Mean age was 54.81 years at baseline. Mean baseline PSS levels were 18.85. Mean baseline weight was 85.30 kgs. and mean HbA1c level was 7.72 mg/dl. After randomization, the intervention group consisted of 57 participants (20 males and 37 females) and the control group consisted of 54 participants (13 males and 41 females). The Intervention group mean age, PSS, weight, and HbA1c were 54.84 years, 18.54, 85.04 kgs., and 7.67 mg/dl respectively. The control group mean age, PSS, weight, and HbA1c were 54.78 years, 19.18, 85.57 kgs., and 7.77 mg/dl respectively. Important demographic, biological, and psychological characteristics of the study population are shown in Table 1.

After randomization, there were no significant differences between the intervention and control groups at the point of randomization in terms of age, gender, HbA1c, weight, depression or perceived stress.

Intervention effects on stress reduction

The initial model examining change in stress fit the data as evidenced by a non-significant chi-square test ($\chi^2 (2) = 1.536, p = 0.4639$). Results examining intervention effects on stress showed that those in the intervention group reported significantly less stress over time than those in the control group ($\beta = -0.475, SE = 0.203, p = 0.02$). These results indicated that participants who received the lifestyle intervention decreased on the PSS .475 points per month more when asked to rate their perceived levels of stress than

those in the control group. This intervention effect remained significant for change in stress ($\beta = -0.497$, $p = 0.019$) after controlling for age ($\beta = 0.018$, $p = 0.208$), gender ($\beta = -0.326$, $p = 0.175$), baseline depression ($\beta = 0.030$, $p = 0.109$), and baseline stress ($\beta = -0.019$, $p = 0.389$).

Estimation of the loading for the slope variable at the 12 month time point indicated that the treatment effect on stress decreased from the 6 month time point to approximately the 8 month time point, where it leveled off and remained stable until the 12 month follow-up time point. As expected, this elucidated a non-linear pattern of change similar to the change previously modeled for weight and HbA1c (Moncrieft et al., 2014).

Associations between stress reduction and weight change

An initial test of model fit where the path between the slope of PSS and slope of weight were constrained equal between groups was performed, yielding the following results: $\chi^2 = 33.180$, $df = 24$, $p = 0.1003$. A second model was then tested for model fit. In this model the path between the slope of PSS and the slope of weight was allowed to vary by group. The unconstrained model yielded the following results: $\chi^2 = 28.061$, $df = 23$, $p = 0.2135$. A significant difference was found between the constrained and unconstrained models (χ^2 difference = 5.119, $P = 0.025$) suggesting a moderation effect of randomization group in this relationship.

Further examination of the significance of the paths between change in PSS and change in weight in the intervention group and in the control group indicated that there was not a significant relationship between change in stress and change in weight either

the control group ($\beta = -.117$, $SE = .09$, $p = .192$) or the intervention group ($\beta = .167$, $SE = .096$, $p = .081$). It should be noted that the relationship between change in PSS and change in weight in the intervention group was approaching significance, suggesting a possible relationship between stress reduction and weight loss in the intervention group but not in the control group.

Associations between stress reduction and improvements in HbA1c

The moderating effect of randomization group in the relationship between change in stress and change in HbA1c was also tested within the SEM framework. An initial test of model fit where the path between the slope of PSS and slope of HbA1c was constrained equal between groups was performed, yielding the following results: $\chi^2 = 33.180$, $df = 25$, $p = 0.1266$. A second model was then tested for model fit. In this model the path between the slope of PSS and the slope of HbA1c was allowed to vary by group. The unconstrained model yielded the following results: $\chi^2 = 32.833$, $df = 24$, $p = 0.1077$. No significant difference was found between the constrained and unconstrained models (χ^2 difference = 0.0347, $P = 0.975$) suggesting no moderation effects of randomization group in this relationship.

Chapter 4

DISCUSSION

In this thesis, we reported on the effects of a lifestyle modification intervention on the reduction of perceived stress in a sample of socio-economically disadvantaged, minority patients with T2D. Results indicate that the CALM-D intervention significantly reduced level of perceived stress for those in the intervention group but not for those in the control group. The lifestyle-modification intervention was shown to be effective for individuals with T2D who participated in a lifestyle modification intervention to reduce their levels of perceived stress by 0.475 points per month, resulting in a total reduction of 4.95 points from baseline to the end of the intervention. Participants in this study reported a higher level of stress at baseline than the national average for both genders, all races, all education levels, and all income levels (Cohen & Janicki-Deverts, 2012). Individuals who received the lifestyle intervention decreased in their PSS score from 17.37 to 12.42 points, a reduction which was both statistically and clinically significant in this population.

This study presents evidence of the efficacy of a stress-reduction intervention, in combination with dietary and physical activity recommendations, in reducing perceived stress in individuals with T2D, even after controlling for age, gender, baseline depression, and baseline stress level. This finding adds important information to the lifestyle modification intervention literature. Firstly, the majority of previous interventions were conducted in individuals at-risk for developing T2D and aimed to reduce the incidence of T2D post-intervention. LookAHEAD, the only previously published study that examined the effects of a lifestyle modification intervention in individuals with T2D, lacked a

stress-reduction component altogether. This intervention was also the first of its kind to examine the effect of a stress reduction component in a lifestyle modification intervention in a population of socio-economically disadvantaged individuals. We selected a primarily minority, low-income, low-educated, depressed sample from the community. Results from epidemiological studies show that these low SES individuals are more likely to be stressed (Baum, Garofalo, and Yali, 1999), making it more difficult for them to attend sessions and follow the intervention regimen. In addition, we selected individuals who had T2D, were obese, and endorsed depressive symptoms, making them less likely to seek medical services (Baum, Garofalo, and Yali, 1999) and less likely to adhere to medical interventions. Positive results for stress reduction in this difficult to treat population may add to treatment options for a low SES community-sample with T2D.

The pattern of change elucidated in this study also indicates that participants were able to reduce their stress quickly within the first 6 months of the intervention, and continue to reduce their level of perceived stress for approximately 2 months before leveling off. The intervention was focused mainly on introducing skills and techniques during the first 6 months and reinforcing and problem solving from the 6 to 12 month time points. However, stress-reduction components were discussed with other diet and physical activity information each week and were oftentimes the full topic of conversation at weekly meetings throughout the intervention. Additionally, intervention participants engaged in a relaxation exercise weekly in session and were encouraged to continue to practice their relaxation techniques at home every week. The relaxation training literature suggests that relaxation skills improve with more exposure to the technique and with greater practice (Martin, 2008). Weekly exposure to a relaxation

intervention, information about stress-reduction techniques, and encouraged independent practice could be responsible for the rapid and continued drop of PSS. Also, results showed that this reduction in stress was maintained for the remainder of the intervention similar to the pattern of change in weight and HbA1c previously modeled (Moncrieft et al., 2014). These results show promise for the long-term value of a behavioral lifestyle intervention with a stress management component for T2D.

We also provided novel data assessing the relationship between reductions in stress and reductions in weight as well as reductions in stress and improvements in glycemic control as a function of randomization group of individuals with T2D. This study extends the findings of previous studies that examined the relationship between stress reduction and weight loss (Epel et al., 2001; Kayman, Bruvold, & Stern, 1990; Torres & Nowson, 2007) and the relationship between stress reduction and improved glycemic control (Inui et al., 1998; Surwit & Schneider, 2002; Peyrot, McMurry & Kruger, 1999). Interventions designed to behaviorally reduce stress in order to improve glycemic control in T2D have often been unsuccessful (Ismail, Winkley, & Rabe-Hesketh, 2004; Surwit et al., 2002).

In this study, no significant associations were found between change in stress and change in weight or change in HbA1c in the intervention group or the control group; however, the relationship between reduction in stress and reduction in weight approached significance in the intervention group, suggesting a stronger association in the intervention group relative to the control group. Due to the small sample size of this study, it is possible that this study may have lacked sufficient power to detect whether or not stress reduction was related to weight loss. A potential factor explaining this trend

toward significance would be the small sample size used in this study. Perhaps in a larger sample, the estimated relationship between change in stress and change in weight would be declared statistically significant. In addition, previous analyses of weight loss in the CALM-D study showed that although the current intervention resulted in significant difference in weight loss between intervention and control groups the amount of weight lost was less than in previous lifestyle modification studies (Moncrieff et al., 2014). It is possible that the reduction in weight was too small to demonstrate a relationship to the reduction in PSS.

A strength of this study is the inclusion primarily of socio-economically disadvantaged, Hispanic and African American participants with T2D. This is the first RCT of its kind to examine the effects of a group-based lifestyle modification intervention in T2D in this kind of population. Hispanics are currently the fastest growing minority group in the United States and have been found to be at particular risk for developing T2D (Ford et al., 2002). How T2D affects Hispanic populations remains understudied and this group has been especially neglected in terms of the efficacy of lifestyle modification interventions for T2D. Moreover, the results of this study conducted on a primarily minority, socioeconomically-disadvantaged population are of particular interest as these individuals are at higher risk for developing more severe diabetes related complications (Roper, Bilous, Kelly, Unwin & Connolly, 2001). A review of the literature by Brown et al. (2004) presents considerable evidence that the socioeconomic status of an individual with T2D influences their risk of mortality and diabetes-related complications, including cardiovascular disease, retinopathy, renal disease, and amputation. More specifically, lower SES has been associated with higher

rates of fatal and nonfatal cardiovascular disease (Dorman et al., 1985; Chaturvedi, Jarrett, Shipley & Fuller, 1998; Robinson, Lloyd & Stevens, 1998), increased risk of microvascular disease (Chaturvedi, Stephenson & Fuller, 1996; Williams, Airey et al., 2004), and overall poorer glycemic control (Weng, Coppini & Sönksen, 2000; Roper et al., 2001) in individuals with T2D. Our research group implemented an intervention that was easy to use and access for these participants was also one of the firsts to include a stress reduction component into the multi-component behavioral modification intervention.

Furthermore, lifestyle modification interventions for individuals already diagnosed with T2D rather than those at risk for developing T2D are scarce. To our knowledge, our study is the first to examine the effects of a lifestyle modification intervention with a stress-management component for those with T2D in a primarily minority population. Another strength of this study was its longitudinal nature. Follow up time points 6 months and 12 months after randomization allowed us to examine the effects of the intervention on stress reduction over time.

This study is limited by its relatively small sample size. In spite of the limited sample size, this study found that individuals who received the lifestyle modification intervention experienced lower levels of stress over time than those in the control group. We also found a relationship approaching significance between reductions in stress and reductions in weight in those who received the lifestyle intervention. As mentioned previously, this relationship is likely to be strengthened with the use of a larger sample size. The present study was also limited by lack of follow-up data beyond the 12 month time point. Therefore, it is difficult to know whether or not reductions in stress were

maintained long-term. However, our findings provide important information about the effects of a stress-management component in a lifestyle modification intervention alongside exercise, diet, and weight loss recommendations for individuals with T2D.

Further research is required to elucidate the association between stress reduction and weight loss using longitudinal research designs with longer periods of follow up and large samples. Additionally, it is important to determine whether the stress reduction component of the intervention was associated with traditional behavioral changes such as increased physical activity and dietary modification.

Chapter 5

CONCLUSIONS

In summary, participants who received the lifestyle modification intervention reported experiencing less stress over time than participants in the control group. However, despite the fact that the lifestyle modification intervention was shown to decrease perceived stress, decrease weight, and lower HbA1c, the decreases in weight and improved glycemic control were not shown to be associated with decreased in perceived stress in the intervention group the control group. However, the relationship between decreases in stress and decreases in weight approached significance in the intervention group but not in the control group, suggesting a possible moderation effect of randomization group that may not have reached significance given the small sample size of this study. Future research is needed in a study with a larger sample size to elucidate the relationships between decreases in perceived stress and change in weight and glycemic control.

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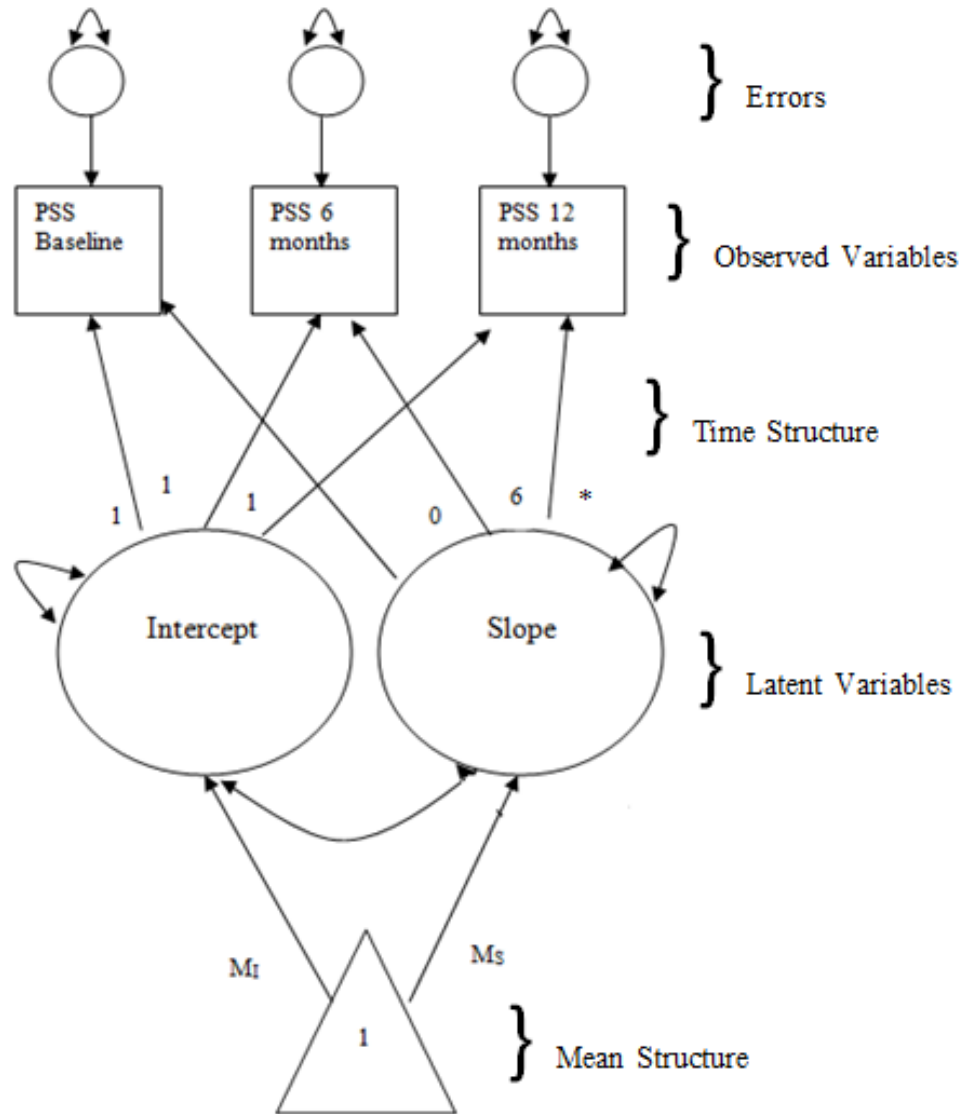
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Table 1. Baseline Sample Characteristics

	Total (N=111)	Control (n=54)	Treatment (n=57)	
	M ± SD / n (%)	M ± SD / n (%)	M ± SD / n (%)	P value
<i>Demographics</i>				
Age, years	54.81 (7.36)	54.84 (8.27)	54.78 (6.34)	.964
Gender, male	32 (28.8)	12(22.2)	20(35.1)	.208
Ethnicity				
Hispanic	94 (84.7)	42 77.78)	52 (91.2)	-
Black	12 (10.8)	7 (13)	5 (8.8)	-
White	5 (4.5)	5 (9.1)	0	-
Household Income, \$	14382 (10832)	14096 (9730)	14674 (1956)	.798
Years of Education	12.46 (3.36)	12.27 (3.57)	12.64 (3.16)	.571
<i>Biological</i>				
HbA1c	7.72 (1.32)	7.67 (1.39)	7.77 (1.23)	.678
Diabetes Duration, yrs	6.89 ± 7.38	7.56 ± 8.43	6.26 ± 6.20	.387
Weight, kgs	85.30 (14.25)	85.04 (12.22)	85.57 (16.19)	.848
BMI	32.59 (4.66)	32.85 (5.54)	32.34 (3.65)	.572
<i>Psychological/Behavioral</i>				
BDI Total Score	20.22 (7.13)	20.31 (7.23)	20.13 (7.10)	.892
PSS	18.85 (8.10)	18.54 (9.15)	19.18 (6.90)	.628

BDI- Beck Depression Inventory; HbA1c- glycosylated hemoglobin; PSS- Perceived Stress Scale
 $\alpha = .05$

Figure 1. Stress reduction growth model



$$\begin{aligned} \text{PSS}@0 &= 1\text{Baseline} + t0\text{Change} + \text{error1} \\ \text{PSS}@6 &= 1\text{Baseline} + t6\text{Change} + \text{error2} \\ \text{PSS}@12^* &= 1\text{Baseline} + t12\text{Change} + \text{error3} \end{aligned}$$

Figure 2. Stress reduction growth model with randomization variable covariate

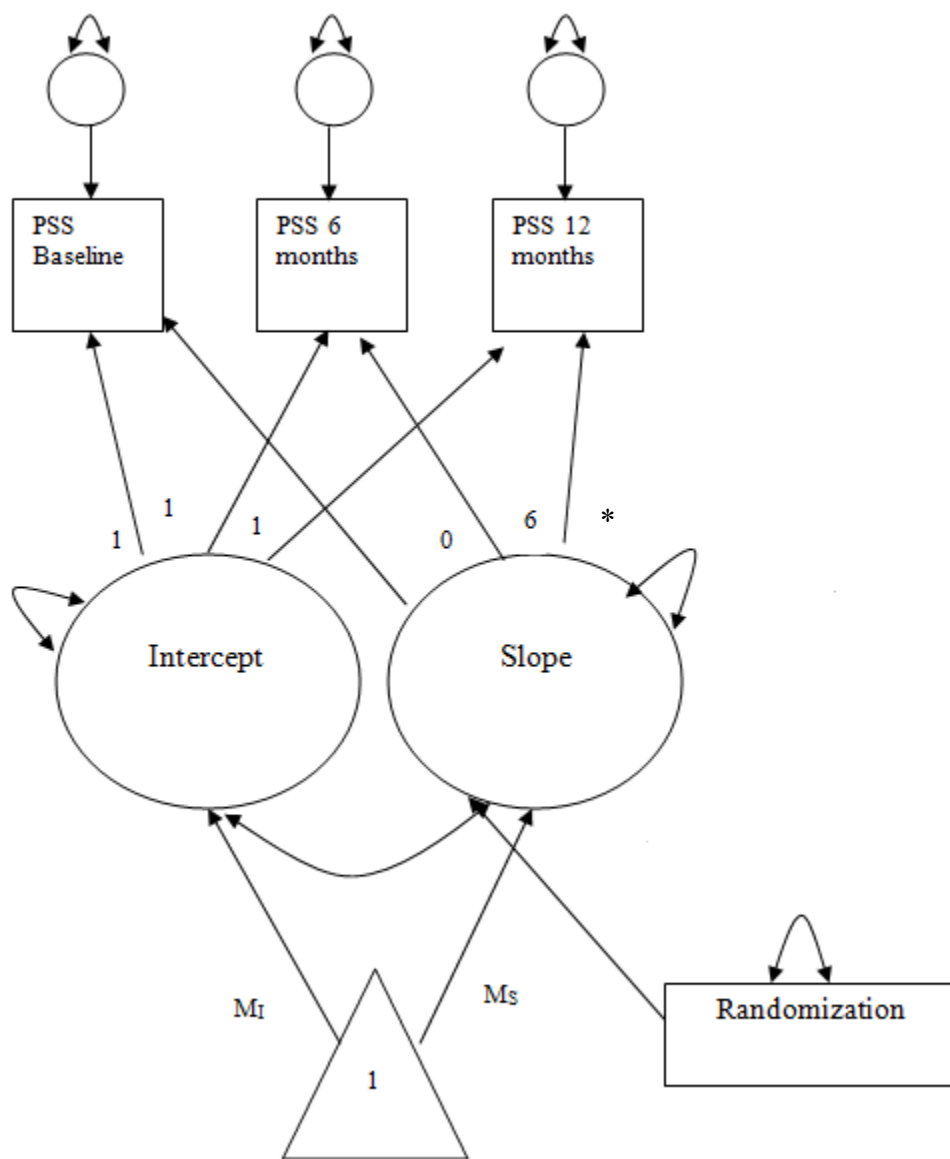


Figure 3. Stress reduction growth model with randomization, age, gender, baseline stress, and baseline depression covariates

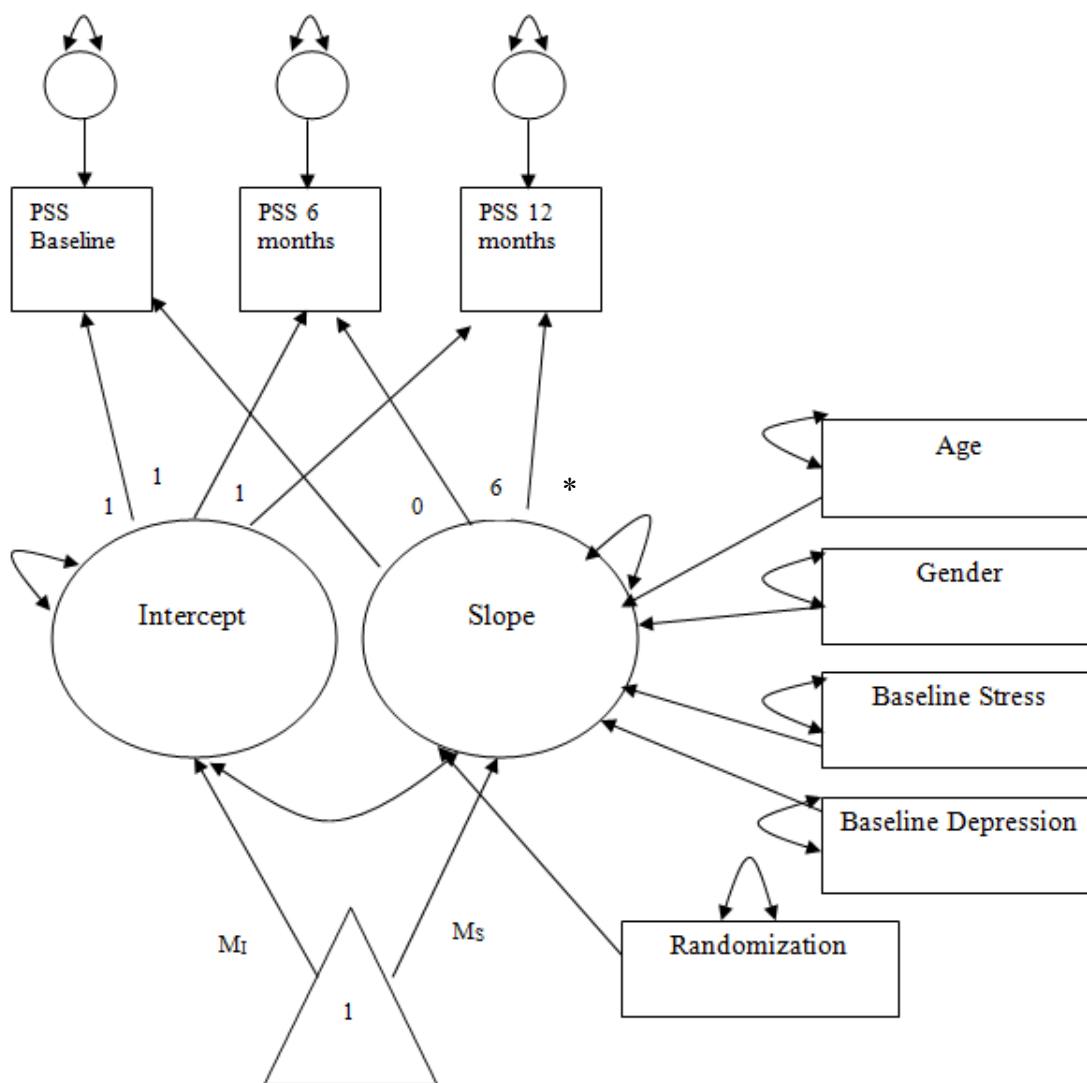


Figure 4. Intervention and Control Means: Perceived Stress

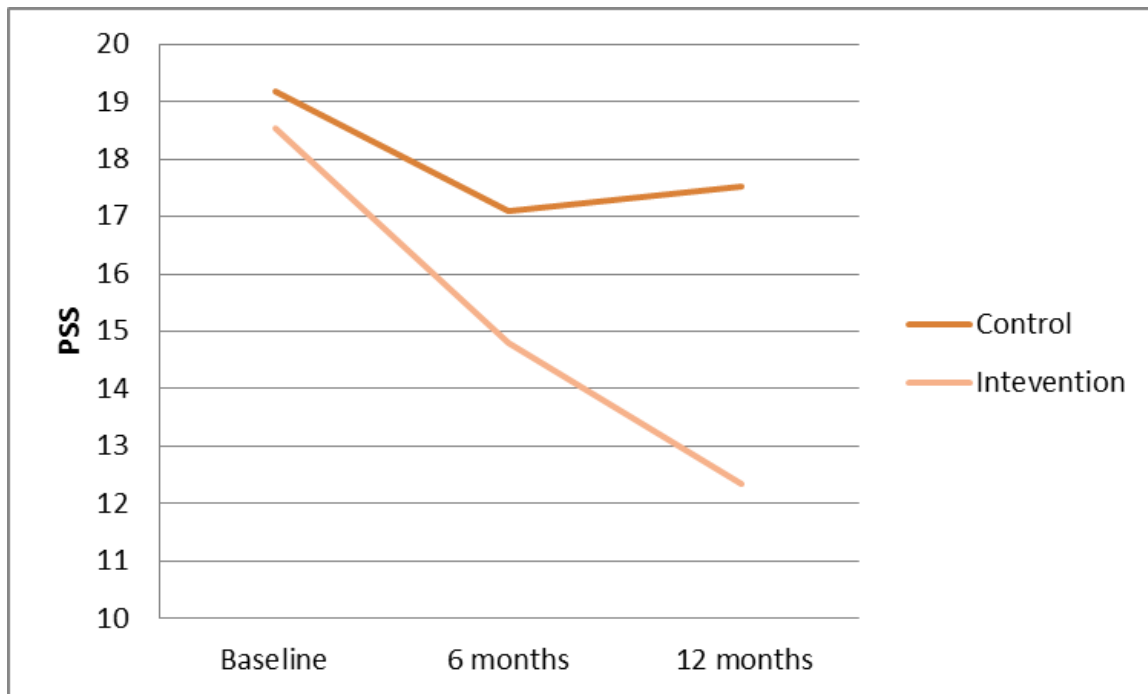


Figure 4 displays mean PSS in at baseline, 6 month, and 12 months for intervention and control participants.

Figure 5. Consort diagram of study participants

