The Influence of Stressful Life Events on the Development of Type 2 Diabetes

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Influence of Stressful Life Events on the Development of Type 2 Diabetes

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A Dissertation Submitted to The Graduate School at the University of Missouri – St Louis in partial fulfillment of the Requirements for the degree
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INFLUENCE OF STRESSFUL LIFE EVENTS ON THE DEVELOPMENT OF TYPE 2 DIABETES
ABSTRACT
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This study examined the relationship between distress and the development of Type 2 diabetes mellitus (T2DM) in the presence of established risk factors. Distress secondary to mental health disparities, stressful life events, and work conditions has been shown to promote insulin resistance and the development of T2DM.

Subjects (N=79) diagnosed with T2DM within the previous six months were recruited from SSM Health Centers and VA Medical Centers in the greater St. Louis area. They completed the Recent Life Changes Questionnaire, ENRICHD Social Support Instrument, and a demographic survey and analyses were conducted to determine differences between the veteran and non-veteran subsamples, as well as determine the influence of distress and social support in the presence the established risk factors of age, BMI, and genetic risk for diabetes.

The average subject’s hemoglobin A1c (HbA1c) was 8.3%, BMI was 34.1, ESSI score was 15, and RLCQ score was 297.6 LCU. Twenty-nine subjects were diagnosed with a mental illness. Age and BMI had significant influence on the development of T2DM for the sample ($\beta=-.241$, $p=.031$ and $\beta=-.293$, $p=0.10$, respectively) while distress was not significant ($\beta=-.040$, $p=.721$). The mean HbA1c for the subgroups were significantly different ($t=2.768$, $p=.007$) The differences in age, BMI ($t=-1.158$, $p=.250$), GRD ($t=-1.279$, $p=.206$), and RLCQ scores ($t=-.487$, $p=.628$) were not significantly different.
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CHAPTER I
INTRODUCTION

Type 2 diabetes mellitus remains a problematic disease of growing proportions due to risk factors such as advancing age, genetic risk for DM, and obesity (Centers for Disease Control and Prevention [CDC], 2011). According to the CDC (2011), T2DM accounted for 90 to 95% of all diabetes cases. In 2012, 29.1 million people – 9.3% of the U.S. population – had diabetes yet only 21 million were diagnosed (CDC, 2014). Half of Americans may develop prediabetes or DM by 2020 (Berkrot, 2010). The CDC (2011) projects that as many as one out of every three people or more in the U.S. may develop DM by 2050. The projected United States population for 2050 is 438 million citizens (Passel & Cohn, 2008). By 2050, 146 million people are expected to be diagnosed with DM.

Total national health expenditure in 2012 was $2.8 trillion dollars (Martin et al., 2014). Diabetes care cost Americans $245 billion in 2012. This cost increased approximately $34.8 billion per year since 2007 (ADA, 2013). In 2050 at the current trajectory of DM care costs, DM care alone will cost Americans over $1.5 trillion dollars.

The average annual cost for healthcare for individuals over 50 years old recently diagnosed with DM was $4,174 greater than someone of the same age without DM between the years 2000 and 2004; this cost increased by approximately $158 per year (Trogdon & Hylands, 2008). Considering the veteran population, the percentage of individuals with diabetes is estimated to be much greater, as approximately 25% of VA patients have been diagnosed with diabetes (U.S. Department of Veteran Affairs, 2015). With nearly 22 million veterans in 2014, the number of veterans with diabetes could be approximately 5.5 million (U.S. Department of Veteran Affairs, 2016). Buddin and Han
(2012) found that DM ranked among the top 10 service-connected disabilities (SCDs) for veterans who began receiving benefits in 2009 (n=23,508; 2.9%).

**Established Influences**

Although genetic predisposition influences the development of T2DM, other factors such as advancing age, exercise, nutrition, and distress also influence the onset of T2DM (American Diabetes Association [ADA], 2004; Guthrie & Guthrie, 2004; LaMonte, Blair, & Church, 2004; Raison & Miller, 2003). The research suggests that genetic predisposition alone may be insufficient to influence the development of T2DM and that other risk factors may need to be present to produce sufficient insulin resistance for a diagnosis of T2DM (Guthrie & Guthrie, 2004; Hamman, 1992).

Since T2DM can occur at nearly any age, the research suggests that lifestyle factors may pose a greater role in the onset of diabetes (DM) than previously suspected (ADA, 2004; Patel & Macerollo, 2010). However, more than 20 years after Wales (1995) stated that the physiological response to stressors is poorly understood, the influence of distress on the development of T2DM remains controversial.

Research has demonstrated a connection between distress and insulin resistance (Chandola et al., 2006; Eriksson, Hilding, Van den Donk, & Ostenson, 2013; Everson-Rose et al., 2004; Heraclides, Chandola, Witte, & Brunner, 2009; Mooy, De Vries, Grootenhuis, Bouter, & Heine, 2000; Novak et al., 2013; Shiloah et al., 2013; Wu, Yang, Thayer, & Andersen, 2014). According to Selye (1976), the state manifested during distress is characterized by increased hypothalamic-pituitary-adrenal (HPA) axis activity and adrenal hormone release. The serum level of cortisol – a glucocorticoid – increases, promotes insulin resistance, and increases blood glucose levels (Chandola, Brunner, &
Marmot, 2006; Innes, Vincent, & Taylor, 2007; McEwen, 2003a). The physiological response to a stressor is in essence what it means to be stressed. As distress influences insulin resistance and insulin resistance leads to the development of T2DM, research indirectly suggests that distress influences the development of T2DM.

**Problem Statement**

Diabetes affects a large portion of society. Despite the extensive research describing the significance of distress to the onset of T2DM, current research fails to adequately describe the influence of distress and its relationship to established risk factors such as aging, family history, and obesity (Chandola et al., 2006; Eriksson et al., 2013; Everson-Rose et al., 2004; Heraclides et al., 2009; Mooy et al., 2000; Novak et al., 2013; Shiloah et al., 2003; Wu et al., 2014). A pilot study was conducted as a precursor to this study to determine how to effectively approach research on the relationship between distress and type 2 diabetes (T2DM) (Minks, 2013).

Examining the relationship among distress, social support, and the development of T2DM, while acknowledging the concurrent risk presented by obesity as indicated by an increased body mass index (BMI), advancing age, and genetic risk for diabetes, could provide a better understanding about the etiology of this multifactorial disease.

**Purpose of Study**

The purpose of the study was to examine the influence of stressful life events, social support, age, body mass index (BMI), and genetic risk for diabetes (GRD) prior to the time of T2DM diagnosis. Stressful life events are limited to six months prior to the onset of diabetes diagnosis in order to further explore the effect of distress. In addition, this
study seeks to determine if there is a difference between veterans and non-veterans for risk of developing T2DM.

**Research Questions**

The research questions guiding this study included:

1. In adults with T2DM, how much distress was present six months prior to the diagnosis of T2DM?
2. What is the individual and combined effect of distress, social support, age, BMI, and GRD on the HbA1c level?
3. In adults with T2DM, what is the difference in risk factors between veteran and non-veteran subjects?

**Definition of Terms**

Definitions reflect variables from the research questions. Theoretical definitions were noted for distress, social support, blood glucose control, BMI, age, genetic risk for diabetes. Operational definitions are also provided in the methods section in Table 1.

**Distress.**

Lazarus and Folkman (1984) theoretically defined distress as harm or loss, threat from anticipated loss, or challenges that pose potential for gain or growth. The theoretical definition of stress considers the impact of environmental demands on an individual’s perception of stressors. Selye (1976) defined stress as the state manifested by a specific syndrome that consisted of all the nonspecifically-induced changes within a biologic system, comparable to McEwen’s (1998) theory of allostasis and allostatic load.

In addition to the distress produced from environmental demands, mental health disorders such as depression can produce distress. Several empirical studies investigated
the effect of distress on insulin resistance and T2DM in terms of depression (Eaton, Armenian, Gallo, Pratt, & Ford, 1996; Everson-Rose et al., 2004; Khambaty, Callahan, & Stewart, 2018; Palinkas, Lee, & Barrett-Connor, 2004; Vrany, Berntson, Khambaty, & Stewart, 2016).

For the purpose of this study, distress caused by stressful life events was operationally defined as a total score on the RLCQ (See Appendix A). The RLCQ is a 73-item survey that measures the degree of distress in terms of life change units (Miller & Rahe, 1997).

**Social Support.**

Social support is conceptually defined as the availability of people, groups, or organizations that an individual can refer to when in need (Vaglio et al., 2004). The availability of such factors can influence how an individual responds to a stressor (Roy & Andrews, 1999). Lack of social support can be identified as attachment insecurity and individuals can have heightened reactivity to stressors and deficits in their regulation of emotions (Diamond & Fagundes, 2010). The pro-inflammatory response and depression that can result from low social support can influence known risk factors for T2DM, including gene expression and obesity (Kiecolt-Glaser, Gouin, & Hantsoo, 2010).

For the purpose of this study, social support was operationally defined as a total score on the ESSI (See Appendix B). The ESSI is a seven-question survey that assesses social support (Vaglio et al., 2004).

**Body mass index.**

An individual’s body mass presents potential risk for the development of T2DM (ADA, 2004). The conceptual definition of BMI is an individual’s weight in proportion to
the individual’s height (Keys, Fidanza, Karvonen, Kimura, & Taylor, 2014). For the purpose of this study, BMI was operationally defined by calculating the BMI. The formula for BMI calculation is: weight in kilograms (kg) divided by height as meters (m) squared or kg/m\(^2\) (Keys et al., 2014).

**Age.**

Age is considered a risk factor for T2DM (ADA, 2004). However, Hamman (1992) argued that the risk associated with age is actually a result of weight gain secondary to sedentary activity that occurs with aging. Another commonly used name for T2DM, adult-onset diabetes, acknowledges the relationship between age and T2DM (ADA, 2004). The conceptual definition of age is the incremental change in time as it relates to an individual’s lifespan. For the purpose of this study, the operational definition of age was the subject’s chronological age in years at the time of diagnosis as noted on the demographic survey (See Appendix C).

**Genetic risk for diabetes.**

Researchers have identified T2DM as a genetic disease (ADA, 2004; Patel & Macerollo, 2010; Guthrie & Guthrie, 2004; Hamman, 1992). For the purpose of this study, GRD is conceptually defined as a family history of diabetes posing genetic risk for the development of the disease (ADA, 2004). Genetic risk for diabetes was operationally defined as the subject answering yes in response to the demographic survey question: “Do you have a parent, grandparent, or sibling with diabetes?” (See Appendix C).

**Blood Glucose Control.**

Blood glucose control is determined by an individual’s blood glucose levels. Individuals may be diagnosed with prediabetes or a category of increased risk, such as
the presence of a fasting glucose 100 to 125mg/dL or an HbA1c between 5.7% and 6.4% (Patel & Macerollo, 2010). Blood glucose control is conceptually defined as the degree of variance between glucose levels and insulin concentrations with higher variance meaning less control. For the purpose of this study, blood glucose control was operationally defined by results of an HbA1c laboratory test.

**Development of Type 2 Diabetes.**

The variance between glucose levels and insulin concentrations may take time to develop until a sufficient number of risk factors are present (Hamman, 1992). For the purpose of this study, the term development refers to the period of time immediately preceding the diagnosis of T2DM where a sufficient number of risk factors are present.

**Diagnosis of Type 2 Diabetes.**

Type 2 diabetes mellitus is diagnosed by an HbA1C greater than or equal to 6.5% (Patel & Macerollo, 2010; NIH, 2008; World Health Organization [WHO], 2011). For the purpose of this study, the term diagnosis refers to the point in time when a provider identifies a patient as having T2DM.

**Justification for the Study**

The number of people with diabetes is only expected to increase. The impact diabetes has on the general population present a clear indication for continued research efforts to determine the influence of risk factors to developing T2DM for effective prevention, treatment, and, particularly, cost control.
Assumptions

The theories proposed by Selye (1976), Lazarus and Folkman (1984), and McEwen (1998) provided assumptions relevant to the study. The assumptions are divided into respective sections, starting with Selye’s (1976) GAS. Assumptions from the GAS included:

1. Stress is a specific state resulting from a syndrome.
2. The amount of adaptability an individual possesses is finite.
3. Diabetes (DM) is not always due to an insufficiency of insulin formation (p. 266).
4. Overwhelming stress can breakdown the body’s protective mechanisms.
5. Poor adaptation influences the development of disease.
6. Each individual responds uniquely to stress due to inherited health-related factors and characteristics acquired from interaction with the environment.

Assumptions pertaining to Lazarus and Folkman’s (1984) stress, appraisal, and coping theory included:

1. An individual’s experiences with various stressors influence that individual’s perception of new stressors.
2. Familiar types of stressors pose little to no distress to an individual while unfamiliar stressors can pose much greater distress.
3. An individual’s perception of a stressor influences that individual’s options for adapting to the stressor.
4. Stakes such as commitments to others and spiritual beliefs influence an individual’s perception of a stressor.
5. Distress can increase if an individual is unable to control the development of an outcome.

6. Distress can increase if an individual is uncertain of the consequences posed by a stressor.

7. Factors such as the time available to appraise stressors and repetition of stressors can influence distress.

8. The ability to cope with stressors is constantly changing and uses a combination of unconscious and conscious processes in response to the perception of a stressor.

Assumptions pertaining to McEwen’s (1998) theory of allostasis and allostatic load included:

1. Complex neuroendocrine processes stimulate a combination of biological changes in response to a stressor.

2. Multiple stressors require greater demands on the neuroendocrine system to stimulate specific biological changes in response to the respective stressors.

3. The overactive response of the neuroendocrine system can increase the risk for the development of diseases such as T2DM.

Assumptions related to the data collection process and the design of the study were:

1. Subjects are honest.

2. Subjects are able to recall events from the previous six months.

3. Subjects can complete the surveys at the clinic where they receive care during a face-to-face interview or by telephone.

4. Subjects speak English.

5. Subjects understand that the term diabetes is not diabetes insipidus.
6. Hemoglobin A1c is a reasonable way to measure an individual’s level of insulin resistance secondary to chronic stress.

Delimitations

The study was limited to adults 18 years or older, excluding pregnant women, residents of prisons or mental institutions, and the mentally handicapped. The adults were diagnosed with T2DM within the previous six months and received diabetes care services from hospitals or clinics within the greater area of St. Louis County, including SSM Health and Veterans Affairs (VA) facilities.

Kang, Rice, Park, Turner-Henson, and Downs (2010) warn that the framework doesn’t recognize the influence of multiple coexisting acute stressors. Retrospective analysis of acute stressors poses unique challenges as a subject’s accuracy in recalling daily stress loads occurring prior to the diagnosis of T2DM, and the investigator’s interpretation of such data, could compromise the results.

The investigator recognizes that the recall timeframe for subjects diagnosed with T2DM up to six months prior to the day of the interview is much longer than subjects diagnosed with T2DM less than a week prior to the day of the interview. Subjects recalling events and support six months prior to a diagnosis of T2DM given six months ago have a greater recall timeframe that could impact their results on the RLCQ and ESSI.

Although social support was evaluated, discussing the coping methods of the subjects was beyond the scope of the study. Because the literature indicated a great degree of complexity regarding appraisal and neuroendocrine response mechanisms, the investigator did not attempt to determine specifics regarding the nature of physiological
mechanisms promoting the development of T2DM (Lazarus & Folkman, 1984; McEwen, 1998; Selye, 1976).

Summary

Despite the known influence of genetic predisposition and environmental factors, T2DM remains a complex disease of multifactorial origin (Hamman, 1992). Individuals with known (or established) risk factors may not develop T2DM. The lack of disease in individuals with established risk factors suggests that other contributing factors must exist.

Many stressors encountered on a daily basis influence the stress response through the activation of the HPA axis (Selye, 1976). Chronic activation of the HPA axis – resulting in constant elevated levels of cortisol – promotes the risk for T2DM (Innes et al., 2007; Kendall-Tackett, 2009; McEwen, 1998). The association between distress and the HPA axis promoting insulin resistance suggests that T2DM may result from ineffective coping in response to distress in the presence of established risk factors.

The problem in determining if distress influences the onset of T2DM is that individuals respond to stressors differently (Shiloah et al., 2003; Wales, 1995). Not to mention, each time a specific stressor occurs, the individual may respond differently in terms of the secondary appraisal as a result of past experience with the stressor (Lazarus & Folkman, 1984). Understanding the influence of distress on the development of T2DM remains a pertinent challenge for further examination.

Several assumptions and limitations regarding the theories developed by Selye (1976), Lazarus and Folkman (1984), and McEwen (1998) and the data collection process formed the foundation for the study. Three research questions were posed.
With the projected healthcare cost of diabetes management alone in 2050 being over $1.5 trillion, further research is needed to better understand the etiology of T2DM. Understanding the relationship of distress and coping with established risk factors such as obesity and familial history of diabetes could improve prevention and treatment measures, as well as reduce the projected expenditure for diabetes management.
CHAPTER II
REVIEW OF THE LITERATURE

The influence of distress on insulin resistance and type 2 diabetes (T2DM), as well as concepts about stress and coping, are reviewed in the literature. Literature regarding glucocorticoids (GCs), insulin resistance, metabolic syndrome, and specific forms of distress such as depression, strain from work demands, and traumatic life events support the plausibility of distress as a risk factor for T2DM. The literature review included theoretical and empirical literature.

Pathophysiology of Stress

Selye (1976) stated that glucocorticoids (GCs) help cells adapt to stressors by preventing excessive cellular activity, which decreases energy demands. The sympathetic nervous system (SNS) and cellular stimulation trigger the stress response. Innes et al. (2007) identified the SNS as the central stimulus of the stress response secondary to the central secretion of catecholamines such as norepinephrine and epinephrine. The SNS responds to an individual’s perception – negative appraisal – of a stressor that triggers the stress response. Selye (1976) stated that cells outside the central nervous system (CNS) could also stimulate a stress response. He identified the stimulant as an alarm signal; injured or strained cells stimulate a stress response to support effective adaptation to inflammation.

Straub, Dhabhar, Bijlsma, and Cutolo (2005) studied the use of dexamethasone to describe the balance between pro-inflammatory and anti-inflammatory factors. Where their research focused on levels of GCs in relation to the immune response, it also indicates that a stress response resulting in elevated levels of GCs influences blood glucose levels.
Selye (1976) argued that distress is the common denominator for all adaptive reactions in the body. When the conceptual model with the physiological components that generate the stress response – limbic system, hypothalamus, pituitary, and adrenal glands – is considered, Selye’s comment becomes clearer.

The hippocampus and amygdala, parts of the limbic system, influence emotional responses to distressing stimuli (Dedovic, Aguiar, & Pruessner, 2009). The limbic system contains memories and life experiences that trigger neuroendocrine response from the hypothalamus down the cascade known as the hypothalamic-pituitary-adrenal (HPA) axis (Fava, 1994; Innes et al., 2007). Ultimately the HPA axis results in the release of cortisol (Innes et al., 2007; Selye, 1976). McEwen (1998) identified this neuroendocrine process as allostasis. Distress stemming from negative perceptions, lifestyle choices, and general health can have considerable influence on cortisol secretion and glucose management.

Delaunay et al. (1997) demonstrated that GCs directly influence insulin production from β cells in the pancreas of transgenic rats. Their research suggests that GCs produced by the stress response can influence blood glucose levels. Allostasis becomes quite complex as GCs influence insulin resistance and insulin production. The progressive research on the relationship between steroids and insulin resistance may promote greater understanding.

Early studies examined exogenous glucocorticoid-induced insulin resistance (Owen & Cahill, 1973; Pagano et al., 1983). In 1951, Kinsell et al. identified a potential relationship between GCs and insulin resistance, noting the suppression of fasting-induced hyperketonemia and ketonuria secondary to exogenous steroids in subjects without endocrinopathies (as cited in Owen & Cahill, 1973). Owen and Cahill (1973)
demonstrated that twice daily injections of cortisone (an exogenous glucocorticoid) increased blood glucose levels within six days while subjects fasted. The data suggest that increased levels of GCs can increase blood glucose levels.

Recognizing the influence of exogenous steroids such as cortisone, endogenous GCs must follow suit and influence blood glucose levels similarly. Distressing non-work and work-related factors influence the stress response and the resulting impact on insulin resistance, a defining characteristic of T2DM.

**Psychological Stress and Diabetes**

Mooy et al. (2000) determined that an increasing number of non-work related stressful life events remained significantly correlated with a diagnosis of T2DM after adjusting for a family history of DM, physical activity, heavy alcohol consumption, and a low level of education ($OR=1.7 \ [1.0-2.7], p<0.05$). After adjusting for age and sex, the odds incrementally increased by roughly 20% for each additional non-work event such as death of a child, friend, partner, or relative ($OR=1.2, CI=1.1-2.5, p<0.05$). Acute psychotic distress has also been associated with hyperglycemia and hyperinsulinemia (Shiloah et al., 2003).

During an eight year study, depression was associated with higher non-fasting plasma glucose levels ($p=0.001$) and risk for T2DM ($OR=2.5, 95\% \ CI \ [1.29-4.87]$) while controlling for BMI, sex, and age (Palinkas et al., 2004). Everson-Rose et al. (2004) found that insulin resistance increased annually for depressed women and that African American women had greater risk for T2DM secondary to depression after controlling for established risk factors ($OR=2.56, p=0.008$). During a nine-year study on the effect of collaborative depression treatment and risk for diabetes, a third of the sample ($n=39$)
developed diabetes (Khambaty et al., 2018). Work stress in the form of high demands and low control increased the risk for T2DM nearly twofold in civil service workers after controlling for age, employment grade, health behaviors, BMI, blood pressure, and cholesterol and C-reactive protein levels ($OR=1.98$, 95% CI [1.14-3.44]; Heraclides et al., 2009).

The impact on veterans may be much greater as they experience not only strain associated with family and work demands, but the potential strain associated with traumatic events that potentially conflict with their individual personalities. The veteran demographic at greatest risk for diabetes are older men with psychiatric disorders such as post-traumatic stress disorder (PTSD) from combat or other trauma (Haas & Watts, 2005). As distress promotes insulin resistance and remains a risk factor for metabolic syndrome, insulin resistance poses a risk for T2DM (Chandola et al., 2006; Vrijkotte, Van Doornen, & De Geus, 1999).

Although primary appraisal of stressful stimuli can trigger a stress response, the response depends on the secondary appraisal in terms of resources and individuals perception of their ability to adapt, as indicated by Lazarus and Folkman (1984); consequently, the degree of influence from the stressful stimuli is difficult to measure and unique to the individual experiencing the stressor. Variables other than an individuals’ adaptability to stressful stimuli include selecting control groups for comparison and not being able to apply results across sociocultural barriers (Wales, 1995). Despite these valid concerns as they relate to measuring the influence of a single stressor, generalizations regarding the cumulative impact of distressing factors according to McEwen (2003a) can be more meaningful than identifying a specific stressor. Identifying that an individual is
experiencing significant distress is more meaningful in terms of health consequences than determining the impact of a specific stressor.

An individual’s perception of available measures for adaptation evolve from individual experiences with stressors. Huxley stated that “Experience is not what happens to a man; it is what a man does with what happens to him” (1933, p. 5). Although likely intended to be more poetic, Huxley acknowledged the significance of an individual’s perception of an event. Exposure to comparable events influence the perception of life experiences can intensify or suppress the outcome of a stress response. The inherent strain from the stress response can be cumulative in effect (Selye, 1976). Recognizing the meaning of Selye’s (1976) remark, responding to various concurrent stressors can have harmful physiological consequences if an individual is unable to successfully adapt to distress. McEwen (1998) expands on this concept with his theory on allostasis and allostatic load. The unresolved stressors remain as in stasis with their independent physical demands. As new stressors arise, the physical demand for coping increases and puts greater strain on the body.

Miller and Rahe (1997) identified the influence of positive and negative experiences using the Recent Life Changes Questionnaire (RLCQ). Life events such as adopting a child or losing a child can cause distress. Regardless of whether the individual has something to gain such as more income or lose such as a loved one, the individual’s appraisal of the situation will influence the stress response. To understand the potential impact of distress on the development of T2DM, Mooy et al. (2000) determined that the death of partner or moving from a house significantly correlated with the development of
T2DM in subjects after adjusting for age and sex (*OR*=1.9, *p*<0.05 and *OR*=1.6, *p*<0.05, respectively).

“Although the predisposition to DM is inherited, the onset depends on how the body responds to distress as a latent diabetic tendency develops into the disease” (Selye, 1976, p.266). Determining the influence of perceived stress on the development of T2DM establishes a more definitive understanding of the extent of environmental influence. As distress may potentiate the impact of known risk factors for T2DM, identifying the potential influence that distress has on the development of T2DM could help healthcare providers in the prevention and treatment of T2DM. Memories and life experiences influence an individual’s ability to adapt to adversity. In turn, memories and life experiences influence neuroendocrine regulation.

**Conceptual Framework**

The investigator-designed conceptual model comprises the risk factors that pose risk for the development of T2DM (See Figure 6). A compilation of Selye’s (1976) General Adaptation Syndrome (GAS) and Roy’s Adaptation Model (RAM) as described by Roy and Andrews (1999) were used for the conceptual framework of the pilot study preceding this study. Considering the variances among subjects with similar stressful life events, the relationship between stressors and individual responses to those stressors appears more complex than previously considered. Where the biological mechanisms of the stress response according to Selye are still applicable, adaptation according to Roy is limited in explaining how an individual’s past experiences influence the perception of stressors, as well as the cumulative effect of stressors on the stress response.

Further analysis of the literature related to stress and coping in nursing research presented non-nursing theories that are more suitable for research on the stress response.

The GAS emphasizes an individual’s biological response to strain while acknowledging an individual’s unique perception of that strain (Selye, 1976). According to Selye (1976), the state manifested during stress is characterized by increased HPA axis activity and adrenal hormone release. The serum level of cortisol, a glucocorticoid, increases, promotes insulin resistance, and increases blood glucose levels (Chandola et al., 2006; Innes et al., 2007; McEwen, 2003a).

Perception is influenced by an individual’s appraisal of the strain. According to Lazarus and Folkman (1984), primary appraisals determine whether that strain is benign, either warranting no need to worry or potentially enhancing an individual’s well-being, or poses risk for harm, loss, threat, or challenge. When significant life events occur, they can present (a) considerable damage to an individual’s physical and or emotional well-being; (b) anticipatory losses as a result of consequences for intended or unintended actions; (c) a sense of danger when values and goals appear to be in jeopardy, and or (d) potential for personal or professional gain at the risk of greater demands on outcomes.

Appraisal is two-fold. First, an individual must determine if the stressor is considered to be a threat or challenge; second, the individual must evaluate all the possible methods for adaptation. The individual must determine if each method can be successfully applied to meet the perceived needs of the stressor (Lazarus & Folkman, 1984). Relatively mild stressors experienced by a large number of individuals can be
exponentially greater in terms of strain for individuals that perceive high stakes at risk with the same stressor. “Even if they have considerable power to control the outcome, any doubt [in an individual’s ability to successfully adapt to a stressor] can produce considerable stress” (Lazarus & Folkman, 1984, p. 35).

As several factors in the appraisal process influence the physiological process of a stress response, opposing endocrine hormones such as aldosterone and cortisol influence the intensity of the stress response (Selye, 1976). Selye (1976) identified cortisol secretion as the adaptive mechanism for effective coping. The GAS being the biological response to a stressor (See Figure 1).

The alarm stage begins with a trigger that stimulates cells to send a signal to the hypothalamus. Considering the process of stress and coping according to Lazarus and Folkman (1984), the alarm stage is comparable to the primary appraisal phase, deeming a
stressor as a threat or a challenge. When a stressor is determined to be a threat or challenge, the hypothalamus secretes corticotropin-releasing hormone (CRH) to activate the stress response via the HPA axis (Selye, 1976).

The stage of resistance is fundamental to adaptation in the GAS. The stage of resistance occurs when a suitable concentration of cortisol suppresses an over-reactive response to the stressor (Selye, 1976). Despite the cognitive-degree of reasoning that occurs to evaluate a stressor of physical or psychological origin, the physiological response to the stressor remains the same. Regardless of the necessity for such a response, the HPA axis leads to the production of cortisol, which enhances cardiovascular function, helps regulate fluid volume levels, and promote mobilization of glucose stores (McEwen, 2003b). The process of appraisal coupled with the GAS presents the interaction between psychological and physiological mechanisms that contribute toward adaptation. The stage of resistance may occur during the process of the secondary appraisal until the initiation of the chosen method of adaptation.

The stage of exhaustion indicates that resistance or adaptation is no longer possible as cellular death occurs (Selye, 1976). In the case of chronic stress, cells exposed to cortisol for an excessive period of time prematurely die as a result of cellular apoptosis (Sapolsky, 2004). The stage of exhaustion may occur if the chosen method of adaptation does not result in resolution of the stressor.

In addition to the three stages of the GAS, Selye (1976) described three components of disease manifestation: the stressor, the forces of resistance, and the forces of submission. Disease manifestation is dependent upon the intensity, sequence of action, systemic influence, and the relative proportions of these components. Regarding
intensity, Selye (1976) stated that the ability to cope with the stressor is more significant than the intensity of the stressor.

In regards to coping and the forces of resistance and submission, Lazarus and Folkman’s (1984) description of an individual’s commitments and beliefs could be representative of Selye’s concepts of resistance and submission. If a stressor threatens a commitment such as a relationship with a partner or friend, a stressor poses greater strain. As Lazarus and Folkman (1984) put it, an individual is more vulnerable to psychological stress from the deeper the commitment and the greater the potential for threat or harm (p. 58). The degree of commitment related to the stressor could be a force of resistance that motivates an individual to devote greater effort to pursuing a successful method of adaptation. On the other hand, a deep commitment could present greater risk for hopelessness and despair if an individual believes that no method of adaptation would be sufficient.

Beliefs can regard premises of faith, hope, and a loci of control. Primary and secondary appraisals can be influenced considerably by an individual’s beliefs (Lazarus & Folkman, 1984). For example, when an individual possesses a high degree of experience or knowledge about a phenomenon of interest, the individual is more cautious of another’s beliefs that present conflicting experience or knowledge. The stressor poses little strain and the primary appraisal of the stressor is likely to be benign rather than threatening. However, if belief is lost, hope can change to hopelessness and present considerable strain from a threatening stressor (Lazarus & Folkman, 1984).

Regarding the loci of control, the secondary appraisal of a stressor is influenced by whether the individual believes he or she has control over events – internal locus of
control – or believes control is left to God or fate – external locus of control. An internal locus of control can present greater strain from an undesirable outcome and guilt that may result from an individual’s belief that he or she should have been able to control the outcome (Lazarus & Folkman, 1984; Roddenberry & Renk, 2010; Sapolsky, 2004; Shupe, 1985). Although undesirable outcome can present greater strain for individuals with an internal locus of control, those individuals are less likely to cope by avoiding stressors than individuals with an external locus of control (Chung, Preveza, Papandreou, & Prevezas, 2006).

The forces of resistance or submission could represent the individual’s perception of the stressor depending on whether the individual previously experienced or understood the significance of the stressor. The individual’s past experience with similar stressors, if any, would in turn influence the individual’s perception of the current stressor. According to Selye (1976), an individual’s ability to cope with stressors is influenced by the events experienced in the individual’s life. The experienced events influence the individual’s perception of the stressor and physiological response to the stressor.

As noted in Figure 2, the stress response is mediated through two pathways, the endocrine system and the nervous system (Selye, 1976). The endocrine system acts through the HPA axis to produce cortisol. The nervous system bypasses the HPA axis and glandular activity during the stress response. Adrenaline and acetylcholine produced by nerve endings act antagonistically in response to stress. For example, adrenaline stimulates a hypertensive response to a psychological stressor producing feelings of agitation while acetylcholine suppresses the hypertensive response (Selye, 1976).
Figure 2. A psychological stressor stimulates the stress response through the endocrine and nervous system pathways. At each level of tissue stimulation (pituitary, nerves, adrenal glands, liver, etc), conditioning factors may support or suppress the neuroendocrine response to distress (Selye, 1976, p. 151). Printed with permission for educational purposes.
The stressor may have a specific or non-specific influence (Selye, 1976). A specific stressor could be a localized injury such as an ankle sprain while the non-specific stressor could be a systemic infection. Apart from the unique consequences posed by either stressor, the resulting stress response depends upon the number of cells affected by the stressor and the individual’s perception of the stressor (Selye, 1976).

Unique contextual factors can also influence primary and secondary appraisals. Primary appraisals can be influenced by an individual’s experience with the stressor or a comparable stressor; predictability of a stressor, warning signs prior to a reoccurring stressful event produce less strain; event uncertainty, different from predictability, can produce strain as individual’s anticipate a stressor that may not occur; and temporal factors such as imminence and duration of a stressful event influence the complexity and intensity of an appraisal process as an individual may have too much or too little time to consider the impact of a stressor with acute or chronic intermittent consequences (Lazarus & Folkman, 1984). Pending the imminence of a stressor, secondary appraisals consider the efficacy of each method of adaptation may be evaluated for difficulty in implementation of a method, extent to which a method can produce specific outcomes or present other consequences, and the likelihood of a method to resolve the stressor (Lazarus & Folkman, 1984). Considering the various types of stressful life events and day-to-day stressors in relation to an individual’s ability to appraise the stressors and each possible method for adaptation, the process of coping presents considerable complexity.

Although the appraisal process – primary and secondary appraisal – suggests a simple algorithm for determining a method for adaptation, the process is far more complex. Each method for adaptation can consist of multiple factors that are relevant to
the stressor. Factors can include how an individual’s desired outcome interacts with the immediate environment, as well as subconscious agendas. An individual may be unaware of subconscious agendas that influence the individual’s appraisal of the stressor (Lazarus & Folkman, 1984). The immediate environment with factors such as support systems like church or interest groups, familial behaviors that influence an individual’s lifestyle choices, and social interactions with family, friends, or partners that result in unique experiences can guide the stress response toward an adaptive or maladaptive response.

Stressors resulting from significant personal events may produce a prolonged rise in serum cortisol dependent on an individual’s ability to adapt to each of the events (Mooy et al., 2000). Limited social support and ineffective coping may allow distress to endure. Prolonged distress can permit persistent elevated serum cortisol levels. If serum cortisol levels remain elevated, insulin resistance and T2DM can result (Cheung & Li, 2012; Everson-Rose et al., 2004; Hankonen, Absetz, Haukkala, & Uutela, 2009; Heraclides et al., 2009; Mooy et al., 2000; Novak et al., 2013; Uchida et al., 2012; Vrijkotte et al., 1999).

Several of the studies suggest that the frequency of stressors can be as concerning as the intensity of stressors. Lazarus and Folkman (1984) identify the variance as acute, time-limited stressors and chronic intermittent or continuous stressors. The occurrence of one or more acute, time-limited stressors coupled with chronic intermittent or continuous stressors is tantamount to what an individual may experience in life. As Kang et al. (2010) indicated, Dr. Bruce McEwen provides an exceptional description of the cumulative effects of stress and stress adaptation in the stress, allostasis, and allostatic load model.
When stressors occur, whether benign or threatening, allostatic responses initiate adaptive processes to cope with stressors via physiological mediators such as glucocorticoids. According to Sterling and Eyer (1988), allostasis is essentially “maintaining stability through [physiological] change” (as cited in McEwen, 2003b, p. 10). The process of allostasis is synonymous with the mediator pathways described by Selye (1976), adaptation triggered by the hypothalamus as part of the HPA axis.

Allostatic responses trigger physiological changes to stressors and as with other mechanisms in the body that respond to demand, greater or sustained change is needed with greater demands. Allostatic load is the cost of adaptation and can lead to pathophysiological consequences if mediators such as glucocorticoids are not efficiently terminated (McEwen, 2003b; McEwen, 1998). Selye (1976) identified the correlation between overwhelming stress, such as the stress posed by worrying, and pathophysiological consequences. In some cases overwhelming stress can even lead to death (Sapolsky, 2004).

McEwen (1998) describes four paradigms associated with allostatic load: frequent stress, repeated stressors of the same type with inefficient adaptation, stressors that cease while allostatic responses persist, and stressors that trigger primary allostatic responses requiring assistance from secondary adaptive mechanisms (see Figure 3). In any of these paradigms, the cost of adaptation includes elevated hormone levels such as epinephrine and cortisol, which are intended to mobilize glucose for a fight-or-flight response to the stressor (McEwen, 2003b; McEwen, 1998; Sapolsky, 2004). Whether the stressor is physical in nature such as aerobic activity or psychological in nature such as the loss of a loved one, an individual mounts the same biological response with varying degrees of
intensity. The intensity of the biological response is influenced by an individual’s appraisal of the stressor (Lazarus & Folkman, 1984). When the total cost of adaptation from stressors over time exceed physical tolerance, pathophysiological consequences such as hypertension and atherosclerosis can occur (McEwen, 2003b).

Figure 3. Frequent stress represented by repeated hits; repeated stressors of the same type with inefficient adaptation represented by lack of adaptation; stressors that cease while allostatic responses persist represented by prolonged response; and stressors that trigger primary allostatic responses requiring assistance from secondary adaptive mechanisms represented by inadequate response. Reproduced with permission from New England Journal of Medicine, Copyright Massachusetts Medical Society.
Combining Selye’s (1976) GAS, Lazarus and Folkman’s (1984) TMS, and McEwen’s (1998) Allostasis Theory creates a conceptual model that identifies essential principles of the stress response. Selye’s (1976) GAS represents the physiological response to stressors. Lazarus and Folkman’s (1984) cognitive appraisal model identifies uniquely human psychological processes in interpreting stressors, the degree of strain if any presented by the stressors, and the possible adaptation measures that could be used to respond to the stressors. McEwen’s (1998) theory of allostasis and allostatic load presents a key component as it represents the phenomenon of chronic stress.

Physiologic changes in the short-term during acute stress are meant to be adaptive. When acute stressors such as running from an attacker, escaping a burning building, or competing in a triathlon occur, elevated levels of hormones such as cortisol and epinephrine promote adaptation. However, these physiologic changes are not meant to be prolonged.

Unfortunately, the human body’s response to chronic stress is the same as the response to acute stress. The human body is not designed to run a triathlon for several weeks, let alone months to years. Persistent, unrelenting strain from any combination of stressors ranging from life changing events such as retirement or a new addition to a family dynamic to being a low-income, single parent raising children with special needs can provoke prolonged physiologic changes that are harmful. As Selye (1976) emphasized, “no disease solely results from maladaptation; however, the onset of many diseases is facilitated by derangements of adaptive mechanisms” (p. 298). Elevated glucose levels posing risk for the development of T2DM is no exception. Regardless of
genetic risk for diabetes, maladaptive responses to stress pose considerable influence on the development of T2DM (Selye, 1976).

Theoretical Literature

Roy, a nurse theorist, stated that the integrity of endocrine function has significant influence on the human body (Roy & Andrews, 1999). She associated endocrine diseases with glandular dysfunction or failure of target cells to respond to specific hormone(s). Roy considered T2DM to be due to unresponsive target cells to insulin (Roy & Andrews, 1999). Endocrine diseases strictly resulted from cellular damage or genetic predisposition. Elevated GCs only indicated pronounced regulator activity, a sign of adaptation difficulty or ineffective coping (Roy & Andrews, 1999).

The literature regarding Roy’s Adaptation Model (RAM) and T2DM is limited to coping with T2DM rather than the prevention of T2DM or other diseases (Roy & Andrews, 1999). However, RAM indirectly suggests that an adaptive response to stressful stimuli prevents insulin resistance as pronounced regulator activity is avoided. The regulator activity presents the neuroendocrine response to the stressor. Minimal regulator activity results in minimal to no secretion of GCs.

Selye (1976) also noted the influence of endocrine function on the body’s protective mechanisms. An overwhelming stressor such as worry was noted to have the ability to breakdown the body’s protective mechanisms; the resulting breakdown potentially causing the development of diseases such as T2DM. Sapolsky (2004) addressed multiple outcomes from excessive cortisol secretion ranging from gastrointestinal complications to the interruption of sensitive immunological and memory processes.
Selye’s General Adaptation Syndrome (GAS) and RAM identified the hypothalamus as the starting point in the endocrine pathway of the stress response (Roy & Andrews, 1999; Selye, 1976). The hypothalamus is the pivotal point of HPA axis activation in response to neuroendocrine factors from the limbic system (Dedovic et al., 2009; Innes et al., 2007). The primary influences from the limbic system include the amygdala and the hippocampus (Dedovic et al., 2009; Innes et al., 2007). Fear-related conditioning and behaviors are characteristics of the amygdala, while the hippocampus is central to learning, memory, and activation of the HPA axis (Innes et al., 2007). Dedovic et al. (2009) suggested that the amygdala potentiates HPA axis activity while the hippocampus suppresses activity.

The initial response to a stressor is a developing emotion in the amygdala. With negative emotions, the hippocampus responds as the individual recalls similar past experiences in the formulation of a stress response. Considering Lazarus and Folkman’s (1984) TMS, the variance could represent the impact of life experience, particularly with negative experiences, as individuals appraise familiar situations as benign.

Fava (1994) concurred with Selye (1976) and Lazarus and Folkman’s (1984) theories about the influence of life events on the stress response, stating that neuroendocrine regulation is dependent upon how an individual perceives events. A benign primary appraisal of a stressor results in little HPA axis activity while appraisals deeming a stressor as threatening or challenging, and potentially impacting commitments or beliefs, demand greater HPA axis activity in response to stress.

Chrousos (2000) stated that the secretion of cortisol typically remains within a stable time-integrated narrow range due to regulatory mechanisms, a negative feedback
Such regulatory mechanisms include hippocampal response to GCs such as adrenocorticotrophin hormone (ACTH) and cortisol (Innes et al., 2007; Selye, 1976). Potential causes of sustained cortisol secretion include depression and visceral obesity. Hyperactivity of the HPA axis may potentiate the onset of a pseudo-Cushing state characterized by overt hypercortisolism and insulin resistance (Chrousos, 2000). Chrousos (2000) concurs with McEwen (1998) as sustained cortisol secretion can result from an overworked neuroendocrine system with an increasing allostatic load.

Depression, a form of distress, can intensify activity of GCs secondary to ineffective coping (Chrousos, 2000). The narrow range of circadian cortisol secretion can be severely influenced by distress (See Figure 4). Individuals with “frequent hits” or a “prolonged response” from a stressor could develop an allostatic load that increases risk for developing T2DM.

![Figure 4. Circadian Cortisol Secretion and Target Tissue Sensitivity](image-url)

Figure 4. (A) Circadian cortisol secretion: comparison of non-stressed (NS) individual (solid black line) with chronic-stressed (CS) individual (dotted line). The CS individual secretes greater levels of cortisol, particular at lunch as noted by the augmented increase in cortisol secretion. Dexamethasone (D) test shows exogenous GC had less influence on the suppression of cortisol secretion in the CS individual. (B) Target Tissue Sensitivity. The image shows the threshold for harmful effects secondary to cortisol concentration in individuals who are hypersensitive (HS), normal (N), and resistant (R) (adapted from Chrousos, 2000, p. S54). Printed with permission for educational purposes.
Early life stress and a history of chronic emotional stress can impair the regulatory mechanisms of cortisol secretion (Chrousos, 2000). According to Chrousos (2000), individuals with chronic distress demonstrate progressive elevations of cortisol concentrations with age. Feedback regulation of cortisol secretion may become dysfunctional with aging and, as a consequence, older individuals have elevated resting levels of cortisol (Sapolsky, 2004). Progressive cortisol elevation that occurs in stressed individuals may potentiate an equally progressive increase in risk for insulin resistance and T2DM as individuals age. Blackburn-Munro and Blackburn-Munro (2001) agreed with Chrousos (2000) and McEwen (1998) by identifying characteristics of chronic stress and chronic depression that affected HPA axis function. The characteristics included increased corticotrophin releasing hormone (CRH), altered circadian rhythmicity of ACTH, increased cortisol, and decreased negative feedback.

**Empirical Literature**

The risk for T2DM associated with genetics, obesity, and advancing age present some potential confounding variables that suggest distress could be a mediating variable in terms of appraisal and coping. During a 30-year study, Li et al. (2012) found that subjects \( n=45,302 \) exposed to maternal bereavement – death of a father, sibling, or maternal grandparent – during prenatal life were 31% more likely to develop T2DM than subjects not exposed to maternal bereavement \( (aIRR=1.31, CI=1.01-1.69) \). Individuals exposed to maternal distress such as bereavement during the prenatal period have an exaggerated stress response to stressors later in life (Sapolsky, 2004). The literature suggests that distress may influence the genetic risk that is associated with the development of T2DM.
The impact of an exaggerated stress response with cortisol secretion is particularly alarming when considering the impact on metabolism and the increase of T2DM among adolescents (Sapolsky, 2004). Obese adolescent males and females are more than two-fold more likely to develop T2DM later in life (OR=2.27 [1.41-3.64] and OR=2.08 [1.34-3.24], respectively) (The, Richardson, & Gordon-Larsen, 2013). Advancing age has also been associated with the development of diabetes as prevalence rates increased for all age groups (20-34 years by 1.0%, 35-64 years by 2.7%, and >64 years by 10.0%; p<0.001). However, obesity explained a greater factor for risk with subjects less than 65 years of age when compared to subjects over 65 years of age. In the study, data from three time periods spanning 22 years was evaluated; the prevalence of diabetes among 22,586 subjects increased by 75% (Cheng et al., 2013).

Advancing age appears to influence the relationship between amygdala and hippocampus activity. Measuring signal change from the amygdala, researchers identified younger individuals as having heightened emotions in response to both positive and negative images while older individuals only have heightened emotions in response to positive images (Carstensen, 2006). Regardless of the risk for T2DM relative to factors such as genetics, obesity, and advancing age, not all individuals with some or all of these risks develop T2DM.

The effect of endogenous cortisol on blood glucose control is difficult to interpret (Netterstrom, Kristensen, Damsgaard, Olsen, & Sjol, 1991). Evaluating the influence that cortisone, an exogenous steroid, has on blood glucose control provides a means for understanding the relationship between elevated levels of GCs in the blood and blood glucose control.
Owen and Cahill (1973) examined the influence of cortisone in six obese volunteers after prolonged starvation. For 35 days, subjects only received one multivitamin, 17 milliequivalents (mEq) of sodium chloride, 13 mEq of potassium chloride, and 1.5 liters of water. Supplements were sugar free. After the period of starvation (day 35), the subjects had blood drawn before and 12 hours following a 100 milligram (mg) injection of cortisone acetate for a period of 6 days. The serum concentrations of glucose and insulin from day 39 through day 42 were significantly different from the precortisone period ($p<0.05$). The limitations of Owen and Cahill’s (1973) study included the small test group ($n=6$), narrow spectrum of subjects (obese men), and that one of the subjects had latent diabetes.

Pagano et al. (1983) caused prednisone-induced insulin resistance in healthy subjects with ideal body weight and no history of diabetes. Six men and four women participated. Six subjects were tested six times (three tests with placebo and three with prednisone) in a random sequence. The four remaining subjects participated in two tests (one placebo and the other with prednisone).

In addition to the 10 healthy volunteers, 16 surgical patients participated in the study of prednisone-induced insulin resistance. All of the subjects were of ideal body weight and had no history of diabetes; all of the surgical subjects planned to receive an elective cholecystectomy. Six subjects received prednisone while the other 10 subjects received a placebo (Pagano et al., 1983).

In each instance with placebo or prednisone, the subjects received an infusion of dextrose and insulin. Prednisone resulted in significantly lower plasma insulin levels and metabolic glucose clearance ($p<0.001$); a significant increase in fasting glucose
production also resulted from the prednisone ($p<0.01$) (Pagano et al., 1983). Figure 5 provides variances in glucose clearance (glucose transport) as a result of prednisone use.

Figure 5. Glucose Transport Variances Between Placebo (●) and Prednisone (■)

Figure 5. Prednisone significantly hinders glucose transport as a result of poor insulin concentrations within cells. $p<0.05$ and $p<0.005$ represent the level of significance for the data in the top section of the figure. 3-OMG stands for 3-orthomethyl-glucose (Pagano et al., 1983, p. 1818). Printed with permission for educational purposes.

Limitations to the study included the mixed pool of subjects: 10 healthy subjects divided into two groups according to the number of tests conducted with prednisone and the placebo, and 16 subjects preparing for elective surgery divided into test ($n=6$) and control ($n=10$) groups. Although the test procedure remained constant, the circumstances
for the surgical group in terms of distress presented a margin for error. As endogenous GCs were not accounted for in the surgical group, the study findings presented a potential for a Type I error.

Despite study limitations, Owen and Cahill (1973) and Pagano et al. (1983) reasonably demonstrated that exogenous GCs cause insulin resistance. As the stress response can stimulate the HPA axis, the relationship between endogenous GCs and insulin resistance was also demonstrated (Owen & Cahill, 1973; Pagano et al, 1983).

Considering the role of allostasis and impact of allostatic load with management of stressors, research on cognitive processes was evaluated. Dedovic et al. (2009) conducted a literature review regarding the use of positron emission tomography (PET) and magnetic resonance imaging (MRI) to examine limbic system activity during stressful events (Dedovic et al., 2009). The PET results from one study comparing 18 social phobia subjects with six control subjects showed increased cerebral blood flow from the amygdala to the hippocampus (Dedovic et al., 2009). In another study, the neural activity of 40 subjects performing mental arithmetic tasks in a controlled environment was examined. MRI evaluation of the subjects’ neural activity following the tasks suggested that hippocampal activity influenced the stress response (Dedovic et al., 2009). Although the data did not specifically address insulin resistance, activation of the HPA axis by the hippocampus suggests potential insulin resistance secondary to cortisol secretion.

Shiloah et al. (2003) examined the influence of distress on insulin resistance in 39 subjects with acute psychotic stress. The subjects were graded using a clinical global impression score (CGI) varying from a score of one to seven with a score of seven
indicating an extremely mentally ill subject who commonly required forced hospitalization.

Shiloah et al. (2003) determined that subjects with a CGI score greater than or equal to six had higher glucose and insulin levels than subjects with a CGI score below six \((p<0.01\) and \(p<0.04\) respectively). Scores from the CGI were positively correlated with glucose and insulin levels \((r=0.47, p=0.003\) and \(r=0.37, p=0.021\), respectively). The data indicated that as psychotic stress increased, insulin sensitivity decreased \((p<0.02)\). The limitations to the study included poor generalizability to populations without psychoses and the relatively high CGI score needed to demonstrate insulin resistance.

The literature also indicates that depression influences insulin resistance in terms of cortisol secretion. In a large sample of women across the United States \((N=2,662)\), depression was associated with an increased risk of 1.66-fold for developing T2DM \((95\% \text{ CI } 1.05-2.61; p < 0.03)\). This increased risk from depression was more than two-fold for African American women \((95\% \text{ CI } 1.27-5.15; p=0.008)\) (Everson-Rose et al., 2004). Subjects with stage II or III breast cancer \((N=227)\) had stress hormones measured over the course of a year. Overall, having any depressive symptoms was positively associated with cortisol levels; however, higher depressive symptoms were associated with lower cortisol levels \((p=0.002)\) (Wu et al., 2014). Wu et al.’s (2014) research findings support Selye’s (1976) GAS, particularly the stage of exhaustion, and McEwen’s (1998) theory of allostatic load. Higher depressive symptoms may increase the allostatic load to a point where neuroendocrine response is insufficient to adapt to the stressor(s).

In a cohort of 1,094 subjects, recurrent episodes of major depression were associated with obesity \((OR=11.63, 95\% \text{ CI } [1.05-128.60])\), although the development of
obesity was not significantly associated with recurrent episodes of major depression \((OR=2.32, \, 95\% \, CI \, [0.82-6.58]; \, \text{Nigatu, Bultmann, \& Reijneveld, 2015})\). Vrany et al.’s (2015) study on depression and insulin resistance indicated that an increase in BMI secondary to somatic-vegetative symptoms was a partial mediator between somatic depressive symptoms and insulin resistance, explaining 23% of the association. Somatic-vegetative symptoms can be an individual’s response to secondary appraisal if management of the stressor – cause for depression – appears to be hopeless or out of the individual’s locus of control (Lazarus \& Folkman, 1984).

An earlier study by Eaton et al. (1996) identified a moderate relationship between major depressive disorder and the development of diabetes \((OR=2.05, \, p=0.113)\); adding obesity slightly increased the risk for T2DM from major depressive disorder \((OR=2.23, \, 95\% \, CI \, [0.90-5.55])\). Although obesity alone has been shown to promote insulin resistance, obesity doesn’t appear to promote the development of major depressive disorder.

Kendall-Tackett (2009) suggested that traumatic events and post-traumatic stress disorder (PTSD) could chronically activate the HPA axis. However, unlike depression, individuals with PTSD have decreased cortisol and increased sensitivity of the HPA negative feedback system (Kendall-Tackett, 2000). Morris, Compas, and Garber (2012) conducted a meta-analysis of 47 studies on the relationship between cortisol and trauma-exposed (TE) subjects \((N=6,008)\) with and without resulting PTSD. The researchers found that although afternoon/evening cortisol levels were lower in TE subjects without PTSD \((d=-0.25, \, \text{SE}=0.09, \, p=0.007)\) and TE subjects with PTSD \((d=-0.27, \, \text{SE}=0.12, \, p=0.007)\).
subjects with PTSD and major depressive disorder had higher cortisol levels
($d=0.49, SE=0.24, p=0.041$).

The decreased cortisol secretion in TE individuals with PTSD may correlate with
the influence of the hippocampus and process of appraisal as described by Lazarus and
Folkman (1984). Traumatic events that promote the development of PTSD may be the
predominant comparative event for individuals during primary appraisal of new stressors.
Although the traumatic event may not seem comparable to other stressors – comparing
sexual assault or active combat to financial turmoil or moving to a new area – the
individual may feel capable of handling new stressors as they are nowhere near as
stressful as the traumatic event. As a result, cortisol secretion of TE individuals with
PTSD may be less than non-TE individuals in similar situations.

The metabolic influence on the development of T2DM secondary to obesity alone
appears to be less influential than when obesity or other known risk factors are combined
with distress such as depression and PTSD. When the researchers control for known risk
factors such as genetic risk and obesity, distress remains a considerable if not significant
factor related to the development of T2DM. Depression can only increase the risk for the
development of T2DM further.

Several studies demonstrated the relationship between insulin resistance and
chronic stress at work (Chandola et al., 2006; Eriksson et al., 2013; Heraclides et al.,
2009; Netterstrom et al., 1991; Vrijkotte et al., 1999). Chronic stress at work increased
the risk for the metabolic syndrome, which increased the risk for T2DM (Chandola et al.,
2006). The metabolic syndrome included abdominal obesity, dyslipidemia, hypertension,
and insulin resistance. Chronic stress at work was defined as having low work social
support and high job demand greater than 75% of time. Subjects \(n=7,034\) from a larger occupational cohort study \(N=10,308\), the Whitehall II study, met selective criteria and were followed over 14 years. Workers with chronic stress were found to be at significant risk for developing metabolic syndrome \(p<0.05\) for men and \(p<0.01\) for women.

The researchers’ findings suggested that strenuous working conditions promoted secretion of cortisol and insulin resistance. However, the findings did not demonstrate the importance of insulin resistance in relation to chronic work stress. Because insulin resistance is a component of the metabolic syndrome, the importance of chronic work stress influence on insulin resistance was implied.

Heraclides et al. (2009) demonstrated greater specificity for the connection between insulin resistance and T2DM when examining a subpopulation of the Whitehall II study. The researchers examined psychosocial work stress in 5,895 subjects \(n=4,166\) men and 1,729 women). Psychosocial work stress was identified by job strain and iso-strain. High work demands and low decisional latitude defined job strain; subjects with the lowest level of work social support had iso-strain. According to Heraclides et al. (2009), job strain increased the risk for T2DM by 60%, and iso-strain doubled the risk for T2DM among women when components of job strain and iso-strain were both present (95% CI). A total of 308 subjects developed T2DM. The results were not significant. Generalization of the findings was limited to Caucasians, 35 to 55 years of age, as the researchers excluded ethnic minorities due to small numbers \(n=532\). The moderate internal consistency reliability of the Job Demands Scale used in the original Whitehall II study presented another potential limitation \(\alpha=0.67\).
Netterstrom et al. (1991), Vrijkotte et al. (1999), and Eriksson et al. (2013) also demonstrated the influence of work stress on insulin sensitivity. The researchers measured the degree of work stress as a balance between work demands and decisional latitude or reward for effort.

The Netterstrom et al. (1991) study consisted of 1,504 men and women, aged 30 to 60 years, and examined the influence of work stress on cardiovascular risk factors. High demands and low decisional latitude on the job accounted for greater stress from work, identified as job strain (Netterstrom et al., 1991). Subjects with job strain had significantly higher hemoglobin A1c (HbA1c) than subjects without job strain ($p<0.01$). The researchers suggested that distress from work influenced insulin resistance in subjects as evidenced by the elevated HbA1c.

The Vrijkotte et al. (1999) study findings demonstrated that insulin resistance occurred in a high over-commitment group of white collar workers. The degree of over-commitment was determined by the sum of four factors: the need for approval, competitiveness, the balance between impatience and irritability, and the inability to stop working due to work expectations. The sample consisted of 124 men, aged 35 to 55 years, working in a large computer company.

Subjects in the high over-commitment group ($n=40$) showed higher insulin and glucose levels ($p=0.034$ and 0.050, respectively) (Vrijkotte et al., 1999). The data complemented the Netterstrom et al. (1991) findings as the high over-commitment group also demonstrated insulin resistance. The data from the two studies suggested that work stress resulting from job demands or ambition produced distress with the risk of developing insulin resistance and potentially T2DM.
Eriksson et al. (2013) conducted a study similar to Netterstrom et al. (1991) following subjects ($N=5,432$) over a period of 8-10 years. The greatest impact from work stress occurred in women. Low decisional latitude increased the risk for T2DM more than two-fold after adjusting for factors such as family history of diabetes and BMI ($OR=2.4$, 95% CI [1.1-5.2]). The risk for women nearly doubled when low decisional latitude was combined with high job demands ($OR=4.2$, 95% CI [2.0-8.7]).

The ability to generalize the data was the primary limitation for the studies. Each study limited generalization in terms of age because the subjects represented an unspecified or small proportion of the population, 35 to 55 year old men and or women. Because Netterstrom et al. (1991) did not specifically identify insulin resistance as a product of job strain, insulin resistance was assumed in connection with the elevated HbA1c; assuming an elevated HbA1c as an indication of insulin resistance seemed permissible with the WHO’s (2011) recognition of HbA1c as diagnostic for T2DM.

Major stressful life events have also been studied related to the onset of T2DM (Mooy et al., 2000). A random sample consisting of 2,262 non-diabetic Caucasians, aged 50 to 74 years, completed a Serious Life Events Survey followed by an oral glucose tolerance test. The survey considered events from the previous five years.

Mooy et al. (2000) determined that each event cumulatively increased the risk for the development of T2DM while controlling for variables such as age and gender (95% CI, $p<0.05$). In addition, subjects ($n=402$) with the highest number of stressful events (three or more) had a 1.6-fold increased risk for developing T2DM after adjusting for age, gender, and family history ($p<0.05$). Five percent ($n=112$) of the subjects had previously undetected T2DM.
Because the sample only included Caucasians, generalization to other ethnicities could not be made. The data also could not be applied to individuals outside the age range of 50-74 years.

The amount of distress, appraisal of the stressor(s), and the allostatic load may play a pivotal role in the development of T2DM over an individual’s lifetime. Novak et al. (2013) analyzed data from the Multifactor Primary Prevention Trial Study, which included a random sample of men ($N=7,251$) that were followed over a period of 35 years. Within the first year, subjective distress evaluations were completed with a single Likert-scaled question, ranging from one – indicating never having experienced stress – to six – permanent stress over the previous five years. The risk for T2DM increased by 42% for men with permanent stress after adjusting for age, SES, physical inactivity, BMI, systolic blood pressure, and use of anti-hypertensive medications (95% CI 1.02-1.96).

Items evaluated in the survey included anxiety or sleeping difficulties secondary to work conditions.

Preliminary work from a pilot study ($N=10$) on the topic suggests a relationship between distress and the development of T2DM. Subjects diagnosed with T2DM within six months of the study completed the Recent Life Changes Questionnaire (RLCQ) to determine the amount of distress in terms of stressful life events present near the time of diagnosis (Miller & Rahe, 1997). Subjects also completed the ENRICHD Social Support Instrument (ESSI) to determine available social support near the time of the T2DM diagnosis (Vaglio et al., 2004). A demographic survey was used to determine BMI, genetic risk for diabetes, age, and HbA1c at the time of the T2DM diagnosis. Analysis of the data suggested a moderate, positive, non-significant correlation between stressful life
events and blood glucose control at the time that T2DM was diagnosed (r=0.494, p=0.147). The limitations included a small convenience sample and rigorous statistical analyses indicated for a larger sample.

**Summary**

In examining theoretical concepts, unique elements from the literature were complementary. The theories presented by Selye, Lazarus and Folkman, and McEwen provided a detailed view of the stress response when combined. Lazarus and Folkman (1984) explained the influence of perception and appraisal resulting from environmental or social factors, and Selye (1976) described the innate process of the stress response and the effect of cortisol on the body.

Further examination of the emotion and memory complexes of the brain strengthened the study’s conceptual framework. The amygdala and hippocampus defined the biological components comprising neuroendocrine regulation secondary to appraisal of a stressor (Lazarus & Folkman, 1984; McEwen, 2003b). In addition, the opposing functions of the amygdala and hippocampus in HPA axis activation complemented Selye’s regard for coping (Dedovic et al., 2009; Innes et al., 2007; Selye, 1976). As Selye noted, “…it is our ability to cope with the demands made by the events in our lives, not the quality or intensity of the events, that counts” (1976, p. 177-178).

Early life stress and chronic emotional stress impair regulation of cortisol secretion; over-activity of the HPA axis promotes insulin resistance (Blackburn-Munro & Blackburn-Munro, 2001; Chrousos, 2000). Essentially, life events influence neuroendocrine regulation (Fava, 1994; Kendall-Tackett, 2009). Effective adaptation is the balance of biological and environmental factors in the process of coping.
The empirical literature regarding insulin resistance and the onset of T2DM also presented potentially confounding factors related to established risk factors such as genetic risk for diabetes and obesity, and described contributing factors to the stress response and secretion of cortisol. Prenatal exposure to maternal distress and obesity secondary to recurrent episodes of major depressive disorder suggest that distress influences established risk factors for T2DM (Li et al., 2012; The et al., 2013).

Owen and Cahill (1973) and Pagano et al. (1983) indirectly supported Selye’s (1976) GAS with their respective studies on exogenous steroids by demonstrating the influence of the drugs on insulin resistance. Novak et al. (2013) started a study shortly after Pagano et al. (1983) published their research to show that endogenous steroids, GCs, can influence insulin resistance over time in men with considerable distress. Acute psychoses promoted insulin resistance and increased the risk for T2DM ($p<0.05$) (Shiloah et al., 2003). Depression also increases the risk for T2DM secondary to obesity and or insulin resistance (Eaton et al., 1996; Everson-Rose et al., 2004; Nigatu et al., 2015; Wu et al., 2014). Individuals who believed that they had high demands and little support at work or worked excessively to meet expectations also demonstrated insulin resistance (Chandola et al., 2006; Eriksson et al., 2013; Heraclides et al., 2009; Netterstrom et al., 1991; Vrijkotte et al., 1999). Unique individual circumstances influenced adaptability to distress.

The distress from unique circumstances became amplified when traumatic life events occurred. Mooy et al. (2000) determined that stressful life events significantly influenced the development of T2DM after adjusting for age, gender, and family history of diabetes ($p<0.05$).
In understanding the nature of the stress response, the psychological influences and adaptability of the individual must be explored. The theoretical literature outlined the psychological influences of the stress response from the amygdala and hippocampus, or the cognator subsystem as described by Roy, and the HPA axis. The empirical literature provided examples of populations that developed insulin resistance and/or T2DM secondary to the stress response.

By combining aspects of the theoretical and empirical literature, an area of concern for further testing of the stress response was developed. An analysis of adaptability in terms of distress and contextual stimuli or social support in relation to stressful life events would strengthen current understanding of the stress response as limited research addresses the topic.
CHAPTER III
METHODS

The purpose of the study was to examine the influence of stressful life events, social support, BMI, age at time of T2DM diagnosis, and genetic risk for diabetes on the development of T2DM. Subjects diagnosed with T2DM within six months of the study completed the Recent Life Changes Questionnaire (RLCQ) to determine the amount of distress in terms of stressful life events present near the time of diagnosis (Miller & Rahe, 1997) (See Appendix A); the ENRICHD Social Support Instrument (ESSI) to determine available social support near the time of the T2DM diagnosis (Vaglio et al., 2004) (See Appendix B); and a demographic survey to determine BMI, age at time of the T2DM diagnosis, and genetic risk for diabetes (See Appendix C)

Design

The research was conducted by using a quantitative descriptive design with correlational and comparative aspects. The pilot study was evaluated to estimate the effect size, although the results were likely influenced by the small sample size ($N=10$; Minks, 2013). The effect size for this study was estimated from data analysis of the pilot study; specifically, subjects with considerable if not significant RLCQ scores ($n=5$) and the standardized coefficient for psychological stress, or distress ($b=0.809, p=0.191$). See Table 1 for concepts and definitions.
<table>
<thead>
<tr>
<th>Concept</th>
<th>Variable</th>
<th>Theoretical Definition</th>
<th>Operational Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Glucose Control (BGC)</td>
<td>Extent of BGC</td>
<td>The degree of variance between glucose levels and insulin concentrations with higher variance meaning less control and possible development of diabetes.</td>
<td>Results of a hemoglobin A1c laboratory test</td>
</tr>
<tr>
<td>Genetic Risk for Diabetes (GRD)</td>
<td>Extent of GRD</td>
<td>A family history of diabetes posing genetic risk for development of the disease (ADA, 2004).</td>
<td>Subject answering yes in response to the question: “Do you have a parent, grandparent, or sibling with diabetes?”</td>
</tr>
<tr>
<td>Aging</td>
<td>Extent of aging</td>
<td>The incremental change in time as it relates to an individual’s lifespan.</td>
<td>Chronological age in years at the time of diagnosis</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>Amount of BMI</td>
<td>An individual’s weight in proportion to the individual’s height (ADA, 2004).</td>
<td>$W = \text{kg/m}^2$</td>
</tr>
<tr>
<td>Distress (D)</td>
<td>Amount of D</td>
<td>The degree of perceived environmental demands requiring adaptation (Lazarus &amp; Folkman, 1984).</td>
<td>The sum of life change units (LCU) from stressful life events</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measurement tool: 1. Recent Life Changes Questionnaire (RLCQ) for major causes of distress (Miller &amp; Rahe, 1997)</td>
<td></td>
</tr>
<tr>
<td>Social Support (SS)</td>
<td>Amount of SS</td>
<td>The degree of perceived availability of people, groups, or organizations that influences an individual’s ability to cope (Vaglio et al., 2004).</td>
<td>SS = CM*Psupport</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measurement tool: 1. ENRICHD Social Support Instrument (ESSI)</td>
<td></td>
</tr>
</tbody>
</table>
The conceptual model comprises the interactions among the variables. See Figure 6.

Figure 6. The conceptual model shows directionality of the influence of variables as they interact with other variables. The extent of genetic risk for diabetes (GRD) encloses the amount of blood glucose control as it influences an individual’s insulin sensitivity. Theoretically, when the amount of social support is unable to suppress the impact of the amount of distress on the extent of blood glucose control, an individual’s extent of blood glucose control expands beyond that individual’s genetic risk for diabetes leading to diagnosis of the disease.

**Setting**

The study was conducted in an urban region of Missouri in the greater St. Louis area at SSM Health and VA Medical Centers. For the purpose of this study, urban was defined as a metropolitan county having 50,000 or more in a population center within its boundaries (United States Census Bureau, 2015). For the purpose of this study, the primary area contributing to the population includes Madison County, IL, St. Charles County, MO, St. Claire County, IL, St. Louis City, MO, St. Louis County, MO (United States Census Bureau, 2015).
The medical centers associated with SSM Health Centers are predominantly in St. Charles County, St. Louis County, and the city of St. Louis (SSM Health, 2016). The locations of the VA Medical Centers are St. Louis County for Jefferson Barracks and the city of St. Louis for John Cochran.

**Population and Sample**

The estimated sample size needed for this study was determined to be 80 subjects as a result of using G-power analysis with a small effect size ($f^2 = 0.10$, $p < 0.05$, and 5 predictors). The target population for this study consisted of 40 non-veterans from SSM Health Centers and 40 veterans from VA Medical Centers, all adults 18 years of age or older diagnosed with T2DM. The accessible population were patients, 18 years or older and diagnosed with T2DM, seen at DePaul, St. Clare, St. Joseph, and St. Mary’s Health Centers (SSM Health Centers) and the John Cochran and Jefferson Barracks (VA Medical Centers) located in the greater St. Louis, Missouri area.

Inclusion criteria were: 18 years of age or older, a diagnosis of T2DM within the previous six months of the study, receiving outpatient diabetes care services from one of the selected medical centers, and willingness to participate in the research. The sample did not include children, pregnant women, residents of prisons or mental institutions, nor the mentally handicapped.

Providers were given copies of a cover letter regarding the study (See Appendix D) to provide to patients if they expressed interest in participation during the time of the clinical appointment. The cover letter introduced potential subjects to the investigator and the purpose of the study, and to help potential subjects make an informed decision about participating in the study. Subjects at the VA received the cover letter in the mail per VA
IRB approval. Subjects at SSM clinics or hospitals were given a copy of the cover letter and or had opportunity to read the contents of the cover letter at the time informed consent was given.

Data regarding the research variables, including age, body mass index (BMI), genetic risk for DM, and hemoglobin A1c (HbA1c) value at the time of T2DM diagnosis were obtained from each subject, or the subject’s health care record if the subject was not certain of specifics related to the questions such as “What was your hemoglobin A1c level at the time of diagnosis?” The HbA1c value represents the extent of blood glucose control, relative to insulin concentrations, for the previous 90-120 days during a period of time that stressful life events may have been experienced. The ethnicity, gender, co-existing mental health diagnoses such as depression or PTSD, level of education, and marital status were acquired from all subjects at the time of the data collection interview to further describe the sample. Completed surveys including demographic information, the Recent Life Changes Questionnaire (RLCQ), and the ENRICHD Social Support Instrument (ESSI) were stored in a safe in the investigator’s home office until processed. Only the primary investigator (PI) has access to the key for subjects recruited from SSM Health Centers. As the VA requires an employee operate as the PI for the study, the PI at the VA was also aware of the identities of subjects recruited from the VA. During data analysis, the investigators will compare and analyze the findings of the raw data at a VA facility, absent of any personal identifiable information for any of the subjects. The raw data from SSM Health Centers will be destroyed one year following the conclusion of the study with a paper shredder while the raw data from VA Medical Centers will be
managed per VA policies and procedures, which requires storage of all data acquired for seven years.

Protection of human subjects was built into the design. Permission to conduct the study and provide appropriate protection of human subjects were obtained from the Committee on Research Involving Human Subjects, College of Nursing, University of Missouri – St. Louis and the medical centers (See Appendix E). Adults 18 years of age or older with T2DM receiving outpatient diabetes care services at an SSM Health or VA Medical Centers were asked to sign a HIPAA release form and a statement of informed consent (See Appendices F & G) at the time of the interview prior to data collection. Implied consent for screening were attributed to subjects or healthcare providers (physicians or diabetes educators) on behalf of the subjects contacting the investigator about participation in the study.

The only foreseeable potential risk to the subjects that could result from participation in the study included emotional distress from discussing life changes and availability of social support. If subjects became emotionally distraught during the interview, an investigator would listen and provide condolences but not attempt to counsel. Subjects at SSM Health Centers would be directed to call Behavioral Health Response, or other entity per IRB preference, for assistance from trained counselors. Subjects at VA Medical Centers were able to contact a psychologist on site per behavioral research protocol.

The potential benefits to subjects include clarifying the influence of known risks for the development of T2DM. Because T2DM is a disease of multifactorial origin,
determining the potential risk that distress presents in the development of T2DM may influence the provider’s approach to preventing and treating T2DM.

One subject from the VA subgroup dropped out of the study. The subject was concerned about the VA using her data for research despite review of informed consent with relative benefits and risks.

**Measurement**

Distress, social support, age, body mass index (BMI), blood glucose control, and genetic risk for DM were examined in the study. The RLCQ measured distress that the subject experienced due to unique life changes (See Appendix A). The ESSI measured social support available to the subject (See Appendix B). The demographic survey provided data to measure age, BMI, blood glucose control, and genetic risk for DM, as well as descriptive details such as gender and level of education (See Appendix C).

**The Recent Life Changes Questionnaire (RLCQ).**

The RLCQ was developed to measure the potential influence of distress on the manifestation of diseases in terms of life change events (Miller & Rahe, 1997). In order to maintain control between subjects interviewed face-to-face, the investigator read the items on the RLCQ to all subjects and allowed time for subjects to answer each item. The investigator completed the survey questionnaire for each subject as appropriate per their response to each question.

The RLCQ consists of 73 life change events that follow a proportionate scaling model (Miller & Rahe, 1997). The subjects scored each applicable event in proportion to a model event. According to Miller and Rahe (1997), subjects usually only acknowledge 10 to 20% of life change events as being influential. To ensure sufficient data for
analysis, the authors recommended asking about 60 to 75 events in order to obtain six to 15 events that apply to the subject.

Lazarus and Folkman (1984) identified the original instrument – The Holmes-Rahe Schedule of Recent Experience – as one of the best, if not the best, known instrument of its time (p.111). However, the original instrument used a complicated proportional scaling method that required calculating arithmetic and geometric mean data (Miller & Rahe, 1997). A simplified scaling method was developed and demonstrated high correlation with the original proportional scaling method ($\rho = 0.92$, $p < 0.001$). Subjects provided numeric evaluation for each relevant event on a scale from 0-100 (Rahe, Ryman, & Ward, 1980). Relevant events may have the same scores as proportional scaling and do not require rank-order scoring for events.

The most recent edition of the RLCQ has further simplified the scoring system. Mean scores were calculated for each event. The PI used the recent edition to simplify the survey process for participants.

According to Miller and Rahe (1997), many studies have been conducted and findings have indicated that the 73-item RLCQ demonstrated significant correlation to perceived stress from life changes when the various samples were compared according to demographic characteristics: age, gender, marital status, and level of education ($r = 0.84$ to $0.96$) (Miller & Rahe, 1997). According to Burns and Grove’s description of construct validity (2009), the findings from the studies suggested strong construct validity as the content effectively identified life events for varying samples and predicted compromised health outcomes from elevated stress.
The RLCQ’s reliability has varied depending on the sample. Pearson and Long (1985) found the RLCQ to be reliable when used to evaluate life change in active military reserves, 18 to 60 years old ($n=109$, $\alpha=0.83$). Lee, Chan, and Berven (2007) found the RLCQ’s reliability to vary from unreliable to reliable in evaluating stress in depressed subjects with chronic musculoskeletal pain ($\alpha=0.47$ to 0.75). Rahe (personal communication, April 15, 2012) reported that an unpublished test-retest run conducted four weeks apart showed acceptable reliability coefficients for the two subscales ($\alpha=0.71$ to 0.85). The data collected from multiple studies, despite Lee et al.’s (2007) findings, indicated that the RLCQ could effectively measure an individual’s perceived distress from life changes (Pearson & Long, 1985; Miller & Rahe, 1997). The reliability coefficient for the pilot study ($\alpha=0.796$) was comparable to Rahe’s reliability coefficients.

According to Miller and Rahe (1997), a total score greater than or equal to 300 life change units (LCU) for a six-month period or greater than or equal to 500 LCU for a one-year period is an indication of high life stress. The scores differed to account for the increased number of events occurring after six months that would influence the level of significance. Total scores greater than 300 LCU or 500 LCU indicated significant distress.

The RLCQ takes 5-10 minutes to complete and generates ratio level data (Proqolid, 2011). The events were addressed as simple questions to account for a subject’s potentially low educational level.

**The ENRICHD Social Support Instrument (ESSI).**

The ESSI is a seven-question survey that assesses social support (See Appendix B) (Vaglio et al., 2004). The first question follows a Likert format with a score ranging from
1-5. A score of one indicates that the subject never had anyone available to talk to while a score of five indicates that the subject always had someone to talk to. The remaining six questions are asked in a yes/no format with dichotomous scoring, one for no and two for yes.

The ESSI has been used to evaluate social support in multiple studies since its creation (Berkman et al., 2003). Although it was initially designed to study patients that experienced a heart attack, it is as applicable for patients with chronic diseases (Gottlieb & Bergen, 2010). In one study of 271 subjects undergoing heart surgery, subjects completed the ESSI monthly for a period of six months following the procedure (Vaglio et al., 2004). According to Vaglio et al. (2004), the ESSI demonstrated significant internal consistency reliability and inter-item associations ($r=0.94$, $\alpha=0.88$, $p<0.001$) and modest but statistically significant correlations when compared to other social support instruments ($p<0.05$).

The ESSI takes approximately 2-3 minutes to complete and generates ordinal level data (Vaglio et al., 2004). A total score could vary from 7-17 with a higher score indicating strong social support.

**Demographic survey.**

The investigator-developed demographic survey included items to measure the variables of age, gender, ethnicity, marital status, BMI, HbA1c, highest level of education, genetic risk for DM, and potential pre-existing diagnosis of a mental health disorder such as depression, anxiety, or PTSD (See Appendix C). Body mass index and HbA1c values at the time of T2DM diagnosis were collected from the subjects’ health records at the respective health care setting. Each subject’s height and weight at time of
diagnosis were gathered from the medical record for accuracy. The existence of a mental health disorder such as depression and the subject’s view of management in the form of a dichotomous question – “Do you feel like your current treatment is effective” – prior to the diagnosis of T2DM was also evaluated. Based upon a review of available literature, the aforementioned variables were relevant to the study about the effect of distress on the development of T2DM, or to provide a typical description of a sample of adult humans (ADA, 2004; Hamman, 1992; Miller & Rahe, 1997; Palinkas et al., 2004).

Age and BMI were noted to be potential risk factors for the development of T2DM (ADA, 2004; Hamman 1992). Ethnicity, gender, marital status, and highest level of education were addressed to further describe the sample. Asking subjects if they had a parent, grandparent, or sibling with T1DM or T2DM acknowledged the genetic influence for the development of the disease.

Genetic risk for DM, ethnicity, gender, pre-existing diagnosis of a mental health disorder, and marital status provided nominal level data. Highest level of education provided ordinal level data. Age, BMI, and HbA1C provided interval/ratio level data.

**Data Collection Procedure**

Subjects were recruited from diabetes clinics and primary health care provider offices affiliated with SSM Health and VA Medical Centers. Flyers with general information and contact information (See Appendix H) hung in exams rooms and the waiting area at participating hospitals of SSM Health Centers. Similar flyers were also created for nursing staff in unit breakrooms.

Patients diagnosed with T2DM in the previous six months receiving care as an outpatient, interested in participating in the study, received a cover letter with information
about the study and methods for contacting the SSM investigator. Implied consent was evident when subjects contacted the SSM investigator for initial screening. Informed consent was obtained from subjects by the SSM investigator where subjects received diabetes care services prior to the interview. Patients diagnosed with T2DM in the previous six months receiving care as an inpatient were offered participation in the study by a nurse or provider. If interested, informed consent was obtained from subjects by the SSM investigator.

The investigator at VA Medical Centers recruited subjects from established programs such as Move 101 orientation, nutrition classes, and primary care providers. Class lists were pre-screened by the VA investigator for inclusion criteria and veterans were contacted by cover letter with informed consent document prior to the date of a scheduled class or appointment. The investigator followed up the cover letter and informed consent by phone to schedule a mutually determined time to meet and complete questionnaires usually pre or post an established VA appointment. The investigator met with each vet interest prior to a class or appointment to determine interest. Those willing to participate completed study questionnaires before or after attending the class or appointment.

At the time of the data collection interview, the investigator asked the questions according to the format of the RLCQ, ESSI, and demographic survey, respectively. The investigators ensured that the RLCQ, ESSI, and demographic survey were completed in entirety at the end of each subject’s interview. Following completion of the instruments, the subjects were thanked for their participation.
Data Analysis

Demographic data were analyzed using descriptive statistics. Descriptive statistics were also used for research questions one and three. Independent samples t-tests were also analyzed for research question three. Multiple regression was used to analyze research question two. The computer program used was SPSS 25.

Descriptive statistics were used for the demographic data of the total sample and for comparison of the SSM and VA subgroups to determine the mean, mode, range, percent, and standard deviation of each demographic characteristic as appropriate. The independent samples t-tests were used to determine if there were significant differences in the mean BMI, HbA1c, and RLCQ scores for the subgroups. Multiple regression was chosen to determine the individual and combined effects of the variables – age, BMI, distress, social support, and genetic risk for diabetes – on the development of T2DM, recognized by HbA1c (≥6.5%). A block-approach to analysis was conducted to determine if any independent variables potentially mediate the effect of GRD, and the variables age and BMI were added in the last two blocks as they are established risk factors for T2DM. An alpha level of 0.05 was used for statistical comparisons.
CHAPTER IV
ANALYSIS OF DATA

This chapter includes data about the study as follows: description of the sample, findings from the data analysis, limitations of the study, and a summary. Data were collected from a sample of subjects (n=79) diagnosed with type 2 diabetes (T2DM) within six months before the date of the interview. Demographic data were reported using descriptive statistics.

Data based on responses to the Recent Life Changes Questionnaire (RLCQ) (See Appendix A), the ENRICHD Social Support Instrument (ESSI) (See Appendix B), and a demographic survey (See Appendix C) were analyzed. The following demographic variables were evaluated in conjunction with total scores from the RLCQ and ESSI: age, body mass index (BMI), and family history of diabetes (DM). As age, BMI, and family history of DM were established risk factors for T2DM (ADA, 2004; Guthrie & Guthrie, 2004; Hamman, 1992), the variables were compared to distress from recent life events and the available social support during the timeframe of the life events to determine the amount of influence each independent variable posed.

Description of the Sample

The subjects were recruited from SSM Health Centers and the VA Medical Centers. SSM Health Centers included DePaul Hospital’s inpatient and outpatient services, St. Joseph’s Hospital’s inpatient services, and St. Joseph’s Hospital West’s inpatient services. The VA Medical Centers’ outpatient clinics located in the greater St. Louis, Missouri area, included John Cochran and Jefferson Barracks. Each health center required unique approaches to subject recruitment.
Potential subjects from SSM Health Centers were screened for eligibility to participate and either invited to participate by providers, nurse educators, or nurses or directed to a flyer about the study hanging in outpatient exam rooms that had a pull-tab with the primary investigator’s (PI) contact information (See Appendix G). Cover letters were provided to providers in outpatient clinics (See Appendix H). If interested in participating, the PI would arrange time to meet with potential subjects, describe the purpose of the study, and confirm the potential subject’s interest in participating. Once interest was confirmed, informed and institutional consents were provided before starting the interview (See Appendices E & F). Subjects were offered a copy of the consent forms.

Potential subjects from VA Medical Centers were pre-screened by the PI onsite as the VA IRB required an employee liaison nurse with PhD to be the PI for the study. Potential subjects that met the inclusion criteria were mailed a cover letter about the study and copy of the consent forms. Potential subjects met with the onsite PI (n=4) or student PI (n=36) before or after the potential subject’s next outpatient appointment regarding the letter that was mailed to them. If interested, the subject met with the PI in a private exam room where the PI described the purpose of the study and determined the potential subject’s interest in participating. If interested, informed consent was provided before starting the interview. One subject later declined participation after completion of the interview.

The average subject was a 58 years old, non-Hispanic, married, Caucasian male with a college degree and a mother with a known diagnosis of diabetes. The average
subject’s hemoglobin A1c (HbA1c) was 8.3% and BMI was 34.1. Twenty-nine subjects were diagnosed with a mental illness.

Subjects varied according to selected demographic variables. Table 2 describes the sample by comparing outcomes for men and women within the subsamples.

Table 2
Demographic Description of Sample Comparing SSM and VA Subjects

<table>
<thead>
<tr>
<th></th>
<th>Overall (N=79)</th>
<th>SSM (n=40)</th>
<th>VA (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men (n=23)</td>
<td>Women (n=17)</td>
</tr>
<tr>
<td>Age in years $\bar{x}$ (SD)</td>
<td>57.63 (12.11)</td>
<td>52.70 (15.28)</td>
<td>62.29 (10.90)</td>
</tr>
<tr>
<td>BMI $\bar{x}$ (SD)</td>
<td>34.08 (6.63)</td>
<td>32.64 (7.91)</td>
<td>34.02 (6.12)</td>
</tr>
<tr>
<td>GRD n</td>
<td>61</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Mental Illness n</td>
<td>29</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Education M</td>
<td>Some College</td>
<td>High school Diploma</td>
<td>Some College</td>
</tr>
<tr>
<td>Married or Living with Partner n</td>
<td>42</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Distress $\bar{x}$ (SD)</td>
<td>297.61 (201.98)</td>
<td>271.43 (192.68)</td>
<td>307.18 (198.64)</td>
</tr>
<tr>
<td>Social Support $\bar{x}$ (SD)</td>
<td>14.97 (2.30)</td>
<td>15.91 (1.38)</td>
<td>14.88 (2.15)</td>
</tr>
<tr>
<td>HbA1c $\bar{x}$ (SD)</td>
<td>8.31 (2.10)</td>
<td>9.26 (2.26)</td>
<td>8.48 (1.97)</td>
</tr>
</tbody>
</table>

The RLCQ presented unique findings in terms of events that affected or did not affect subjects. Of the 73 events listed, 7 events did not apply to the sample within six months prior to their diagnoses: a demotion, pregnancy, birth of a child, adoption, parents
divorce, a parent remarried, or held in jail. Of the 73 events listed on the RLCQ, 14 events applied to the sample within six months prior to their diagnoses with considerable frequency \((n\geq18)\). Events listed in table 3 with frequency. To avoid inflating RLCQ scores for subjects that were inpatients at the time of the interview, two events were not counted at the time of the interview: an illness or injury that kept the subject in bed for more than a week or sent the subject to the hospital did not count if the only occurrence occurred at the time of the interview.

Table 3
Recent Life Changes Questionnaire Events with Frequency \(\geq18\) for the Sample \((N=79)\)

<table>
<thead>
<tr>
<th>Event</th>
<th>Frequency (Percent of Sample)</th>
</tr>
</thead>
<tbody>
<tr>
<td>An illness or injury that you kept in bed for more than a week or sent you to the hospital ((74\ LCU))</td>
<td>23 (29.1%)</td>
</tr>
<tr>
<td>An illness or injury that was less serious than above ((44\ LCU))</td>
<td>26 (32.9%)</td>
</tr>
<tr>
<td>Major change in eating habits ((27\ LCU))</td>
<td>22 (27.8%)</td>
</tr>
<tr>
<td>Major change in sleeping habits ((26\ LCU))</td>
<td>24 (30.4%)</td>
</tr>
<tr>
<td>Major change in usual type and or amount of recreation ((28\ LCU))</td>
<td>18 (22.8%)</td>
</tr>
<tr>
<td>Major change in living conditions ((42\ LCU))</td>
<td>18 (22.8%)</td>
</tr>
<tr>
<td>Change in family get-togethers ((25\ LCU))</td>
<td>18 (22.8%)</td>
</tr>
<tr>
<td>Major change in health or behavior of a family member ((55\ LCU))</td>
<td>19 (24.4%)</td>
</tr>
<tr>
<td>Change in personal habits ((26\ LCU))</td>
<td>25 (31.6%)</td>
</tr>
<tr>
<td>Change in social activities ((27\ LCU))</td>
<td>18 (22.8%)</td>
</tr>
<tr>
<td>Vacation ((24\ LCU))</td>
<td>26 (32.9%)</td>
</tr>
<tr>
<td>Major decision about immediate future ((51\ LCU))</td>
<td>24 (30.4%)</td>
</tr>
<tr>
<td>Major purchase ((37\ LCU))</td>
<td>19 (24.4%)</td>
</tr>
<tr>
<td>Moderate purchase ((20\ LCU))</td>
<td>22 (27.8%)</td>
</tr>
</tbody>
</table>

Note. The frequency score of 18 was chosen due to the mode \((n=4)\) and the next highest frequency score was 14 with only one occurrence. Other frequency scores with considerable mode values were less than a frequency score of 10.

Scores from the ESSI varied from 8 to 17. The mean ESSI score was 15.0 \((SD=2.3)\). The predominant modes were ESSI scores of 16 and 17 \((n=22\ and\ n=22,\)
respectively). Fifteen subjects had ESSI scores less than 14. The majority of subjects had a strong social support system (See Table 4 and Table 5).

Table 4
Determining the Availability of Support Using the ENRICHD Social Support Instrument (N=79)

<table>
<thead>
<tr>
<th>Question</th>
<th>Amount of Time</th>
<th>None</th>
<th>Little</th>
<th>Some</th>
<th>Most</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there someone available to whom you can count on to listen when you need to talk?</td>
<td></td>
<td>8 (10.1%)</td>
<td>2 (2.5%)</td>
<td>4 (5.1%)</td>
<td>20 (25.3%)</td>
<td>45 (57.0%)</td>
</tr>
</tbody>
</table>

Table 5
Describing the Availability of Support Using the ENRICHD Social Support Instrument (N=79)

<table>
<thead>
<tr>
<th>Description of Support</th>
<th>‘Yes’ Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Someone available to give [the subject] good advice about a problem</td>
<td>67 (84.8%)</td>
</tr>
<tr>
<td>Someone available who shows [the subject] love and affection</td>
<td>74 (93.7%)</td>
</tr>
<tr>
<td>Someone available to help with daily chores</td>
<td>60 (75.9%)</td>
</tr>
<tr>
<td>Anyone available to provide [the subject] with emotional support (talking over problem or helping make a difficult decision)</td>
<td>70 (88.6%)</td>
</tr>
<tr>
<td>Have as much contact as [the subject] would like with someone [the subject] feels close to in whom [the subject] can trust and confide in</td>
<td>63 (79.7%)</td>
</tr>
<tr>
<td>Currently married or living with a partner</td>
<td>45 (57.0%)</td>
</tr>
</tbody>
</table>

Note. ‘Yes’ responses consists of all subjects that responded ‘yes’ to having the specific type of support available.

Research Question (RQ) #1: In adults with T2DM, how much distress was present six months prior to the diagnosis of T2DM?

An individual with an RLCQ score greater than or equal to 300 life change units (LCU) is considered to have significant stress. Scores from the RLCQ varied from 0 to 801 LCU. The mean RLCQ score was 297.6 LCU (SD=202.0). The median RLCQ was
Two subjects had RLCQ scores of 0 LCU. Despite the mean and median RLCQ scores being less than 300 life change units (LCU), 36 of the 79 subjects had significant distress, scores greater than 300 LCU, within the six-month period prior to the diagnosis of T2DM.

Discussion.

The mean RLCQ score was not significant as it was less than 300 LCU. Although it was not significant, the subjects had a high amount of distress on average.

Per Miller and Rahe’s (1997) initial RLCQ design, 73 life change events were addressed with each subject when measuring distress with the goal of 10-20%, or 6-15 events, applying to each subject. From the sample, 33 subjects experienced less than six events within the previous six months. The majority of the sample (n=46) experienced more than six stressful life events.

If the 33 subjects were considered outliers as less than six events on the RLCQ applied to them, and the mean and median were recalculated, a more representative mean and median may be determined. Only considering subjects that experienced six or more events (n=46) resulted in a mean RLCQ score of 431.74 LCU (SD=152.5) and a median RLCQ score of 408 LCU. These scores are greater than 300 LCU and considered significant.

RQ #2: What is the individual and combined effect of distress, social support, age, BMI, and GRD on the HbA1c level?

Age, BMI, GRD, distress, and social support explained 8.9% of the variation in the dependent variable, represented by HbA1c (adjusted $R^2=.089$, $F=6.910$, $p=.010$). Two
variables, age and BMI, significantly explained portions of the total variance in the
dependent variable ($\beta=-.241, p=.031$ and $\beta=-.293, p=0.10$, respectively) (See Table 6).

Further analysis was done to examine collinearity and the adjusted $R^2$ value. The
VIF values for the variables ranged from 1.034 to 1.063. The range of values is much less
than 8 and suggests no collinearity among variables.

The adjusted $R^2$ value was 8.9%, therefore a regression analysis was conducted
using only the established risk factors age, BMI, and GRD. The established risk factors
explained 11.1% of the variation in HbA1c (adjusted $R^2=.111$, $F=4.259$, $p=.008$).

Table 6
Hemoglobin A1c: Examining Risk Factors with Regression Models

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Genetic Risk</td>
<td>4.907E-5</td>
<td>.000</td>
<td>.089</td>
</tr>
<tr>
<td></td>
<td>Distress</td>
<td>-.001</td>
<td>.001</td>
<td>-.075</td>
</tr>
<tr>
<td>2</td>
<td>Genetic Risk</td>
<td>5.353E-5</td>
<td>.000</td>
<td>.097</td>
</tr>
<tr>
<td></td>
<td>Distress</td>
<td>-.001</td>
<td>.001</td>
<td>-.075</td>
</tr>
<tr>
<td></td>
<td>Social Support</td>
<td>.052</td>
<td>.106</td>
<td>.057</td>
</tr>
<tr>
<td>3</td>
<td>Genetic Risk</td>
<td>4.368E-5</td>
<td>.000</td>
<td>.079</td>
</tr>
<tr>
<td></td>
<td>Distress</td>
<td>-.001</td>
<td>.001</td>
<td>-.092</td>
</tr>
<tr>
<td></td>
<td>Social Support</td>
<td>.022</td>
<td>.105</td>
<td>.024</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>-.039</td>
<td>.020</td>
<td>-.224</td>
</tr>
<tr>
<td>4</td>
<td>Genetic Risk</td>
<td>5.925E-5</td>
<td>.000</td>
<td>.108</td>
</tr>
<tr>
<td></td>
<td>Distress</td>
<td>.000</td>
<td>.001</td>
<td>-.040</td>
</tr>
<tr>
<td></td>
<td>Social Support</td>
<td>-.011</td>
<td>.102</td>
<td>-.012</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>-.042</td>
<td>.019</td>
<td>-.241</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>-.093</td>
<td>.035</td>
<td>-.293</td>
</tr>
</tbody>
</table>
Discussion.

Age and BMI had the most profound effect on the development of T2DM based on the analysis of the data collection. These findings are consistent with the wealth of literature on the risk for T2DM posed by advancing age and obesity (ADA, 2004; Patel & Macerollo, 2010; The, Richardson, & Gordon-Larsen, 2013). The American Diabetes Association (2004) summarized the impact of advancing age and obesity on insulin resistance as T2DM may go undiagnosed for many years. Patel and Macerollo (2010) stated that clinical practice recommendations are encouraged to diagnose or rule out diabetes if patients present with hypertension or hyperlipidemia. Assuming practice recommendations are followed by providers treating patients with a new diagnosis of hypertension or hyperlipidemia; the only potential issue that would delay early diagnosis of T2DM, or hypertension or hyperlipidemia, would be a patient that does not see a provider at least once annually. An assessment leading to a diagnosis of T2DM may be delayed due to a patient’s undervaluation of the benefit of a well-patient exam.

This study is consistent with others regarding the significant impact of obesity on the development of T2DM. For example, The et al. (2013) found that obesity persisting since adolescence can increase the risk for developing T2DM more than two-fold. The mean age of subjects being less than 65 years in this study also supports the greater impact of obesity versus age on the development of T2DM for the sample. Cheng et al. (2013) stated that the prevalence of diabetes for subjects >64 years was nearly four-times more than for subjects between 35-64 years; however, obesity explained greater risk for subjects <65 years.
Distress from stressful life events was not significant to the development of T2DM for the subjects in this study. There are two possible explanations. First, the onset of T2DM may have occurred more than 6 months prior to the diagnosis. Measurement of distress for the six months prior to the diagnosis of T2DM may not be relevant if the patient has delayed assessment by a provider until complications from hyperlipidemia, hypertension, or T2DM arise. Second, distress is more than stressful life events. Reviewing the limitations for the study and the conceptual framework, particularly McEwen’s (1998) theory of allostatic load, an analysis of distress should include an inventory of daily stressors.

RQ #3: In adults with T2DM, what is the difference in risk factors between veteran and non-veteran subjects?

SSM subgroup.

The average subject was a 57 year old, married, non-Hispanic, white male, who had at least a high school diploma, and a mother, father, or sibling with a known diagnosis of diabetes. The average subject’s HbA1c was 8.9%, BMI was 33.2, stress score was 287.0 LCU, and had no history of mental illness. Removing the outliers for the subgroup, 21 subjects experienced six or more events with a mean RLCQ score of 432.1 LCU (SD=146.2).

VA subgroup.

The average subject was a 58 year old, married, non-Hispanic, white male, who had a college degree, and a mother with a known diagnosis of diabetes. The average subject’s HbA1c was 7.6%, BMI was 34.9, stress score was 308.9 LCU, and had no history of
mental illness. Removing the outliers for the subgroup, 25 subjects experienced six or more events with a mean RLCQ score of 431.5 LCU (SD=160.6).

Analyses to understand the differences in mean BMI, GRD, HbA1c, and RLCQ scores were conducted. An independent samples t-test and Lavene’s test for equality of variances were run for each variable in SPSS (See Tables 7, 8, 9, & 10). There was a significant difference in HbA1c (t=2.768, p=.007). The difference in BMI was not significant (t=-1.158, p=.250; F=1.040, p=.311). The difference in RLCQ scores was not significant (t=-.487, p=.628; F=.248, p=.620).

Table 7
Independent Samples T-Test: BMI Comparison for SSM and VA Subgroups

<table>
<thead>
<tr>
<th>Levene’s Test</th>
<th>t-test for Equality of Means</th>
</tr>
</thead>
<tbody>
<tr>
<td>F, Sig.</td>
<td>t, df, Sig. (2-tailed)</td>
</tr>
<tr>
<td>SUM Equal variances assumed</td>
<td>1.040, .311</td>
</tr>
<tr>
<td>SUM Equal variances not assumed</td>
<td>-1.161</td>
</tr>
</tbody>
</table>

Table 8
Independent Samples T-Test: GRD Comparison for SSM and VA Subgroups

<table>
<thead>
<tr>
<th>Levene’s Test</th>
<th>t-test for Equality of Means</th>
</tr>
</thead>
<tbody>
<tr>
<td>F, Sig.</td>
<td>t, df, Sig. (2-tailed)</td>
</tr>
<tr>
<td>SUM Equal variances assumed</td>
<td>7.055, .010</td>
</tr>
<tr>
<td>SUM Equal variances not assumed</td>
<td>-1.343</td>
</tr>
</tbody>
</table>
### Table 9
Independent Samples T-Test: HbA1c Comparison for SSM and VA Subgroups

<table>
<thead>
<tr>
<th>Levene’s Test</th>
<th>t-test for Equality of Means</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
<td>t</td>
<td>df</td>
<td>Sig. (2-tailed)</td>
</tr>
<tr>
<td>SUM</td>
<td>Equal variances</td>
<td>.967</td>
<td>.329</td>
<td>2.768</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>assumed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Equal variances</td>
<td></td>
<td></td>
<td>2.773</td>
<td>76.012</td>
</tr>
<tr>
<td></td>
<td>not assumed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 10
Independent Samples T-Test: RLCQ Score Comparison for SSM and VA Subgroups

<table>
<thead>
<tr>
<th>Levene’s Test</th>
<th>t-test for Equality of Means</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>Sig.</td>
<td>t</td>
<td>df</td>
<td>Sig. (2-tailed)</td>
</tr>
<tr>
<td>SUM</td>
<td>Equal variances</td>
<td>.248</td>
<td>.620</td>
<td>-.487</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>assumed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Equal variances</td>
<td></td>
<td></td>
<td>-.486</td>
<td>75.950</td>
</tr>
<tr>
<td></td>
<td>not assumed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discussion.**

The average subject from each group had relatively similar ages. Subjects from the SSM subgroup were more likely to have more than one family member with a known diagnosis of diabetes while the average subject in the VA subgroup had a mother with a known diagnosis of diabetes.

The variance in BMI and HbA1c appeared to present an inverse relationship to each other in examining the outcomes for each subgroup. While the HbA1c was higher for the SSM subgroup, the age, BMI, and RLCQ scores for the SSM subgroup were lower in comparison to the VA subgroup.

The relationship between distress and BMI could be explained by coping mechanisms described by Lazarus and Folkman (1984) and McEwen (1998). The immediate environment for each subject may present a weak or strong support system.
relative to the type of stressor encountered. For example, where a good friend may have experience with a challenging process such as adoption, that friend may have conflicting values in terms of how to raise a child. With no one to help, each subject could choose from a myriad of measures for coping with a challenge that are also influenced by subconscious agendas. Agendas could include hope or hopelessness and a loci of control; if the situation is appraised as hopeless or the subject has no control over the situation, coping mechanisms may be maladaptive (Lazarus & Folkman, 1984).

Maladaptive responses could also be more complex than excess calorie consumption for some subjects, where chronic distress from stressful life events may persist well beyond the six month to one year timeframe used by Miller and Rahe (1997). In such cases, insulin resistance secondary to chronic or chronic-intermittent secretion of cortisol. McEwen (1998) identifies such cases as a prolonged response or repeated “hits” of distress influencing an individual’s allostatic load.

Some subjects shared more detail than required for the interview. Where the RLCQ only requires yes or no answers in regards to whether or not the subject experienced the event, some subjects elaborated on the event. The subjects indicated that although one or more events may not have occurred within the previous six months, the event(s) were still troubling them. Multiple subjects stated such when asked if they lost a family member or friend within the previous six months. The response about the relative event would be “no, but I’m still depressed” or “not within the past six months, but it’s still difficult.”

Considering the theories of Lazarus and Folkman (1984) and McEwen (1998), subjects may have had trouble coping with the loss of a loved friend or family member. In response they may have chosen maladaptive coping mechanisms that complicated their
respective allostatic loads and cortisol secretion. Such maladaptive responses to coping may be learned behaviors from family members. In the case of distress and BMI, family members may show support but undermine healthy eating in terms of poor food choices during times of distress (Wang, Phert, & Lemon, 2014).

Several of the subjects who indicated still struggling with the loss of a loved one also indicated having a mental illness, typically depression, and that their treatment was effective. Further clarification of the term “treatment” may be needed in future studies as subjects in this study may have only considered how they were feeling at the time of the interview, or included maladaptive coping techniques such as malnutrition as a part of effective treatment for mental illness.

The relationship between depression and the development of T2DM was well explained in the literature (Palinkas et al., 2004; Everson-Rose et al., 2004; Khambaty et al., 2018). The subjects that indicated the loss of a loved one was still difficult or that they were still depressed also indicated that they believed their treatment for mental illness was effective. This finding supports Khambaty et al.’s (2018) findings from a nine-year study on depression and the risk for diabetes; regardless of treatment, a third of the researchers’ sample (n=39) developed diabetes.

The lower HbA1c in the VA subgroup could be evidence of greater coping mechanisms from distress regardless of the presence of mental illness, or due to the number of veterans diagnosed with mental illness. Although the average subject had no diagnosis of mental illness, nearly half the VA subgroup had a diagnosis of mental illness (n=19), 10 of which had depression and 8 of which had PTSD (not exclusive of comorbid depression).
The lower mean HbA1c for the VA subgroup could indirectly support a meta-analysis of 47 studies conducted by Morris et al. (2012) that concluded subjects with PTSD and PTSD with major depressive disorder (MDD) had lower daily cortisol output ($d= -.36, SE=.15, p=.008$ and $d=-.65, SE=.25, p=.008$, respectively). Nineteen of the studies reviewed by Morris et al. (2012) included participants with PTSD and PTSD with MDD secondary to combat/war experience; 21 of the studies, likely not all exclusive of the 19 studies regarding combat/war experience, included PTSD and PTSD with MDD secondary to torture or witnessing a trauma.

Morris et al. (2012) suggest that individuals with PTSD may have lower daily cortisol production as a form of adaptation to allow for an adequate response to future threats. Indirectly, this lower daily cortisol production in response to stressful life events may also result in lower HbA1c levels. Although this adaptive response may be helpful for individuals with PTSD, diagnosed with T2DM or potentially exposed to future threats, several authors such as Pervanidou (2008) state that reduction of daily cortisol output could lead to unregulated sympathetic nervous system activity and increasing norepinephrine levels leading to sustained hyperarousal and increased sensitivity to fear and threats promoting anxiety (as cited in Morris et al., 2012).

The variance in stress scores between the two groups presents an interesting finding. Examining stressful life events up to six months prior to the diagnosis of T2DM required an RLCQ score of $\geq 300$ LCU to be significant (Miller & Rahe, 1997). Although the variance was not significantly different from the SSM subgroup, the average subject from the VA subgroup had significant distress prior to their diagnosis of T2DM.
Summary

For the sample (N=79) the average subject was a 58 years old, non-Hispanic, married, Caucasian male with a college degree and a mother with a known diagnosis of diabetes. The average subject’s hemoglobin A1c (HbA1c) was 8.3%, BMI was 34.1, had no history of mental illness, an ESSI score of 15, and an RLCQ score of 297.6 LCU.

Age, BMI, GRD, distress, and social support explained 8.9% of the variation in HbA1c (adjusted $R^2=.089$, $F=6.910$, $p=.010$). Age and BMI were significant ($\beta=-.241$, $p=.031$ and $\beta=-.293$, $p=0.10$, respectively).

The comparison of the average subjects from the SSM and VA subgroups presented slight differences in age, BMI, GRD, and distress in terms of RLCQ scores. While the mean HbA1c for the subgroups were significantly different, the differences in age, BMI, and RLCQ scores were not significantly different.
CHAPTER V
SUMMARY AND CONCLUSIONS

Summary of the Study

Type 2 diabetes mellitus (T2DM) appears to be a disease of multifactorial origin as multiple factors influence insulin sensitivity. Genetic risk for disease (GRD), age, BMI, and distress, from a variety of sources, can promote insulin resistance and the development of T2DM. The purpose of this study was to examine the influence of stressful life events, social support, BMI, age, and GRD on the development of T2DM.

The research questions guiding this study included:
1. In adults with T2DM, how much distress was present six months prior to the diagnosis of T2DM?
2. What is the individual and combined effect of distress, social support, age, BMI, and GRD on the HbA1c level?
3. In adults with T2DM, what is the difference in risk factors between veteran and non-veteran subjects?

The estimated sample size needed for this study was determined to be 80 subjects as a result of using G-power analysis with an effect size between small and medium ($f^2 = 0.17$, $p < 0.05$, and 5 predictors). Subjects ($N=79$) were recruited from SSM Health Centers and VA Medical Centers in the greater St. Louis area. Subjects diagnosed with T2DM within six months of the potential time of recruitment completed the Recent Life Changes Questionnaire (RLCQ), ENRICHD Social Support Instrument (ESSI), and an investigator-developed demographic survey following completion of informed consent at the time of the potential interview.
The data was analyzed using SPSS 25. Statistical analyses included descriptive, multiple regression, and independent sample t-test analyses. An alpha level of 0.05 was used for statistical comparisons.

Results

The average subject was a 58 years old, non-Hispanic, married, Caucasian male with a college degree and a mother with a known diagnosis of diabetes. The average subject’s hemoglobin A1c (HbA1c) was 8.3%, BMI was 34.1, and the subject had no history of mental illness.

The mean RLCQ score was 297.6 LCU ($SD=202.0$). Despite the mean RLCQ scores being less than 300 life change units (LCU), 36 of the 79 subjects had significant distress. Only considering subjects that experienced six or more events ($n=46$) resulted in a mean RLCQ score of 431.74 LCU ($SD=152.5$) and a median RLCQ score of 408 LCU.

Age, BMI, GRD, distress, and social support explained 8.9% on the variance in HbA1c ($R^2=.089$, $F=6.910$, $p=.010$). Age and BMI significantly explained portions of the total variance in the dependent variable ($\beta=-.241$, $p=.031$ and $\beta=-.293$, $p=0.10$, respectively). Distress was not significant in the model ($\beta=-.040$, $p=.721$).

The VA subgroup had an insignificantly greater mean BMI (34.9 vs 33.2, $p=.311$) and mean stress score (308.9 LCU vs 287.0 LCU, $p=.620$) compared to the SSM subgroup. However, the VA subgroup had a significantly lower HbA1c in comparison to the SSM subgroup despite having greater mean BMI and stress score (7.6% vs 8.9%, $p=.007$).
Implications

The implications for healthcare include the prevention or management of T2DM and the management of mental health disparities, particularly among individuals diagnosed with major depressive disorder (MDD) or post-traumatic stress disorder (PTSD). While distress in terms of stressful life events was not significant in this study, the analyses support existing literature in that advancing age and elevated BMI remain important factors for consideration in the prevention and management of T2DM. The inverse relationship between the hemoglobin A1c (HbA1c) and the examined risk factors BMI and distress among the VA subgroup, in comparison to the SSM subgroup, presented an unexpected finding. The finding may suggest that individuals with mental health disparities such as MDD and PTSD may be at greater risk for comorbidities secondary to hypocortisolism such as irregular immune function or conditions related unsuppressed norepinephrine release.

Comparison with Literature Review

Building on the research of Li et al. (2013), Mooy et al. (2000), and Novak et al. (2013), this study used the RLCQ as a more comprehensive assessment of distress. It examined the amount of available social support in relation to RLCQ scores. Subjects recalled the six-month period preceding their diagnosis of T2DM and indicated if any of the events applied to that six-month period of time. This study also revealed an unexpected qualitative component as some subjects elaborated on life experiences beyond the yes or no questions that were asked.

Where Li et al. (2013) and Mooy et al. (2000) focused more on their respective subjects’ experiences with or exposure to loss of loved ones, this study also examined
other forms of distressing circumstances that may ultimately be a positive experience such as getting a promotion with its added responsibilities, or a negative experience such as financial challenges. The RLCQ questions regarding loss of loved ones had LCU scores consistent with the impact of such losses described by Li et al. (2012) and Mooy et al. (2000). The LCU scores for such events ranged from “death of a close personal friend” at 70 LCU to “loss of a spouse” at 119 LCU (Miller & Rahe, 1997). The impact of cumulative events identified in Mooy et al.’s (2000) study and McEwen’s (1998) theory of allostasis supported use of the RLCQ for the measurement of distress in this study. Analysis revealed that many subjects experienced non-loss related events such as having a major change in living conditions ($n=18$) or needing to make a major decision about their immediate future ($n=24$) that contributed toward their total RLCQ scores.

This study also examined the differences between veteran and non-veteran subjects. Examining the combined contribution of distress, social support, age, BMI, and GRD provided a method for comparing the impact of the risk factors between the subgroups. Considering the process of appraising distress and the various coping responses described by Lazarus and Folkman (1984), veterans may have learned to respond to distress differently as a result of their experiences serving in the military. While their exposure to the events on the RLCQ may be similar to a non-veteran, the resulting impact on glucose levels, and ultimately their HbA1c, may be different as a result of a unique appraisal process and physiological response that uses less cortisol.

**Recommendations for Future Research**

The gaps in the literature included a comprehensive assessment of distress including daily or weekly stressors and a comprehensive assessment of mental illness with
respective treatments in relation to distress. Future research needs to include a comprehensive assessment of distress and mental illness to better understand the relationship between distress and the developing of T2DM.

While identifying and understanding the potential risk for T2DM from stressful life events can be helpful for treating patients struggling with a recent history of multiple calamities, a methodological approach that incorporates a measure of exposure to stress similar to Novak et al.’s (2013) study may provide a greater understanding of the relationship between distress and the development of T2DM. Some individuals may still experience considerable distress from life and work demands not identified as pinnacle or unique events on the RLCQ. A daily or weekly stress inventory for individuals at risk for diabetes with an HbA1c between 5.7% and 6.4% per ADA’s (2019) criteria would provide greater insight into the impact distress has on the development of T2DM.

A next step is to follow individuals newly diagnosed at risk for diabetes for 6-12 months. A daily distress inventory with a numeric scaling system would be maintained by subjects. The inventory would evaluate the stressor in terms of who was involved, duration of the stressful period, and what the individual perceived was at stake (Almeida, Wethington, & Kessler, 2002). The RLCQ needs to be conducted at six months and or 12 months during follow-up appointments. Analyses would be conducted to examine the combined effect of stressful life events and daily stressors to provide a broader or two-fold definition of distress.

Future research should also address the relationship between mental illness, particularly MDD and PTSD, and distress as they relate to the development of T2DM. As this study suggested that individuals with mental illness may have lower HbA1c levels
than individuals without mental illness, examining how mental illness and associated treatments impact distress and coping could provide greater understanding of how an individual’s primary appraisal of a stressor influences insulin resistance secondary to the cortisol secretion that occurs with the appraisal (Chrousos, 2000; Lazarus & Folkman, 1984; Kendall-Tackett, 2009).

Individuals diagnosed as being at risk for T2DM and being treated for a mental illness would be followed for 6-12 months. A control group with no mental illness would also be followed. A daily or weekly distress inventory and mental wellbeing assessment would be analyzed in relation to scheduled BMI, cortisol, and HbA1c assessments. The mental illness and control groups would be compared in terms of distress, mental health, BMI, cortisol levels, and HbA1c.

These approaches to future research would aim to understand how distress and individual responses to distress, coping, can influence the development of T2DM; especially in consideration of the conceptual framework comprising the theories of the stress response, stress appraisal and coping, and allostatic load. Recognizing the complexity of the stress response and the potential harm posed by dysregulation of cortisol secretion in homeostasis, understanding how individuals manage distress or perceive their ability to cope with mounting distress could help clinicians provide optimal resources or support in the prevention of T2DM.
REFERENCES


## Recent Life Changes Questionnaire

### Health

<table>
<thead>
<tr>
<th>Event</th>
<th>LCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>An illness or injury that kept you in bed for more than a week or sent you to the hospital</td>
<td>74</td>
</tr>
<tr>
<td>An illness or injury that was less serious than above</td>
<td>44</td>
</tr>
<tr>
<td>Major dental work</td>
<td>26</td>
</tr>
<tr>
<td>Major change in eating habits</td>
<td>27</td>
</tr>
<tr>
<td>Major change in sleeping habits</td>
<td>26</td>
</tr>
<tr>
<td>Major change in your usual type and/or amount of recreation</td>
<td>28</td>
</tr>
</tbody>
</table>

### Work

<table>
<thead>
<tr>
<th>Event</th>
<th>LCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change to a new type of work</td>
<td>51</td>
</tr>
<tr>
<td>Change in your work hours or conditions</td>
<td>35</td>
</tr>
<tr>
<td>More work responsibilities</td>
<td>29</td>
</tr>
<tr>
<td>Fewer work responsibilities</td>
<td>21</td>
</tr>
<tr>
<td>A promotion</td>
<td>31</td>
</tr>
<tr>
<td>A demotion</td>
<td>42</td>
</tr>
<tr>
<td>A transfer</td>
<td>32</td>
</tr>
<tr>
<td>Trouble with your boss</td>
<td>29</td>
</tr>
<tr>
<td>Trouble with your coworkers</td>
<td>35</td>
</tr>
<tr>
<td>Trouble with those you supervise</td>
<td>35</td>
</tr>
</tbody>
</table>
### Work

<table>
<thead>
<tr>
<th>Event</th>
<th>LCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other work troubles</td>
<td>28</td>
</tr>
<tr>
<td>Major business readjustment</td>
<td>60</td>
</tr>
<tr>
<td>Retirement</td>
<td>52</td>
</tr>
<tr>
<td>Laid off</td>
<td>68</td>
</tr>
<tr>
<td>Fired</td>
<td>79</td>
</tr>
<tr>
<td>Took a course to help your work</td>
<td>18</td>
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### Home and family

<table>
<thead>
<tr>
<th>Event</th>
<th>LCU</th>
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<tbody>
<tr>
<td>Move within same city or town</td>
<td>25</td>
</tr>
<tr>
<td>Move to different town, city, or state</td>
<td>47</td>
</tr>
<tr>
<td>Major change in living conditions</td>
<td>42</td>
</tr>
<tr>
<td>Change in family get-togethers</td>
<td>25</td>
</tr>
<tr>
<td>Major change in health or behavior of a family member</td>
<td>55</td>
</tr>
<tr>
<td>Marriage</td>
<td>50</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>67</td>
</tr>
<tr>
<td>Miscarriage or abortion</td>
<td>65</td>
</tr>
<tr>
<td>Birth of a child</td>
<td>66</td>
</tr>
<tr>
<td>Adoption of a child</td>
<td>65</td>
</tr>
<tr>
<td>Relative moves in with you</td>
<td>59</td>
</tr>
<tr>
<td>Spouse begins or stops work</td>
<td>46</td>
</tr>
<tr>
<td>Child leaves home to attend college or for marriage</td>
<td>41</td>
</tr>
<tr>
<td><strong>Home and family</strong></td>
<td><strong>LCU</strong></td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Child leaves home for other reasons</td>
<td>45</td>
</tr>
<tr>
<td>Change in arguments with spouse</td>
<td>50</td>
</tr>
<tr>
<td>Problems with relatives or in-laws</td>
<td>38</td>
</tr>
<tr>
<td>Parents divorce</td>
<td>59</td>
</tr>
<tr>
<td>A parent remarries</td>
<td>50</td>
</tr>
<tr>
<td>Separation from spouse due to work</td>
<td>53</td>
</tr>
<tr>
<td>Separation from spouse due to marital difficulties</td>
<td>79</td>
</tr>
<tr>
<td>Divorce</td>
<td>96</td>
</tr>
<tr>
<td>Birth of grandchild</td>
<td>43</td>
</tr>
<tr>
<td>Death of spouse</td>
<td>119</td>
</tr>
<tr>
<td>Death of child</td>
<td>123</td>
</tr>
<tr>
<td>Death of parent</td>
<td>100</td>
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<td>Death of a brother or sister</td>
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<table>
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<th><strong>Personal and social</strong></th>
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<tbody>
<tr>
<td>Change in personal habits</td>
<td>26</td>
</tr>
<tr>
<td>Beginning or ending school</td>
<td>38</td>
</tr>
<tr>
<td>Change of school or college</td>
<td>35</td>
</tr>
<tr>
<td>Change in political beliefs</td>
<td>24</td>
</tr>
<tr>
<td>Change in religious beliefs</td>
<td>29</td>
</tr>
<tr>
<td>Change in social activities</td>
<td>27</td>
</tr>
<tr>
<td>Personal and social</td>
<td>LCU</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>-----</td>
</tr>
<tr>
<td>Vacation</td>
<td>24</td>
</tr>
<tr>
<td>New, close personal relationship</td>
<td>37</td>
</tr>
<tr>
<td>Engagement to marry</td>
<td>45</td>
</tr>
<tr>
<td>Girlfriend or boy friend problems</td>
<td>39</td>
</tr>
<tr>
<td>Sexual difficulties</td>
<td>44</td>
</tr>
<tr>
<td>An accident</td>
<td>48</td>
</tr>
<tr>
<td>“Falling out” of a close personal relationship</td>
<td>47</td>
</tr>
<tr>
<td>Minor violation of the law</td>
<td>20</td>
</tr>
<tr>
<td>Being held in jail</td>
<td>75</td>
</tr>
<tr>
<td>Major decision about immediate future</td>
<td>51</td>
</tr>
<tr>
<td>Major personal achievement</td>
<td>36</td>
</tr>
<tr>
<td>Death of a close personal friend</td>
<td>70</td>
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<table>
<thead>
<tr>
<th>Financial</th>
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<tbody>
<tr>
<td>Major loss of income</td>
<td>60</td>
</tr>
<tr>
<td>Major increase in income</td>
<td>38</td>
</tr>
<tr>
<td>Investment and/or credit difficulties</td>
<td>56</td>
</tr>
<tr>
<td>Loss/damage to personal property</td>
<td>43</td>
</tr>
<tr>
<td>Major purchase</td>
<td>37</td>
</tr>
<tr>
<td>Moderate purchase</td>
<td>20</td>
</tr>
<tr>
<td>Foreclosure on mortgage or loan</td>
<td>58</td>
</tr>
</tbody>
</table>
APPENDIX B

ENRICHD Social Support Instrument

1. Is there someone available to whom you can count on to listen to you when you need to talk?
   i. Most of the time
   ii. All of the time
   iii. None of the time
   ii. A little of the time
   iii. Some of the time

2. Is there someone available to you to give you good advice about a problem?

3. Is there someone available to you who shows you love and affection?

4. Is there someone available to help with daily chores?

5. Can you count on anyone to provide you with emotional support (talking over problems or helping you make a difficult decision)?

6. Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide in?

7. Are you currently married or living with a partner?
APPENDIX C

Demographic Survey

Date of diagnosis: ________________
HbA1C level: ________________
Age at time of diagnosis: ____________
Height and weight or BMI: __________

Any current diagnosis of mental illness? _____
- Depression
- Anxiety
- PTSD
- Other
If yes to previous question, do you feel like your current treatment is effective? YES / NO

Gender: MALE / FEMALE

Ethnicity: LATINO / NON-LATINO

Race:
- Arab
- Asian/ Pacific Islander
- Black
- Hispanic
- Caucasian/ White
- Multiracial
- Other: ____________________________

What is your marital status?
- Married
- Divorced
- Separated
- Single
- Widowed
- Living with partner

Do you have a family member that was diagnosed with diabetes? YES / NO
If so:
- Mother
- Father
- Grandparent
- Sibling
- Aunt
- Uncle

What was your highest level of education?
- 10th grade or less
- High school diploma
- GED
- Some college
- College degree
SSM Health Center
University of Missouri – St. Louis
Informed Consent Cover Letter
Stress and Type 2 Diabetes

Dear Potential Research Study Participant,

Thank you for your interest in this study. My name is Joshua Minks, and I am a doctoral student in the nursing department at the University of Missouri – St. Louis.

This research study is designed to look at the relationship between distress and type 2 diabetes. Results of this research will be used to compare the effect of distress to known risk factors such as family history and obesity at the time a person is diagnosed with type 2 diabetes.

If you volunteer to participate in this study, you will be asked to complete two surveys and some background information during a face-to-face interview. The interview may take 10-15 minutes, depending on the time taken to answer questions.

The surveys look at stressful life events and social support. For some individuals, recalling such events may cause emotional discomfort. The research may benefit future diabetes studies and the prevention and management of diabetes.

No one will be able to see your personal identifiable information except for myself. No names will be placed on the surveys. There will be no publicly-known way to connect you with the information collected as only I will have the consent forms and the information provided will be coded. Your signed consent will be kept in another file from your information. You may choose to withdraw at any time during the interview. If you have any questions about your rights as a research participant, please contact the Human Subjects Research Office at the College of Nursing, University of Missouri – St. Louis (314-516-5928).

This research project has been reviewed and approved by the Human Subjects Research Office at the College of Nursing, University of Missouri – St. Louis and the Human Subjects Committee associated with the diabetes clinic that you attend.

Again, I thank you for your interest in participating in this study. Please keep this cover letter for your records.

Sincerely,

Joshua Minks, MSN-FNP, RN
Doctoral Student
Department of Nursing
University of Missouri – St. Louis
You are invited to participate in a research study with Deborah Fritz PhD, a Nurse Practitioner at VA St. Louis Health Care System and Joshua Minks MSN-FNP, a Doctoral Student with the University of Missouri. The purpose of this study is to look at the relationship between stressful life events to known risk factors such as family history and obesity at the time a person is diagnosed with type II diabetes. This research may benefit future diabetes studies and the prevention and management of diabetes.

If you decide to volunteer:

You will be asked to fill out 3 surveys during a face to face interview. Completing all 3 surveys should not take more than 45 minutes.

The surveys look at stressful life events and social support over the past 6 months, basic background information, and information regarding diabetes history.

Basic background information includes: age, gender, ethnicity, race, marital status, education, and current diagnosis of mental illness.

Diabetes history includes most recent Hemoglobin A1c (test which gives an overall picture of average blood sugars over about 3 months), height and weight, and family history of diabetes.

For some individuals, recalling such stressful life events may cause emotional discomfort. Should you experience emotional discomfort, a psychologist is on call to meet with you.

If you have any questions, please call Deborah Fritz PhD at cell number 314-403-3600 during normal business hours, 9am to 5pm.

Participating in research is voluntary. It won’t affect your treatment at the VA Saint Louis Health Care System. In the next week, you will be contacted by phone to tell us if you would like to participate in this study. Attached is the consent form associated with this study for your review.

Thank you for your consideration,

Sincerely,

Deborah Fritz  PhD FNP  
Nurse Practitioner  
VA St. Louis Health Care System

Joshua Minks MSN-FNP  
University of Missouri, St. Louis
APPENDIX E

Human Subjects Approvals

University

Office of Research Administration

One University Boulevard
St. Louis, Missouri 63121-4499
Telephone: 314-516-5599
Fax: 314-516-0709
E-mail: ora@umsl.edu

DATE: March 14, 2017
TO: Joshua Minks, MSN-FNP
FROM: University of Missouri-St. Louis IRB
PROJECT TITLE: [1034753-1] The influence of stressful life events on the development of type 2 diabetes
REFERENCE #: 
SUBMISSION TYPE: New Project
ACTION: APPROVED
APPROVAL DATE: March 14, 2017
EXPIRATION DATE: March 14, 2018
REVIEW TYPE: Expedited Review
REVIEW CATEGORY: Expedited review categories # 5, 7

The chairperson of the University of Missouri-St. Louis IRB has reviewed the above mentioned protocol for research involving human subjects and determined that the project qualifies for expedited review under Title 45 Code of Federal Regulations Part 46.110b. The time period for this approval expires one year from the date listed below. You must notify the University of Missouri-St. Louis IRB in advance of any proposed major changes in your approved protocol, e.g., addition of research sites or research instruments.

You must file an annual report with the committee. This report must indicate the starting date of the project and the number of subjects to date from start of project, or since last annual report, whichever is more recent.

Any consent or assent forms must be signed in duplicate and a copy provided to the subject. The principal investigator must retain the other copy of the signed consent form for at least three years following the completion of the research activity and they must be available for inspection if there is an official review of the UM-St. Louis human subjects research proceedings by the U.S. Department of Health and Human Services Office for Protection from Research Risks.

This action is officially recorded in the minutes of the committee.
NOTICE OF APPROVAL FOR HUMAN RESEARCH

DATE: April 01, 2016
TO: Minke, Joshua, Nursing
FROM: Fowlor, Karyn, MD, CMO, SSMSTL IRB
PROTOCOL TITLE: The influence of stressful life events on the development of type 2 diabetes
FUNDING SOURCE: NONE
PROTOCOL NUMBER: 16-11-2991
APPROVAL PERIOD: Approval Date: December 20, 2017 Expired Date: December 19, 2018

The Institutional Review Board (IRB) has reviewed and approved the protocol submission and the pertinent attachments listed in the Event history for protocol 16-11-0991 CONTINUING REVIEW titled The influence of stressful life events on the development of type 2 diabetes, in accordance with the SSMSTL Human Research Protection Program. The approval is issued under SSM Health Care - St. Louis Federalwide Assurance Number 00008120 issued by the Office for Human Research Protections (OHRP).

The protocol must be renewed on a yearly basis as long as the research remains active unless it is approved as an Exempt study. Should the protocol not be renewed before expiration, all activities must cease until the protocol has been reviewed and renewed by the IRB.
Memorandum

Date: March 20, 2017

From: Associate Chief of Staff, Research and Development Service (151/JC)

To: Deborah Fritz, FNP, Ph.D. Principal Investigator (PI)

Subj: Associate Chief of Staff for R&E- Study Implementation Memorandum – “Influence of Stressful Life Events on the Development of Type II Diabetes.” Epromise #1193622

1. This study has been reviewed and approved by the appropriate Veterans Affairs St. Louis Health Care System (VASTLHCS) research committees and can be implemented effective the date of this memorandum. Continued approval is contingent upon satisfactory annual reviews by the appropriate sub-committees prior to the expiration date. Report forms from the sub-committees will be forwarded to you no later than two months prior to the date of expiration. If you have not received the forms by that date, please contact our office. Should your study be completed or terminated prior to that date, please contact our office so that forms can be forwarded to you for submission of your final report.

2. The Research and Development committee has concurred with the approvals of the subcommittees on March 20, 2017.

3. The Institutional Review Board (IRB), at its February 1, 2017 meeting, reviewed and contingently approved your study. Geoffrey Gorse, M.D., IRB Chair reviewed your study on February 24, 2017 and fully approved your study under the expedited process. The Main informed consent, Authorization for Release of Protected Health Information (PHI), and your recruitment tools are approved and stamped. These are the versions that must be used. Your study was not selected for flagging. In addition, your study was determined to have a minimal risk level. The IRB’s approval of this study expire will on February 1, 2018.

4 Study personnel must complete the prescribed training requirements for research from the Collaborative Institutional Training Initiative (CITI) and Talent Management System (TMS) websites prior to participating in the research and annually thereafter. Study personnel are also required to update their Scope of Practice annually. Failure to comply with annual training and scope requirements will result in administrative suspension of VA research until all requirements are in compliance. Administrative holds pending beyond 30 days will result in the revocation of a Without Compensation (WOC) appointment for non-VA employees.

5. Publications resulting from this study must maintain patient confidentiality and must acknowledge the VA and your VA appointment consistent with the guidelines in VHA Handbook 1200.19.

6. Please direct any questions concerning this approval to the IRB Administrator at (314) 289-6333 ext. 55521.
Associate Chief of Staff for R&E- Study Implementation Memorandum – “Influence of Stressful Life Events on the Development of Type II Diabetes.” Epromise #1193622

Ziyad Al-Aly, M.D.
ACOS, Research and Education Service

Attachments: Approved documents
HIPAA AUTHORIZATION FORM

Authorization for the Use and Disclosure of Personal Health Information
Resulting from Participation in a Research Study

Project Title: The Influence of Stressful Life Events on the Development of Type 2 Diabetes

You have agreed to participate in the study mentioned above. This authorization form explains how your Protected Health Information will be safeguarded. Please read carefully to be sure you agree to all of the following statements.

Description of the Protected Health Information

My authorization applies to the information described below. Only this information may be used and/or disclosed in accordance with this authorization:
Date of type 2 diabetes diagnosis, hemoglobin A1c level at time of diagnosis, age, weight, height, potential family history of diabetes, gender, ethnicity, marital status, level of education, potential concurring diagnosis of depression/anxiety/PTSD/or other mental health diagnosis, amount of distress preceding your diagnosis of type 2 diabetes, and amount of social support preceding your diagnosis of type 2 diabetes

Who may use and/or disclose the information

I authorize the following persons (or class of persons) to make the authorized use and disclosure of my PHI: Joshua Minks (PhD Student) and diabetes care providers, including nurses and diabetes educator

Who may receive the information

I authorize the following persons (or class of persons) to receive my personal health information: Joshua Minks (PhD Student)

Purpose of the use or disclosure of information

My PHI will be used and/or disclosed upon request for the following purposes:
☐ Auditing  ☐ My treatment during the study
☐ Study outcomes including safety and efficacy  ☐ Administrative and billing
☐ Submission to government agencies that may monitor the study
☐ Publications and presentation of results that may identify me as a subject
☐ Other:  __determine the potential influence or relationship of each factor (i.e. potential family history)  with the development of type 2 diabetes____

Expiration date or event
This authorization expires upon:
☐ The following date: ________________
☒ End of research study
☐ No expiration date
☐ Other: ________________

Right to revoke authorization
I understand that I have a right to revoke this authorization at any time. My revocation must be in writing in a letter sent to the Principal Investigator at College of Nursing, 1 University Blvd., St. Louis, MO 63121-4400. I am aware that my revocation is not effective to the extent that the persons I have authorized to use and/or disclose my PHI have already acted in reliance upon this authorization.

Statement that re-disclosures are no longer protected by the HIPAA Privacy Rule
I understand that my personal health information will only be used as described in this authorization in relation to the research study. I am also aware that if I choose to share the information defined in this authorization with anyone not directly related to this research project, the law would no longer protect this information. In addition, I understand that if my personal health information is disclosed to someone who is not required to comply with privacy protections under the law, then such information may be re-disclosed and would no longer be protected.

Right to refuse to sign authorization and ability to condition treatment, payment, enrollment or eligibility for benefits for research related treatment
I understand that I have a right not to authorize the use and/or disclosure of my personal health information. In such a case, I would choose not to sign this authorization document. I understand I will not be able to participate in a research study if I do not sign.

Suspension of right to access personal health information
I agree that I will not have a right to access my personal health information obtained or created in the course of the research project until the expiration of this authorization.

If I have any questions or concerns about my privacy rights I should contact, the HIPAA Compliance Officer at 314-516-5362.

I have read the above statements and have been able to express my concerns, to which the investigator has responded satisfactorily. I believe I understand the purpose of the study, as
well as the potential benefits and risks that are involved. I authorize the use of my PHI and give my permission to participate in the research described above. I certify that I have received a copy of the authorization.

All signature dates must match.

<table>
<thead>
<tr>
<th>Participant’s Signature</th>
<th>Date</th>
<th>Participant’s Printed Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent or Guardian’s Signature</td>
<td>Date</td>
<td>Parent or Guardian’s Printed Name</td>
</tr>
<tr>
<td>Witness’ Signature</td>
<td>Date</td>
<td>Witness’ Printed Name</td>
</tr>
<tr>
<td>Researcher’s Signature</td>
<td>Date</td>
<td></td>
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The Notice of Privacy Practices (a separate document) describes the procedures used by UM-SL to protect your information. If you have not already received the Notice of Privacy Practices, the research team will make one available to you.

I have been offered a copy of the UM-SL Notice of Privacy Practices.

Initial
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH PURPOSES

The Health Insurance Portability & Accountability Act (HIPAA) is a Federal law that helps to protect the privacy of your health information and to whom this information may be shared within and outside of DePaul, St. Clare, St. Joseph, or St. Mary’s Health Centers. This Authorization form is specifically for a research study entitled “The Influence of Distress on the Development of Type 2 Diabetes” and will tell you what health information (called Protected Health Information or PHI) will be collected for this research study, who will see your PHI and in what ways they can use the information. In order for the Principal Investigator, Joshua Minks, and the research study staff to collect and use your PHI, you must sign this authorization form. You will receive a copy of this signed Authorization for your records. If you do not sign this form, you may not join this study. Your decision to allow the use and disclosure of your PHI is voluntary and will have no impact on your treatment at DePaul, St. Clare, St. Joseph, or St. Mary’s Health Centers. By signing this form, you are allowing the researchers for this study to use and disclose your PHI in the manner described below.

Generally the Principal Investigator and study staff at DePaul, St. Clare, St. Joseph, or St. Mary’s Health Centers who are working on this research project will know that you are in a research study and will see and use your PHI. The researchers working on this study will collect the following PHI about you: date of type 2 diabetes diagnosis, hemoglobin A1c level at time of diagnosis, age, weight, height, potential family history of diabetes, gender, ethnicity, marital status, level of education, potential concurring diagnosis of depression/anxiety/PTSD/or other mental health diagnosis, amount of distress preceding your diagnosis of type 2 diabetes, and amount of social support preceding your diagnosis of type 2 diabetes. This PHI will be used to determine the potential influence or relationship of each factor with the development of type 2 diabetes. Your access to your PHI may be limited during the study to protect the study results.

Your PHI will not be identifiable by an investigator assisting with research collection at John Cochran and Jefferson Barracks. Your completed survey will be coded and only the Principle Investigator at your hospital, Joshua Minks, will have the key that links your name with your completed survey. DePaul, St. Clare, St. Joseph, or St. Mary’s Health Centers, including the SSMSTL Research Compliance department, and Government representatives or Federal agencies will only have access when required by law.

Your permission to use and disclose your PHI does not expire. However, you have the right to change your mind at any time and revoke your authorization. If you revoke your authorization, the researchers will continue to use the information that they previously collected, but they will not collect any additional information. Also, if you revoke your authorization you may no longer be able to participate in the research study. To revoke your permission, you must do so in writing by sending a letter to Joshua Minks, 11830
Westline Industrial Drive, Suite 106, St. Louis, MO 63146; If you have a complaint or concerns about the privacy of your health information, you may also contact the SSM Office of Research Compliance at 314-989-2032 or the CRP/Regulatory Coordinator at 636-496-2538.

The researchers and staff agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and Federal law. SSMSTL is committed to protecting your confidentiality. Please understand that once your PHI has been disclosed to anyone outside of SSMSTL, there is a risk that your PHI may no longer be protected; however other Federal and State laws may provide continued protection of your information.

________________________________________
Signature of Subject or Legally Authorized Representative

________________________________________
Date

____________________________
Print Name of Subject or Legally Authorized Representative

____________________________
Description of Legally Authorized Representative’s Authority
Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research

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<thead>
<tr>
<th>Subject Name (Last, First, Middle Initial):</th>
<th>Subject SSN (last 4 only):</th>
<th>Date of Birth:</th>
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<tr>
<th>VA Facility (Name and Address):</th>
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<tr>
<td>VA St. Louis Health Care System</td>
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<tr>
<td>915 North Grand Blvd</td>
</tr>
<tr>
<td>St. Louis, MO 63109</td>
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<tr>
<th>VA Principal Investigator (PI):</th>
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<tr>
<td>Deborah Fritz PhD</td>
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</table>

PI Contact Information:
Project cell: 314-xxxx-xxxx

Study Title:
Influence of stressful life events on the development of Type II Diabetes

Purpose of Study:
The purpose of this study is to look at the relationship between stressful life events to know risk factors such as family history and obesity at the time a person is diagnosed with type 2 diabetes. This research may benefit future diabetes studies and the prevention and management of diabetes.

USE OF YOUR INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION (IIHI):

Your individually identifiable health information is information about you that contains your health information and information that would identify you such as your name, date of birth, or other individual identifiers. VHA is asking you to allow the VA Principal Investigator (PI) and/or the VA research team members to access and use your past or present health information in addition to new health information they may collect for the study named above. The investigators of this study are committed to protecting your privacy and the confidentiality of information related to your health care.

Signing this authorization is completely voluntary. However, your authorization (permission) is necessary to participate in this study. Your treatment, payment, enrollment, or eligibility for VA benefits will not be affected, whether or not you sign this authorization.

Your individually identifiable health information used for this VA study includes the information marked below:

- Information from your VA Health Records such as diagnoses, progress notes, medications, lab or radiology findings
- Specific information concerning:
  - alcohol abuse
  - drug abuse
  - sickle cell anemia
  - HIV
- Demographic Information such as name, age, race
- Billing or Financial Records
- Photographs, Digital Images, Video, or Audio Recordings
- Questionnaire, Survey, and/or Subject Diary
- Other as described:
Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

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<tr>
<th>Subject Name (Last, First, Middle Initial):</th>
<th>Subject SSN (last 4 only):</th>
<th>Date of Birth:</th>
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USE OF YOUR DATA OR SPECIMENS FOR OTHER RESEARCH: (Instruction: When banking or further analysis is an optional research activity, complete page 5 and leave this section blank. If banking is a required research activity to store "Data" and/or "Specimen" for future use or if "Not Applicable" is selected, remove page 5 in its entirety.)

☐ Not Applicable - No Data or Specimen Banking for Other Research

An Important part of this research is to save your

☐ Data

☐ Specimen

in a secure repository/bank for other research studies in the future. If you do not agree to allow this use of your data and/or specimen for future studies approved by the required committees, such as the Institutional Review Board, you will not be able to participate in this study.

DISCLOSURE: The VA research team may need to disclose the information listed above to other people or institutions that are not part of VA. VA/VHA complies with the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Privacy Act of 1974 and all other applicable federal laws and regulations that protect your privacy. The VHA Notice of Privacy Practices (a separate document) provides more information on how we protect your information. If you do not have a copy of the Notice, the research team will provide one to you.

Giving your permission by signing this authorization allows us to disclose your information to other institutions or persons as noted below. Once your information has been disclosed outside VA/VHA, it may no longer be protected by federal laws and regulations and might be re-disclosed by the persons or institutions receiving the information.

☐ Non-VA Institutional Review Board (IRB) at _who will monitor the study_

☐ Study Sponsor/Funding Source:
  VA or non-VA person or entity who takes responsibility for; initiates, or funds this study

☑ Academic Affiliate (institution/name/employee/department): University of Missouri, St. Louis, Joshua Minks
  A relationship with VA in the performance of this study

☐ Compliance and Safety Monitors: Data Monitoring Committee
  Advises the Sponsor or PI regarding the continuing safety of this study

☐ Other Federal agencies required to monitor or oversee research (such as FDA, OHRP, GAO):
  Federal agencies such as the Office for Human Research Protection (OHRP), the Government Accounting Office (GAO), Office of Research Oversight (ORO), St. Louis VAMC IRB, VA Audit Committees and accrediting agencies will have access to the records or that records are subject to audit or inspection by a funding agency or sponsor. A copy of this consent form will be filed in your medical records.

☐ A Non-Profit Corporation (name and specific purpose):

☐ Other (e.g. name of contractor and specific purpose):
Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

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<th>Date of Birth:</th>
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Note: Offices within VA/VHA that are responsible for oversight of VA research such as the Office of Research Oversight (ORO), the Office of Research and Development (ORD), the VA Office of Inspector General, the VA Office of General Counsel, the VA IRB and Research and Development Committee may also have access to your information in the performance of their VA/VHA job duties.

Access to your Individually Identifiable Health Information created or obtained in the course of this research:

☑ will have access to your research related health records
☐ will not have access to your research related health records

This will not affect your VA healthcare including your doctor's ability to see your records as part of your normal care and will not affect your right to have access to the research records after the study is completed.

REVOCATION: If you sign this authorization you may change your mind and revoke or take back your permission at any time. You must do this in writing and must send your written request to the Principal Investigator for this study at the following address:

VA St. Louis Health Care System
915 North Grand Blvd
St. Louis, MO 63109

If you revoke (take back) your permission, you will no longer be able to participate in this study but the benefits to which you are entitled will NOT be affected. If you revoke (take back) your permission, the research team may continue to use or disclose the information that it has already collected before you revoked (took back) your permission which the research team has relied upon for the research. Your written revocation is effective as soon as it is received by the study's Principal Investigator.

EXPIRATION: Unless you revoke (take back) your permission, your authorization to allow us to use and/or disclose your information will:

☑ Expire at the end of this research study
☐ Data use and collection will expire at the end of this research study. Any study information that has been placed into a repository to be used for future research will not expire.
☐ Expire on the following date or event:
☐ Not expire
Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

<table>
<thead>
<tr>
<th>Subject Name (Last, First, Middle Initial):</th>
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<th>Date of Birth:</th>
</tr>
</thead>
</table>

**TO BE FILLED OUT BY THE SUBJECT**

Research Subject Signature. This permission (authorization) has been explained to me and I have been given the opportunity to ask questions. If I believe that my privacy rights have been compromised, I may contact the VHA facility Privacy Officer to file a verbal or written complaint.

I give my authorization (permission) for the use and disclosure of my individually identifiable health information as described in this form. I will be given a signed copy of this form for my records.

<table>
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<tr>
<th>Signature of Research Subject</th>
<th>Date</th>
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<tr>
<th>Signature of Legal Representative (if applicable)</th>
<th>Date</th>
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To Sign for Research Subject (Attach authority to sign: Health Care Power of Attorney, Legal Guardian appointment, or Next of Kin if authorized by State Law)

Name of Legal Representative (please print)

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114
Informed Consent Form

Project Title: The Influence of Stressful Life Events on the Development of Type 2 Diabetes
Investigator: Joshua Minks, MSN-FNP, PhD Candidate
Department: Nursing
University of Missouri – St. Louis
Phone Number: 314-403-3600

I understand that the purpose of this research project is to examine the influence of stressful life events on the development of type 2 diabetes. I have been chosen to participate in this study because I was diagnosed with type 2 diabetes within the previous 6 months. I understand that as a research subject I will complete the Recent Life Changes Questionnaire (RLCQ) to determine the amount of distress in terms of stressful life events that I experienced near the time of diagnosis. I will complete the ENRICHD social support instrument (ESSI) to determine available social support present during the same period of time. I will also provide demographic data (background information) that may not be available in my medical records.

I understand that the interview may take 10-15 minutes depending on my ability to recall and answer questions asked of me by the investigator.

I understand that my participation is voluntary; I may refuse to participate and/or discontinue my participation at any time without penalty or prejudice. The health care services I receive by the provider that manages my diabetes will not be influenced by my participation in this study, refusal to participate, or withdrawing from the study.

I understand that all information collected in this study will be held confidential. My name will not appear on any of the research instruments. My identity will not be revealed while the study is being conducted or when the study is reported. All data will be reported as grouped data. Only the investigator will have access to the raw data.

I understand that there may be risk for emotional distress as I recall stressful life events that I have experienced in the last 6 months to 1 year. If I do become emotionally distressed, the investigator will listen and allow me to express my concerns but will not attempt to counsel. The investigator will provide a telephone number for community counseling or social work services should I become emotionally distressed. While I may
not personally benefit from the study, study findings may assist those who work in the area of diabetes management to better serve individuals in need of care.

I understand that by agreeing to participate in this study and signing this form, I have not waived any of my legal rights.

I understand that any questions or concerns I have regarding my participation in the project will be addressed by the above named investigator. Should I have any questions about the rights of research subjects, I may contact the Human Subjects Research Office at the College of Nursing, University of Missouri – St. Louis (314-516-5928).

___________________________   ___________________
Subject’s Signature                Date
SSM Health Center

Project Title: The Influence of Stressful Life Events on the Development of Type 2 Diabetes
Investigator: Joshua Minks, MSN-FNP, PhD Candidate
Department: Nursing
University of Missouri – St. Louis

I understand that the purpose of this research project is to examine the influence of stressful life events on the development of type 2 diabetes. I have been chosen to participate in this study because I was diagnosed with type 2 diabetes within the previous 6 months. I understand that as a research subject I will complete the Recent Life Changes Questionnaire (RLCQ) to determine the amount of distress in terms of stressful life events that I experienced near the time of diagnosis. I will complete the ENRICH social support instrument (ESSI) to determine available social support present during the same period of time. I will also provide demographic data (background information) that may not be available in my medical records.

I understand that the interview may take 10-20 minutes depending on my ability to recall and answer questions asked of me by the investigator.

I understand that my participation is voluntary; I may refuse to participate and/or discontinue my participation at any time without penalty or prejudice. The health care services I receive by the provider that manages my diabetes will not be influenced by my participation in this study, refusal to participate, or withdrawing from the study.

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___________________________   ________________________
Subject’s Signature            Date
Title of Study: Influence of stressful life events on the development of Type II Diabetes

Principal Investigator: Deborah Fritz PhD FNP
VAMC: St. Louis, MO
Subject Name: ___________________________ Date: ___________________________

1. Research Statement.
This is a research study. Such studies include only participants who choose to take part. Take your time to make a decision and ask the person obtaining your consent any questions you have regarding the study. You may discuss this with your family and friends.

The purpose of this research is to determine what effect stressful life events and known risk factors have on the development of Diabetes type II. Eighty total subjects will be enrolled. Forty Veterans from the VA Saint Louis Health Care System and forty from SSM Health Care System will be enrolled.

You will be asked to fill out 3 surveys during a face to face interview. Completing all 3 surveys should not take more than 45 minutes. There is no compensation for being a part of this study.

The surveys look at stressful life events and social support over the past 6 months, basic background information, and information regarding diabetes history.

Basic background information includes: age, gender, ethnicity, race, marital status, education, and current diagnosis of mental illness.

Diabetes history includes: most recent Hemoglobin A1c (test which gives an overall picture of average blood sugars over about 3 months), height and weight, and family history of diabetes.

2. Reasonably Foreseeable Risks or Discomforts.
For some individuals, recalling such stressful life events may cause emotional discomfort. Should you experience emotional discomfort, a psychologist is on call to meet with you. An additional risk is loss of confidentiality.

3. Reasonably Expected Benefits to Subjects or Others.
The information gathered from the questionnaires may assist with the prevention and management of diabetes and future research for diabetes care, with no compensation or benefit to you.
Title of Study: Influence of stressful life events on the development of Type II Diabetes

Principal Investigator: Deborah Fritz PhD FNP
VAMC: St. Louis, MO

Subject Name: ____________________________ Date: ____________

4. Appropriate Alternatives.
None.

5. Extent of Confidentiality.
No one will be able to see your information except for Deborah Fritz PhD and Joshua Minks MSN-FNP, a Doctoral student from the University of Missouri. Your name will not be placed on the surveys, but will be given a code. There will be no way to connect you with the information you give once surveys are completed. Your consent form will be kept in a separate file from the completed surveys. This signed Informed Consent Document is subject to destruction after the required retention period has ended in accordance with the VHA Record Control Schedule (7 years).

Federal agencies such as the Office for Human Research Protection (OHRP), the Government Accounting Office (GAO), Office of Research Oversight (ORO), St. Louis VAMC IRB, VA Audit Committees, University of Missouri, St Louis, SSM Healthcare and accrediting agencies will have access to the records. A copy of this consent form will be filed in your medical records, and for your safety, your medical records may be flagged to alert other healthcare providers that you are participating in the study. Your medical records will include a note that you have consented to participate in the study.

6. Compensation or Treatment for Injury.
The VA medical facility shall provide necessary medical treatment to you as a research subject injured as a result of participation in a research project approved by the VA R&D Committee and conducted under the supervision of one or more VA employees in accordance with Federal regulations. There is no compensation associated with this study.

In case there are medical problems or questions, you can call:
Deborah Fritz PhD FNP at 314-403-3600 during normal business hours, 9am – 5pm.

If you have any questions about your rights as a research subject, or you wish to voice a concern; obtain information about the VA St. Louis Health Care System IRB approved study; or offer

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<tr>
<th>IRB Approval Date: 01/3/2016</th>
<th>Expiration Date: 01/31/2019</th>
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<td>10-1086</td>
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</table>
Title of Study: Influence of stressful life events on the development of Type II Diabetes

Principal Investigator: Deborah Fritz PhD FNP

VAMC: St. Louis, MO

Subject Name: ____________________________ Date: ______________

Input of any kind you may call the St. Louis VA Research & Development Office, IRB administrator or R&D Committee administrator at (314) 289-6333, or Patient Advocate Office at (314) 289-6373.

RESEARCH SUBJECT’S RIGHTS:

"My rights as a research subject have been explained to me and I voluntarily consent to participate in the study. The purpose of the study and my participation in the study has been explained to me. I have been advised that I will receive a signed copy of this consent form. I understand that VA patients may have a copy of this consent form filed in their VA medical records.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled. I voluntarily consent to participate in this study. The reasons for the study and its procedures have been explained.

______________________________    ________________
Subject’s Signature            Date

______________________________    ________________
Consenter’s Name               Date

______________________________    ________________
Signature of Person Obtaining Consent Date of Signature

IRB Approval Date: 01/31/2019 Expiration Date 01/31/2019 by __________ Subject’s initials
APPENDIX H
Flyer for Patients

DIABETES RESEARCH STUDY

Were you diagnosed with type 2 diabetes in the past 6 months?
Are you 18 years or older?
10-20* minutes of your time could make a considerable contribution to research on type 2 diabetes.
*Duration depends on time needed to answer questions.
Contact me, arrange a meeting, sign a consent, and complete 3 short surveys.

I appreciate your time and consideration.
Sincerely,
J. Minks, Doctoral Student