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Association of Biological and Self-Reported Stress Measures with Cardiovascular Disease and Risk Factors among Adults with Type II Diabetes Mellitus

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Abstract

Purpose and Background/Significance: Cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) are prevalent comorbid health conditions in adults, affecting roughly 65% of U.S. adult population, and are among the leading causes of premature disability and mortality. An underlying inflammatory mechanism is hypothesized in the development and progression of CVD. Poor T2DM control, depression, and stress are inflammatory processes that are associated with an increased risk of CVD events, including hypertension, myocardial infarction, stroke, and kidney disease. The purpose of this thesis was to test a model of the relationships between T2DM control, depression, and stress measures as predictors of CVD risk factors and events in a sample of adults (N=45) with T2DM and depressive symptoms. It was hypothesized that, after controlling for socio-demographic characteristics and clinical characteristics, there would be: (a) a positive association between biological and self-report stress measures with self-reported cardiovascular events and risk factors, and; (b) A1c and smoking status would be positively related to biological and self-report distress measures and to self-reported CVD risk factors/events. Methods: A secondary analysis was done using baseline (pre-intervention) data from a randomized trial of a 12-week patient-centered decision support intervention (n=45) to improve patient decision-making about managing depressive symptoms in context of T2DM. Standardized measures included glycemic control (A1c), depression (Patient Health Questionnaire-9), self-reported and biomarker stress measures (Diabetes Distress Scale; salivary α-amylase), and a dichotomized self-report measure of four CVD risk factors and events (0 = no risk factors/events; 1 = at least one risk factor/event). Regression analysis was used to model relationships of glycemic control, depression, and, in predicting CVD risk factors/ events (hypertension, heart disease, kidney disease, stroke), after initially controlling for socio-demographic characteristics (age, gender, race) and smoking status. Results: Unadjusted bivariate relationships were statistically significant for PHQ-9 and DDS (r = .550, p < .05), DDS and A1c (r = .314, p < .05), and smoking status and A1c (r = .299, p < 05). A logistic regression analysis revealed three statistically significant and positive predictors of CVD risk factors events (all p < .05): PHQ-9, DDS, and smoking status. In the first regression model, salivary α-amylase was used as a continuous variable and trended towards significance (p = .082), and when used as a binary predictor, approached statistical significance (p = .051) in predicting CVD risk factors/events. Conclusion: This study contributes to knowledge about relationships between potentially modifiable psychological factors (depression, stress), risky health behaviors (smoking), and glycemic control in predicting CVD risk factors/events. This knowledge can inform improved healthcare interventions to reduce the morbidity and mortality associated with cardiovascular disease and diabetes.

Keywords: Cardiovascular Disease, Type II Diabetes

1. Introduction

Diabetes is the seventh leading cause of death in the United States. Cardiovascular events including myocardial infarction and stroke account for 70% of deaths in patients with type 2 diabetes mellitus (T2DM). Diabetes is a

chronic disease that destroys the arterial vasculature in both small and large capillaries. This disease process, if inadequately managed, can result in clinically significant cardiovascular disease (CVD), and heightened risk for adverse cardiovascular events. The interrelationships between diabetes and CVD are a priority area for additional research in order to reduce premature morbidity and mortality associated with diabetes and adverse cardiovascular events[6].

There are multiple types of diabetes syndromes, with diabetes mellitus type 2 comprising the majority of diagnosed diabetes. Type 1 Diabetes (T1DM) is marked by a lack of insulin-secreting beta cells in the pancreas. Without sufficient insulin, there is a resultant buildup of glucose in the vasculature, and exogenous insulin is required. T1DM is generally diagnosed relatively early in life and is understood as an autoimmune disorder. By contrast with T1DM, type 2 diabetes (T2DM) makes up approximately 95% of cases among adults. In T2DM, cells become resistant to insulin and are unable to store glucose and glycogen. An underlying pro-inflammatory mechanism is hypothesized to be the link between hyperglycemia and cell damage. The result of insulin resistance is hyperglycemia, which has detrimental effects on the vascular system, resulting in significantly higher risk of adverse cardiovascular disease (CVD) events such as myocardial infarction, kidney dysfunction, stroke, and peripheral vascular disease

A number of behavioral lifestyle factors can increase the likelihood of developing T2DM, including a sedentary lifestyle and an unhealthy diet. T2DM is often accompanied by other CVD risk factors, such as elevated LDL cholesterol, hypertension, hyperglycemia, elevated BMI, and other psychosocial issues such as stress and depression. These CVD risk factors are targets of behavioral lifestyle change interventions to prevent development or progression of T2DM and to reduce risk of CVD events. These types of interrelationships between diabetes and CVD are a priority area for additional research within a goal to reduce premature morbidity and mortality associated with diabetes and adverse cardiovascular events[6]. The overall goal of this thesis is to contribute to theoretical knowledge in this area by using an existing dataset to test a model of relationships between diabetes control and psychological distress measures (stress, diabetes-related distress, and depression) in accounting for CVD risk factors and events.

2. Review of Literature

2.1 Hyperglycemia and Cardiovascular Disease

Long-standing hyperglycemia accelerates the rate of atherosclerosis and is related to increased incidence of cardiovascular events. A recent meta-analysis that examined the relationship between A1c and cardiovascular-related mortality in patients with T2DM found that for every 1% increase in A1c there was a 25% increase in CVD mortality[34]. Microvascular disease involves smaller arterial pathways, such as in the eyes, kidneys, and peripheral nerves, while macrovascular disease involves larger arteries. Examples of macrovascular disease include cardiovascular disease, hypertension and stroke. The relationship between glucose and microvascular disease has been shown to be very strong, but it is less clear how strong the relationship is to macrovascular disease[27]. The Kumamoto Study and The Diabetes Control and Complications Trial research group have both shown conclusively that improved glycemic control decreases the incidence of microvascular disease and neuropathic problem[30, 23]. Cardiovascular outcomes were then examined in relation to improved glycemic control but did not show as large of a correlation as with microvascular disease. The relationship between glycemic control and CVD, the leading cause of death for those with diabetes, is less clear. The Diabetes Control and Complications trial saw a trend towards a positive correlation between improved glycemic control and decreased incidence of CVD and follow-up 9 years later did show a significant reduction in the risk for cardiovascular related death. Three other large trials (ACCORD, ADVANCE, and VADT) found no reduction of CVD with increased glycemic control[28]. An extension of the VADT study found that if patients had less severe atherosclerosis at baseline, intensive glycemic control could significantly reduce their chances of cardiovascular events[26]. More long-term follow up studies may provide more information on the relationship between glycemic control and macrovascular disease.

2.2 Stress, Depression and Cardiovascular Disease

A substantial relationship exists between psychological stress, depression and cardiovascular health. Clinically significant stress can contribute to adverse cardiovascular events. For example, stress causes an increase in heart rate and blood pressure which can cause atherosclerotic plaques to dislodge. People with diabetes often experience

complex ongoing psychosocial stressors, and relatively less is known about the impact these stressors have on cardiovascular health[4]. Salivary α-amylase, an enzyme in the saliva, increases in response to physical or psychological stress and has been used as a stress biomarker in research on cardiovascular physiology[14]. Psychosocial stress is associated with a higher likelihood of smoking, hypertension and sedentary lifestyle, all of which are risk factors for T2DM[13]. Depression, one of the major causes of disability and disease burden worldwide, is also a risk factor for development of heart disease. A bidirectional association between depression and cardiovascular disease has been shown to exist. Several studies show that individuals diagnosed with depression have higher mortality, especially cardiovascular related mortality[3]. Those who are diagnosed with cardiovascular disease often also have an increased incidence of depression[15]. This correlation can be explained by a number of factors including higher vulnerability and decreased access to healthcare[3]. Another recent study has shown that although depression often accompanies CVD, and depression can best be seen as a "variable risk marker." However, there has been no evidence that shows that treating depression alters CVD outcomes[22].

2.3 Stress and Glycemic Control

Individuals with T2DM have the added stress of managing their diet, exercise, and medications on a daily basis. Diabetes self-management needs can be complex and require substantial, highly challenging changes in lifestyle. For example, people with diabetes often must regularly check their blood glucose, make significant changes in physical activity and diet, and administer medications, sometimes including insulin injections or use of other insulin administration devices. Added stress can decrease confidence in self-management abilities and worsen hyperglycemia. Stress can be generalized, reflecting general psychosocial stressors, or more specific to living with and managing diabetes on a daily basis. Regardless of the specific sources of stress, there is evidence that interventions to reduce stress can help to improve chronic hyperglycemia[29]. However, additional research is needed to examine the relationships between specific types of stress and glycemic control.

2.4 Depression, Diabetes-related Distress, and Diabetes Self-Management

Depression has been found in a variety of studies to be associated with poor metabolic control[12]. The mechanisms for this relationship are complex, and include issues such as reduced treatment adherence and impaired self-management of diabetes. People with diabetes are more likely to have depression when compared to the rest of the population[7]. Even mild depressive symptoms are associated with greater likelihood of suboptimal self-care behaviors, including decreased adherence to diet, exercise and medication regimens[13]. Compared to people without diabetes and/or depression, people who have both diabetes and depression have increased functional impairment, spend more days in the hospital, and miss more days of work[25, 7], have poorer glycemic control[19], incur higher health care costs[7], and have a higher risk of death and sickness[18]. The impact of depression is related to but conceptually distinct from stress and diabetes-related distress. Diabetes-related distress has been found to be more predictive of behavioral and biological outcomes compared to depressive symptoms[7]. The relationships between depression, diabetes-related distress, and diabetes self-management are important areas for further research in relation to health outcomes.

2.5 Diabetes-Related Distress and Hyperglycemia

A1c is a biomarker that reflects extent of blood glucose control over a 3-month period and is a useful test to measure adequacy of T2DM management. A1c is now being used as a screening measure for disease prevention and health promotion. A strong and positive relationship has been found between diabetes-related distress and A1c[10]. However, research has shown that when interventions were implemented to improve depression among adults with diabetes, no subsequent decreases in A1c were noted[18]. Thus, the study of diabetes-related distress is promising in regard to potential for improving glycemic control. For example, interventions research could be conducted to target sources of diabetes-related distress and to evaluate intervention effectiveness in relation to A1c improvements over time. Refining existing interventions to improve T2DM control is important to decrease the risk for CVD.

2.6 Summary and Purpose

After an extensive literature review, no research studies were located that specifically examined diabetes-related distress, glycemic control, stress, and depressive symptoms in relation to self-reported CVD risk factors and events.

Many studies have explored linkages between two or three of the variables, but not all in conjunction. Therefore, the purpose of this thesis is to use an existing dataset to test a model of relationships between longer-term diabetes control (A1c), stress (salivary α-amylase), diabetes-related distress (Diabetes Distress Scale; DDS) and depressive symptoms (Patient Health Questionnaire-9; PHQ-9) in predicting CVD risk factors/ events (hypertension, heart disease, kidney disease, stroke), after initially controlling for socio-demographic characteristics (age, gender, race) and smoking status.

3. Theoretical Model

The theoretical model that guided this research is presented in Figure 1. The model was created by the research team to better show the hypothesized directional relationships between sociodemographic and clinical characteristics, biological and self-report distress measures, stress, and cardiovascular risk factors/events.

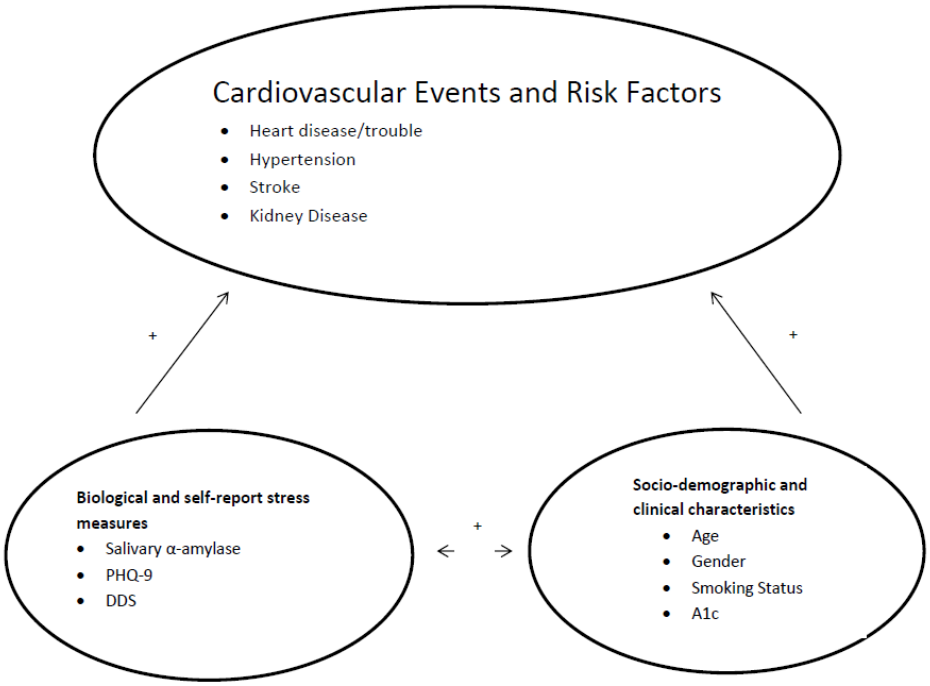

Figure 1. Conceptual Model

3.1 Hypotheses

1. After controlling for sociodemographic and clinical characteristics, each biological and self-report measures of distress (salivary α-amylase, PHQ-9, and DDS) will be positively related to self-reported CVD risk factors/events.
2. A1c and smoking status will be positively related to biological and self-report distress measures and to self-reported cardiovascular risk factors/events.

4. Methods

This correlational descriptive study was a secondary analysis of a randomized pilot intervention study done with 45 adults with T2DM and depressive symptoms to test a novel decision support intervention (DSI) to improve decision-making about managing depressive symptoms. This thesis analysis used the baseline (pre-intervention) data to test the hypothesized model.

4.1 Participants

A socio-demographically diverse sample with multiple chronic co-morbidities, significant psychosocial stressors and significant health care barriers was used in the primary study. Participants were recruited from multiple sites including OSU Primary Care Research Network sites Advertisements, postings in local community centers and libraries, OSU diabetes clinic and Central Ohio Diabetes Association (CODA) advertisements, on site recruitment at community health fairs and diabetes health fairs, study invitations sent via the NIH CTSA-sponsored *ResearchMatch* health volunteer database, and advertisements in local print media. Once participants were recruited and screened they were randomly assigned into one of two study groups (experimental – DSI + Usual Care, or control – Usual Care) based on a stratified (depressive symptom severity x gender) randomized block design. Participants met the following inclusion/exclusion criteria:

4.2 Inclusion and Exclusion Criteria

Inclusion criteria included mild to moderate depression symptoms assessed with PHQ-9 depression scale, access to telephone and transportation, and ability to complete required forms. Exclusion criteria included severe levels of psychological and physical distress, age, substance abuse disorders, history of psychiatric hospitalizations, history of suicidality, and severe physical pain or terminal illness.

4.3 External and Internal Validity

The primary study used a sample representative of the population of adults who have T2DM and mild to moderate depressive symptoms and complex psychosocial stressors in central Ohio, potentially making the results of the study potentially generalizable to a comparable population of adults. The randomized study design helped to minimize threats to internal validity in the primary study.

4.4 Measures

All measures used have been previously used in similar research with adults with T2DM and depression and have known psychometrics. An overview of the measures used in this secondary analysis is included below.

4.5 Health Conditions Questionnaire

In the primary study, patients were asked to identify any current health conditions from a list of 16 conditions besides T2DM. A sum score was calculated for the total number of health conditions. For the purposes of this secondary analysis, four health conditions (heart disease/trouble, kidney disease/trouble, hypertension, stroke), and one additional behavioral variable (smoking status) were used in the analysis.

4.6 Salivary α-amylase

Salivary α-amylase is a point-of-care test used to measure sympathetic nervous system (SNS) activity or short term stress. salivary α-amylase for this study was collected, centrifuged and kept frozen until ready to be examined. A Salivette kit was used to collect samples and patients were instructed on how to properly use the instrument. The alpha-amylase is measured using a quantitative enzymatic kinetic method. Intra-assay variation is usually less than 7.5% and inter-assay variability among duplicates less than 6%[5].

5. Patient Health Questionnaire-9

The Patient Health Questionnaire (PHQ-9) is used to screen for depressive symptoms and has validated cut points for no/minimal, mild, moderate, moderately severe, and severe levels of depression. Respondents report the frequency of bother from depressive symptoms over the past two weeks (0 = not at all; 1 = several days; 2 = more than half the days; 3 = nearly every day). Scores for individual items are summed for a depressive symptom severity score, which can range from 0 (no depression) to 27 (severe depression). The PHQ-9 has been found to have satisfactory sensitivity and specificity for diagnosis of major depressive disorder in diabetic patients[19]. Major depressive disorder differs from depressive symptoms in terms of symptom severity and length. For example, a cut-off score of 12 has been recommended for diagnosing major depressive disorder and has relatively high specificity in this patient population; e.g., sensitivity of 75.7% and a specificity of 80.0%. However, a cut point of 10 or higher can be appropriate for epidemiological research because it captures a larger group of patients with possible depressive disorders[32]. In the present study, the PHQ-9 demonstrated moderately high internal consistency reliability (α = .84), which is similar to values of .89 and .86 in prior validation research[19].

5.1 A1c

Hemoglobin A1c is a point of care test obtained through a capillary finger stick and is used to measure longer term glycemic control. The test indexes the 3-month average of blood glucose levels, providing a longer-term indicator of blood glucose control. The relationship between A1c levels and mean plasma glucose levels from data in the international A1c- Derived Average Glucose trial found that the correlation between serum glucose and A1c was substantial (r = 0.92). The ADAG trial found no significant differences between racial and ethnic groups. Keeping the A1c level below 7% has shown to reduce the incidence of microvascular and possibly macrovascular disease[1].

5.2 Diabetes Distress Scale

Diabetes-related distress refers to the psychological distress associated with the burden of diabetes. The Diabetes Distress Scale (DDS) has four distress-related subscales: emotional burden, physician-related distress, regimen-related distress and diabetes-related interpersonal distress. Respondents rate items using a 1 (not a problem) to 6 (serious problem) scale to indicate extent of diabetes-related distress. Polonsky[24] validated the DDS using four diverse sites. The mean correlation between the total score of the DDS and the four subscales was high (r = 0.82). The DDS had good internal reliability (α > 0.87) and validity across all four clinical sites. Younger subjects had higher DDS scores than older subjects and insulin users reported the highest DDS scores. Total DDS scores was positively associated with depressive symptoms, poor adherence to meal planning and little exercise[30]. In the present study, the DDS had high internal consistency reliability (α = .92).

6. Results

6.1 Data Analysis

SPSS v. 20 statistical analysis software was used to analyze the data. Mean scores, standard deviations, and percentages (N %) were used to summarize sociodemographic and clinical characteristics of the sample. A bivariate correlation matrix was used to compare the relationships between the unadjusted variables. Multivariate logistic regression analysis was used to model the relationships of glycemic control, depression, and stress in predicting the odds of CVD risk factors/events, after initially controlling for other socio-demographic characteristics and smoking status.

6.2 Participant Characteristics

The participants in this study represented a sociodemographically diverse sample with clinically significant psychological distress and cardiovascular risk factors on average. The sample was 28.9% male, 42.2% minority, and the mean age was 49.16 years. The average A1c for the sample was 8.3% (normal value < 6.5%). The sample had clinically significant cardiovascular risk factors; i.e., 48.8% of the sample reported at least one CVD risk factor

or event, 42.2% reported hypertension, and 17.8% reported being smokers. The mean PHQ-9 score was 10.67, which indicates mild to moderate depressive symptoms on average in the sample. The DDS mean score was 3.07, with a range of scores from 1-6, which indicates a moderately distressed sample in relation to diabetes-related sources of distress. The sample had a mean baseline alpha amylase values of 76.08 U/ml while an average of 92.4 U/ml has been reported in adults (Salimetrics, 2012). However, there was substantial variation in baseline alpha amylase values for this sample, ranging from 2.95 to 321.77 U/ml. See Table 1 below.

Table 1. Socio-demographic Characteristics

		Mean	Standard Deviation	Range	Frequency	Valid Percentage
Age		49.16	11.473	27-69		
PHQ-9		10.67	5.681	0-24		
A1c		8.27	2.327	5-14		
DDS		3.069	1.054	1-5.47		
Alpha amylase		76.08	65.53	2.95-321.77		
Sex	Male				N=13	N=13
	Female				N=32	N=32
Race	American Indian				N=1	N=1
	Asian				N=2	N=2
	Black/African American				N=15	N=15
	Caucasian				N=26	N=26
	Other				N=1	N=1
Sum of 4 CVD Risk factors/events						
	0				N=23	51.1%
	1				N=17	37.8%
	2				N=4	8.9%
	3				N=1	2.2%

6.3 Bivariate Correlation Matrix

A bivariate correlation matrix was computed to assess the unadjusted relationships between each pair of study variables. Correlations were computed using the parametric Pearson correlation (*r*). The non-parametric equivalent correlations, Kendall's Tau-B (*tau*) and the Spearman rank order correlation coefficient (*rho*) were also examined in context of a relatively small sample size and non-normal distribution of some study variables. As shown in the table, several unadjusted bivariate correlations were statistically significant. The observed correlations are partially consistent with the hypotheses of the association between A1c and smoking status with biological and self-report distress measures (PHQ-9, DDS, α-amylase) and cardiovascular risk factors/events (heart disease/trouble, hypertension, stroke, kidney disease). Age, gender, and A1c were not significantly correlated with cardiovascular risk factors and events. Smoking status was the only significant correlate of cardiovascular risk factors and events. The largest correlation of smoking status was with hypertension (r =.309, p < .05), and smoking status was also positively associated with A1c as expected (r = .299, p < .05). A1c was associated with diabetes-related distress as expected (r = .314, p < .035). Other relationships between biological and self-report measures of distress and CVD risk factors/events were statistically non-significant in the unadjusted bivariate correlation matrix. See Table 2 below.

Table 2. Bivariate Correlation Matrix

	Smoking	A1c	PHQ-9	DDS	α-amylase
Smoking		r=.299*	r=.214	r=.075	r=-.048
A1c			r=.091	r=.314*	r=.023
PHQ-9				r=.550*	r=.082
DDS					r=.141
α-amylase					

6.4 Multivariate Logistic Regression Analysis

After controlling for sociodemographic characteristics (age, race gender), A1c, and smoking status (*W*= 4.632, p=.031), PHQ-9 (*W*=4.679, p=.031), and DDS (*W*= 4.345, p=.047) remained statistically significant in predicting cardiovascular events and risk factors. When used as a continuous variable, salivary α-amylase trended in the direction hypothesized (*W*= 3.021, p=.082), and was likely non-significant in the model due to limited statistical power. A second model using a dichotomized α-amylase score (< 92.4 U/ml; ≥ 92.4 U/ml) based on the reported 92.4 U/ml average in adults approached statistical significance (p = .051) in predicting CVD risk factors/events. The Nagelkerke R Square for the overall model was .825, showing that 82.5% of the results were explained by the model. The Hosmer and Lemeshow test was .983, showing that the model had an excellent overall fit to the data. See Table 3 below.

Table 3. Logistic Regression Analysis Results

	Wald	sig
Sex	.530	.467
Age	.126	.722
Race	4.308	.366
Smoking	4.632	.031
A1c	1.913	.167
PHQ-9	4.679	.031
DDS	4.345	.037
α-amylase	3.021	.082

7. Discussion

Hypotheses were partially supported in the study model for the associations between DDS, PHQ-9, α-amylase and smoking status in the prediction of CVD risk factors and events. For the first hypothesis, DDS, PHQ-9 and smoking status remained statistically significant predictors of CVD risk factors/events in the full regression model, after adjusting for age, race, gender, and A1c. A dichotomized alpha amylase approached statistical significance in predicting CVD risk factors/events, but this result and replication of the other findings would need to be replicated in future research with a larger sample size. For the second hypothesis, in the unadjusted bivariate correlation

analysis, smoking status and A1c were positively associated as expected, but only A1c was associated with diabetes-related distress and only smoking status was positively related to self-reported CVD risk factors/events.

The results of this thesis have implications for refining interventions related to psychological health in order to favorably influence the course of T2DM and CVD risk factors and events. The findings replicate prior research on the role of stress, smoking and depression in the development of CVD risks and event. However the findings contribute to new knowledge about the relationship between potentially modifiable psychological risk factors and CVD risk factors and events. This thesis used both biomarker (α-amylase and A1c) and self-report data (psychological distress) variables, and showed that there were statistically reliable relationships between self-reported distress and biomarkers, as well as ability to predict self-reported CVD risk factors and events from both biological and self-report variables.

Psychological health plays a large role in the progression of both T2DM and cardiovascular diseases, and health care interventions should be used by nurses and other types of health care providers to modify the risk status of vulnerable patients. For example, self-reported smoking status was a relatively best predictor of self-reported CVD risk factors/events, and underscores the central importance of smoking cessation as an intervention that must continue to be offered (including provided comprehensive resources needed to support patients to stop smoking). Depression screening and similar resources should continue to be part of best practice in settings in which patients with T2DM are seen for healthcare services. This is especially vital as inadequately treated depression further exacerbates risk for CVD risk/events and worsens the distress of an individual's diabetes regimen. New patients who self-report CVD risk/events and who have T2DM should be prioritized for additional assessment and resources to reduce CVD risk factors. Stress, whether long-term or short-term, can also affect glycemic control and CVD risk. Given the significant impact of stress in T2DM, health care providers must prioritize attention and time to explain the importance of stress reduction and to provide needed educational and other resources; e.g., education on self-management stress-relieving activities such as exercise, yoga and meditation. Diabetes-related distress is a potentially useful measure to inform tailored interventions to reduce distress in T2DM, but is not widely-used by healthcare providers to inform care. The DDS or a similar standardized tool to assess diabetes-related distress could be usefully incorporated into primary health care for adults with T2DM. Although time constraints often impact counseling time in primary care and other settings for healthcare, the results of this thesis underscore the priority importance of taking the time to carefully explain self-care management of T2DM to improve A1c levels and reduce CVD risk factors, which in turn can significantly reduce the incidence of CVD and CVD-related health events.

7.1 Implications for Nursing Practice

Nurses are one of the few health care professionals that are with patients at the bedside for the majority of the day in acute care settings. This allows hospital-based nurses the unique opportunity to form a rapport with patients to be able to recognize the need for managing psychological issues that can complicate T2DM self-management and medical treatment. The results of this thesis research underscore the central importance of intervening with modifiable risk factors for which nurses can make a significant difference. For example, nurses can advocate and teach patients who are smokers about smoking cessation treatment and the consequences smoking has for the progression of CVD and T2DM. Nurses can offer basic screening tools for depression and diabetes-related distress to improve patient outcomes. Patients and nurses alike must recognize the impact and potential consequences of insufficiently managed depression, and that even "minor" depression can have a major impact on quality of life, ability to manage T2DM, and CVD risk factors and events. Many people still see depression as something that should be dealt with alone or avoid bringing symptoms to the attention of healthcare professionals, even when symptoms are clinically significant.

Nurses can assist with reflecting on the importance of addressing symptoms and relating taking action to prevention of adverse health events and improved quality of life. Nurses can also identify significant issues and resource needs for hospitalized patients for whom standard discharge teaching may not be sufficient to assure follow-through with T2DM management, including advocating organizing needed resources and follow-up prior to discharge from the hospital. Discharge teaching should go beyond providing information only to including verbal teach back of discharge instructions in relation to T2DM, and may usefully even involve a short quiz to assess understanding. This way, issues and misunderstandings with the T2DM management plan can be addressed while the patient is still in the inpatient setting, has the resources and staff to help improve understanding, and/or the needed resources beyond the patient can be mobilized before the patient leaves the hospital. Primary care providers and nursing staff in these facilities can also use these approaches at outpatient visits to improve patient outcomes. Many patients with T2DM are treated on an outpatient basis if complications are not present. Primary care providers and nursing staff can identify developing pyscological issues using assessment and the screening tools

discussed earlier. Patients should be empowered to improve their self-management of T2DM via activity and dietary modifications. Lifestyle changes such as improved diet, a workout regimen, weight loss and stress-relieving activities should be emphasized just as much as medication adherence during hospital discharge teaching and throughout the continuum of care in the community.

7.2 Limitations and Future Research

There are some study limitations that may impact the generalizability. While statistically significant findings were documented that were consistent with *a priori* hypotheses, a larger sample size should be used to potentially replicate findings. Alpha amylase, while trending towards significance, was not statistically significant in the logistic regression models, probably due to low statistical power (small sample size) and substantial variability in α-amylase values. The assay results were reconfirmed by the laboratory that provided the analysis in order to check for any technical problems with laboratory procedures and the results were replicated. However, the individual test results could be impacted by a variety of other non-controlled factors, such as smoking or a very recent stressful event, aside from longer-term average stress level. Diabetes-related distress scores could be impacted by the length of time an individual has had diabetes, which would allow more time to adjust to living with diabetes; e.g., a recently-diagnosed individual may feel more distress than an individual who has been living with their T2DM diagnosis for years. The Health Conditions Questionnaire is a self-report measure that was used to assess CVD risk factors and events, and diagnoses were not confirmed via medical records audits. Therefore it is possible that participants could have either under- or over-reported their CVD risk factors and events. Last, the A1c point-of-care test that was used has a maximum percentage value of 14% that can be assessed. Thus it is possible that some participants may have had an A1c value over 14%, but the A1c test apparatus would not report the actual value beyond 14%. This could have resulted in truncation of the actual A1c values for some participants, reducing the sensitivity of the A1c measure in the reported analyses.

8. Conclusion

This analysis contributes to the theoretical understanding of the relationships between stress, depression, diabetes and cardiovascular disease and can lead to more informed health care treatment to refine tailored interventions to reduce poor outcomes for patients with CVD risk factors and T2DM.

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