DEPRESSION AND DIABETIC CONTROL AMONGST A CHRONIC DISEASE CLINIC IN TRINIDAD

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ABSTRACT

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Objectives: The goals of this study were to evaluate the relationship between two outcomes; depression and uncontrolled diabetes as well as to determine the prevalence and associated factors of these two main outcomes amongst diabetics attending a chronic disease clinic in Trinidad. **Research Design and Methods**: A cross-sectional study utilizing a researcher-administered questionnaire with a sample of 239 diabetic patients from the St Joseph Enhanced Health Centre. The Patient Health Questionnaire was used to determine the presence of depression whilst history from patients and laboratory data from the files were used to determine the HbA1C and other factors. **Results**: Depressed patients had increased odds for uncontrolled diabetes (OR 8.24 95%CI 3.37-20.17 p <0.000). Mann-Whitney U testing showed significant differences between the median and variance of the HbA1C between the depressed and non-depressed group, with the depressed group having a median HbA1C 9.0% and the non-depressed group a median of 7.1%. Prevalence of depression was 23.4% in this population and 59.4% of patients had HbA1C >7.0%. Factors associated with increased odds for depression were females, unemployment, no exercise and treatment with insulin. Decreased odds for depression was associated with religious participation, frequent exercise, compliance with medication and Afro-Trinidadian ethnicity. With respect to uncontrolled diabetes, housewives and those on insulin had increased odds whilst single persons and those who comply with medications had decreased odds for uncontrolled diabetes. **Conclusions**: The presence of depression is associated with 8x increased odds of uncontrolled diabetes, with depressed persons having higher average HbA1Cs than non-depressed. Persons treated with insulin had increased odds of both depression and uncontrolled diabetes whilst those compliant with medication had lowered odds for both.

(272 Words)

Keywords: Depression; Diabetic Control; Primary Care; Trinidad

Introduction

The study of comorbid depression and diabetes has amassed great interest since Willis first eluded "the long sorrow" as a potential cause of diabetes in 1684.[1] Much of this collective interest has been due to the effect of both illnesses on individuals, the possibility of the effect of their comorbidity on disease progression, as well as their respective increasing impacts on global health.

Diabetes is a disease that is increasing in numbers worldwide. Globally, the World Health Organization (WHO) report on diabetes, showed that the prevalence of diabetes in the last 30 years has risen from 4.7% or 108 million persons to 8.5% or 422 million persons in the adult population. This rise is more rapid in middle and low-income countries.[2]

Regionally, the prevalence of Diabetes in the Caribbean was last estimated to be 9%.[3] The Pan American STEPs Chronic Non-Communicable Disease Risk Factor Survey in Trinidad and Tobago determined a prevalence of 20.5% for persons with high fasting blood glucose or who were on medication for diabetes.[4] This was conducted in 2012. The International Diabetes Federation (IDF) estimates prevalence of diabetes in Trinidad and Tobago in 2015, to be 14.1% or 140,000 persons[5]. These figures are higher than that of US (10.8%), UK (4.7%) and most other individual Caribbean countries (Grenada – 11.4%, Barbados – 13.6%, Antigua -13.6%, St Lucia – 10.9%, St Vincent – 11.9%, Guyana – 11.2%, Jamaica – 11.9%). Only Belize, with a prevalence of 16.5%, has a greater percentage of diabetics in the region. Worldwide, Trinidad and Tobago is ranked number 23 for diabetes prevalence amongst adults 20-79 yrs.[6]

The high prevalence of diabetes, along with the treatment and long-term support of its complications as well as reduced productivity amongst affected individuals has led to a large economic burden worldwide. The IDF estimates that, in most countries, 5-20% of health expenditure is spent on diabetes.[7] Worldwide expenditure in 2015 was estimated to

be 673 billion US Dollars.[8] In the US, the American Diabetes Association (ADA) estimated in 2012, a cost of $245 billion US dollars for known cases of diabetes, over half of which was due to the direct medical costs and of which nearly 30% was spent in costs related to reduction in productivity. Their last estimate of total health care costs for diabetes in 2007 was 41% less or $174 billion US dollars. The estimated cost of diabetes in Trinidad in 2015 was $177.2 - 296.2 million US dollars[9]

Diabetes is also a major cause of deaths both regionally and internationally. In 2015, IDF estimated 5 million deaths worldwide were caused by diabetes which is greater than the number of deaths caused by HIV/AIDS, tuberculosis and malaria.[7] They estimated over 1500 deaths due to diabetes in Trinidad in 2015. Diabetes is currently the second leading cause of death in Trinidad.[10] Worldwide, the WHO has projected diabetes to be the 7th leading cause of death in 2030.[2]

For those who survive, diabetes can cause multiple potential long-term complications. These add to both the economic and psychological/physical burden of the disease. It is a major cause of coronary artery disease and stroke as well as kidney, retinal and nerve damage[2]. It can lead to multiple disabilities including blindness, coma, partial paralysis and limb amputation, which can in turn lead to less productivity and increased dependence and stress on health care systems.

Brandle et al in 2003 conducted a study to evaluate medical costs associated with type 2 diabetes. They found that both insulin therapy and diabetic complications had substantial impact on the cost of diabetes. Factors associated with a 10-30% increase in cost were; increased BMI, being treated with an oral agent, having diabetic nephropathy and associated cardio or peripheral vascular disease whereas treatment with insulin, angina or MI increased costs by 60-90%. [11]

Despite its numerous complications and potential for mortality, diabetes is a treatable disease. Lifestyle and dietary changes impact greatly on outcomes as well as the various treatment regimens available. The majority (90-95%) of cases of diabetes in the US are Type 2 Diabetes[12] Of these, most are either overweight or obese.[13] Poor compliance with medications and lifestyle changes are responsible for improper glycaemic control which in turn leads to complications and deaths.

Depression, in comparison to diabetes and other non-communicable diseases, is a profound negative determinant of health. The WHO World Health Survey (WHS) evaluated determinants of health and related outcomes in adults aged 18 years and older. They noted that of adults with chronic physical diseases, between 9.3-23% also are found to have depression. They also found that depression led to the largest overall effect on worsening health scores amongst the differing countries and demographics.[14]

Worldwide, high rates of depression and diabetes comorbidity have been reported. Also, there has been a volume of evidence to suggest that this comorbidity results in poorer health outcomes and even increases mortality for diabetics.[15,16] With the potential for these worsening health outcomes in the expanding diabetic population, emphasis on detecting and treating depressive symptoms continues to be of great value in the routine care of diabetic patients.

Diabetics in Trinidad are mainly seen and followed up at local health centers (primary health care facilities). The various Regional Health Authorities, which govern these health centers are separate entities and as such the standards of care vary widely across the country. There is no guideline to date that addresses depression screening in primary care in Trinidad. The Caribbean Health Research Council has published guidelines for management of Diabetes in primary care, however, the most recent guideline does not include any protocol concerning mental health in diabetics.[17]

This study was intended to determine the prevalence of depressive symptoms amongst diabetics in a chronic disease clinic in Trinidad and to evaluate its effect, if any, on diabetic control as determined by the HbA1c. We also intended to look at socio-demographic factors in an attempt to determine if any are associated with higher rates of depression. By determining these figures, it is our hope to highlight the impact of depression on a diabetic population of Trinidad. This may, in turn, lead to increased awareness of the importance of this comorbidity and allow for integration of universal screening for depression amongst diabetics in primary care facilities nationwide.

Research Questions

What is the prevalence of uncontrolled diabetes in diabetic patients attending St Joseph Enhanced Health Centre?

What are the risk factors associated with uncontrolled diabetes amongst diabetics attending St Joseph Enhanced Health Centre?

What is the prevalence of depressive symptoms in diabetic patients attending St Joseph Enhanced Health Centre?

What are the risk factors associated with presence of depressive symptoms amongst diabetics attending St Joseph Enhanced Health Centre?

Is there an association between depression and glycaemic control?

Objectives

1) To determine prevalence of uncontrolled diabetes and associated risk factors in diabetic patients attending St Joseph Enhanced Health Centre.

2) To determine prevalence of depressive symptoms and associated risk factors in diabetic patients attending St Joseph Enhanced Health Centre.

3) To evaluate the relationship between presence of depressive symptoms and diabetic control.

Literature Review

For information pertaining to this research topic, two main databases were used; PubMed and the UWI Library online database system. Hand searches of the most recent CARPHA conference listings were done in an attempt to locate any unpublished regional work in the field.

An initial Pub Med search using the search terms “Depression and Diabetes” produced over 10000 articles. This was narrowed down to articles published in the last ten years which revealed 6687 articles. In order to attain the most robust evidence initially, the search was filtered to include systematic reviews and meta-analysis only, which produced 1022 articles. These abstracts were then read to determine relevance and the full texts, when available, were saved. The UWI online database was useful in attaining articles that were not free via PubMed through direct online journal access. The studies used in the systematic reviews and accompanying references were searched and attained when possible to build the background of previous work in this review.

The online forum ResearchGate was also found to be useful in uncovering conference papers that were not published in journals. It is a searchable database that connects fellow researchers locally and internationally and allows direct contact with authors for full text requests.

One of the forerunners of research in the field of diabetes and depression internationally is Prof PJ Lustman, a professor of psychiatry at the Washington University School of Medicine in St Louis. One of the most useful papers published entitled “Recent Advances in Understanding Depression in Adults with Diabetes” provided a lot of useful information and references regarding this topic.[18]

The prevalence of depression in diabetes is a subject that has been widely studied. Anderson et al conducted a meta-analysis published in 2001 entitled "The Prevalence of Comorbid Depression in adults with diabetes." They combined studies on prevalence and found that diabetics are twice as likely to have comorbid depression than non-diabetics. (Odds Ratio 2.0 95% CI 1.8 –2.2). The meta-analysis estimated a lifetime prevalence of major depression in diabetics to be 11% and elevated depression symptoms, a prevalence of 31%. They also noted higher odds of depression in female diabetics (OR 1.6, 95% CI 1.4 –1.8) [19]

In 2005, Ali et al combined 10 studies to determine prevalence of depression amongst diabetics. This review differed in that only studies including Type 2 Diabetes separately from Type 1 were used and they specified use of controlled studies only. They reported a prevalence of depression in Type 2 Diabetes to be 17.6%. [OR = 1.6, 95%, confidence interval (CI) 1.2-2.0].[20] They also derived a similar finding of higher prevalence of diabetes in the female diabetic population (17.0 vs males 8.1% p <0.000) as Anderson et al.

Another meta-analysis done in 2010 by Nouwen et al attempted to combine longitudinal studies on depression in Type 2 diabetes to determine incidence rates.[21] They found that diabetes was associated with a 24% increased risk of incident depression compared to the general population. The rate for depression in people with type 2 diabetes found in this study (OR 1.19– 1.47) was lower than the finding in two previous mentioned studies. This may be due to the fact that this meta-analysis focused on longitudinal studies of diabetes, attempting to determine incidence of depression rather than prevalence. Because prevalence refers to proportion of persons who currently have a condition during a certain time period, as opposed to incidence which refers to the proportion of persons who are diagnosed with a condition during a certain time period,[22] this would result in higher proportions noted when prevalence rates are quoted vs incidence rates.

Locally, a study conducted by Maharaj et al in primary health care facilities in the southwest region of Trinidad, to determine the prevalence of depression in patients with chronic diseases, estimated a prevalence of 28%.[23] They found associations between the presence of depression and female gender, having multiple complaints (>3), a lower level of education and presence of osteoarthritis. This study did not focus solely on diabetes. They concluded that diabetes on its own did not independently increase the odds for having depression but when combined with other chronic diseases, the odds of having depression were significantly increased. This is in keeping with findings that depression amongst diabetic patients may be attributed to the overall burden of chronic disease.[24,25]

This author also did a study based on patients attending private GP practices in northwest Trinidad which revealed a prevalence of depression to be 12.6%.[26] The populations studied in these two studies would vary as the characteristics of patients attending private GP's would differ from those attending public facilities. Public health facilities in Trinidad are free for nationals whilst private GP's operate via fee for service, therefore, persons of lower economic status would be more likely to attend the public health facilities for their health concerns. Also, the first study was performed on chronic disease patients whilst the latter sampled consecutive patients of a GP clinic whose reasons for visiting the doctor greatly differed from the prior. The geographic location also differed. The finding of lower educational status increasing the odds of depression in this study was similar to that earlier reported.

Another local study by Frederick et al published in 2013 determined a prevalence of comorbid depression in diabetes to be 17.9%.[27] This finding was close to prevalence found in the international studies. The population in this study consisted of patients from outpatient clinics of the major hospitals from all regions of the country. These patients are still under the care of the secondary institutions, however, so their characteristics may differ from those in primary care clinics. They noted gender and presence of other medical conditions in addition to diabetes, were associated with depression with females and those with coexisting conditions scoring higher mean scores on the Zung scale.

One other study done locally reported a prevalence of depressive symptoms of 49%.[28] This study was a comprehensive assessment of diabetes self-care conducted at Penal Health Centre in 2010-2011. They used the Patient Health Questionnaire-8 (PHQ 8) which assesses for depression using 8 questions on a Likert scale. They defined depressive symptoms as present if the score was ≥5 and a score ≥10 to indicate presence of major depression. 18% of persons were found to have scores ≥10.

The high prevalence of depression in diabetics worldwide has prompted a large amount of research in an attempt to deconstruct the relationship between the two. One widely-purported theory is that depression in diabetics is as a result of so called "burden of disease".

Supporting this theory, Van Bastelaar et al found that emotional distress associated with diabetes appears to be an "important mediator" in the association with depression and glycaemic control.[24] They analyzed the relationship between diabetes associated emotional distress, depressive symptoms, and HbA1C. The HbA1C or glycated haemoglobin is used as a measure of long term glycaemic control[29]. Its value represents the percentage of Haemoglobin or red blood cells that have irreversibly bonded to glucose and is dependent on the level of glucose present in the bloodstream. As the red blood cell has a lifespan of 120 days, it gives an average of glycaemia over the previous 8-12-week period. The American Diabetes Association (ADA) and National Institute for Health and Care Excellence (NICE) recommend an HbA1c of <7.0% for non-pregnant adults with diabetes.[30,31] Van Bastelaar found 3X higher odds of having high levels of HbA1C in those who had depressive symptoms in combination with distress specific to diabetes.[24]

To further evaluate the relationship between diabetes and depression, a look at the factors associated with this comorbid condition is necessary. As previously mentioned, local

studies found female gender and lower educational background to be associated with higher rates of depression in diabetics. Several international studies also looked at influences that are associated with depression amongst diabetics. One such study was done by Katon et al and looked at behavioral and clinical factors associated with depression amongst diabetics.[32] They also reported an association with lower educational status and female gender. They noted associations as well, with being younger, unmarried, obese or a smoker. With respect to clinical factors, being treated with insulin and having other medical comorbidities also were found to be associated with presence of depression.

Predictors were also evaluated by a cross-sectional study in 2016 by Habtewold et al which examined several biopsychosocial factors to determine which could be possible predictors of depression amongst diabetics.[33] They found that patients who were divorced, housewives, had diabetic nephropathy, poor social support or a recent negative life event had increased mean depressive symptoms score on the PHQ-9. They also noted the same associations mentioned before such as female gender and lower educational background as being significant predictors. An interesting finding was that regular physical activity reduced odds of depression in this sample. (This was defined as aerobic exercise 30min/day 3-5 days a week).

A more robust study into the relationship between diabetes and depression was done in 2011 by Renn et al who conducted a systematic review of literature on this topic.[34] Findings from the literature suggest a bidirectional relationship. They state, "The biochemical and physiological changes associated with diabetes, as well as the psychosocial burden of a chronic disease, lend modest evidence to the argument that depression is a consequence of diabetes. It remains unclear, however, if it is the diagnosis of a chronic illness or the actual disturbance to the glucoregulatory system that precedes depressive symptomatology, or if both factors contribute bidirectionally." They also acknowledged the increasing evidence that suggests that depression may actually precede diagnosis of diabetes but noted that the mechanism of this relationship was still unclear.

They provided suggestions such as poor lifestyle/dietary choices associated with depression and altered physiological responses as possible risk factors for the development of diabetes in depressed patients.

Looking at depression as a risk factor for the development of diabetes was first described in the landmark prospective study done by Eaton et al in 1981 on >1700 patients with a 13 year follow up. This study demonstrated a Relative Risk >2 for the association between major depressive disorder and development of diabetes, but was not statistically significant (95% CI, 0.90–5.55), which the authors attributed to possible under-detection of diabetes diagnosis using the self-reporting method of diagnosis and a small number of persons meeting criteria for depression in 1981. These findings though, were important in paving the way for further study into the possibility of depression as a risk factor for diabetes. [35]

A number of other significant studies followed including a number of large cohorts. One such cohort was done by Arroyo et al in 2004, in which, over 70,000 adult female nurses were followed up after four years to examine the effect of the presence of depression on developing diabetes[36] They found significantly increased risk for developing Type 2 diabetes in women who had depressive symptoms (RR 1.55 (95% CI 1.27-1.90)). However, this effect was only moderate when adjusted for other risk factors (RR, 1.22; 95% CI, 1.00–1.50). The prevalence of depression is higher in the general female population, however, so this study was limited by selection bias including females only.

A meta-analysis conducted by Knol et al in 2006 combined studies to determine the overall risk of developing diabetes in depressed adults.[37] They concluded that the relative risk for developing diabetes in persons with depression was 1.37 (95% CI, 1.14– 1.63).

The results of these studies are robust enough to encourage one to enquire about the processes behind the relationship of depression and diabetes outside of the so-called "burden of disease".

One theory about why the presence of depression may lead to the onset of diabetes was proposed by a case control study done by Anderson et al in 2009 which suggested that the weight gain caused by chronic antidepressant use (>24 months) in depressed patients can lead to increased risk for development of diabetes (incidence rate ratio=1.84, 95% CI=1.35– 2.52).[38] The association was found for both selective serotonin reuptake inhibitors (SSRI's) and tricyclic antidepressants. This being a case control study however, the cause and effect relationship could not be inferred.

Weight gain alone however cannot explain the increase in incidence of diabetes in patients with major depressive disorder. For this reason, numerous studies look at the biologic effect of depression on diabetes. Musselman et al reviewed literature including the biology of depression in diabetes in 2003 and reported biologically, there were several ways that depression can affect diabetes and its oucomes.[39] They reported findings of increased counter-regulatory hormones in times of psychological distress which could impair the hypo glycaemic effect of insulin and raising blood glucose levels. These include cathecolamines, glucagon, glucocorticoids and growth hormone. The evidence also suggested that persons with depression have decreased glucose activity in the left lateral prefrontal cortex which is postulated to be due to alterations in the GLUT-1 and GLUT-3 transporters. This implies that abnormalities in the peripheral transporters may also exist which can lead to hyper glycaemia. Also, increased immune-mediators such as tumor necrosis factor in depression may impair insulin action.

The relationship of depression and diabetes is still debatable, however, the effect of this comorbidity on glycaemic control is significant. To investigate this, the aforementioned Lustman et al conducted a meta-analysis combining 24 studies in 2000.[40] They concluded

that depression is significantly associated with higher blood sugar readings in diabetes ($P < 0.0001$) but were unable to determine the directional nature of this relationship.

In a cross-sectional study done on > 4000 diabetic patients in 2004, it was found that depressed persons engaged in less exercise, were less likely to eat healthy and were less compliant with medications for diabetes, hypertension and cholesterol, which are the three main types of drugs prescribed in diabetics.[41] They stated that diabetic patients with depression used ~ 20 less days of oral hypo-glycaemic medication compared to non-depressed patients. They noted however that preventative care (such as routine foot inspections) and self-monitoring of diabetes were similar for depressed and non-depressed patients.

Having examined literature on the prevalence and possible causative relationship between diabetes and depression, we then turned to examining the effect of the comorbidity on the affected populations. Firstly, we examined whether the presence of depression is associated with worsened diabetic complications. De Groot et al studied this relationship in 2001 and found that the presence of depression was significantly associated with diabetes complications, including both micro and macro-vascular outcomes [15] This was done via meta-analysis of 27 studies published between 1975 and 1999.

Secondly, we looked at the possibility that depression in diabetes may also increase mortality of those affected. Van Dooren et al conducted a meta-analysis published in 2013 to examine the association between depression and mortality in people with diabetes.[16] They found, that after adjusting for the presence of diabetic complications and socio-demographics, depression was associated with increased mortality in diabetics (both all-cause and cardiovascular).

The course of depression amongst diabetics has also been studied. It has been found that depression amongst diabetics can be more persistent and recurrent and this in turn lead to further worsening of glycaemic control and long-term complications.

Nefs et al conducted a study on 2460 primary care patients with type 2 diabetes who were screened for depression in 2005 and followed up in 2007 and 2008 in attempt to shed light on the course of depression in diabetics and the associated demographic and clinical factors.[42] They examined and compared those with depression at baseline to those without and then further examined all patients 2-3 years later for depression. They detected a 14% incidence of depression (those with depression at follow up who were not previously depressed) and 66% prevalence of persistent depression (those who were found to be depressed at both points). The associated factors for depression at any time were again female gender, low education and presence of other chronic diseases in addition to stressful life events and a history of depression. History of depression increased odds of both incident and persistent depression as well.

In 2009, Peyrot et al assessed persistence of depression symptoms amongst a diabetic population in relation to the patient's involvement in an educational outpatient program targeting diabetes self-care. The education program was one week long.[43] They found that this program resulted in a large (53%) reduction in depressive symptoms. Thirteen percent (13%) of patients were found to have persistent depressive symptoms which was defined as having symptoms at all three time points. They also evaluated predictors of persistent depression finding that lower educational status, a greater number of complications of diabetes, and not being treated with insulin had increased the odds of being persistently depressed.

Huang et al in 2012 also conducted a prospective study which looked at depressive symptoms in diabetics and the effect of changes in these symptoms on patients' disability status, which they measured by their activities of daily living (ADL).[44] This study

measured depressive symptoms (using PHQ-9) and ADL scores at baseline and 5 year follow up. They found that at both time points increased depressive symptoms were associated with worsened disability status. ($p<0.001$).

In 2017 Deschenes et al conducted a prospective study which evaluated both depressive symptoms and diabetic complications at baseline and annually for 5 years.[45] They found that in addition to these complications being strongly associated with depressive symptoms, they also were associated with recurrent or persistent depressive symptoms. The effect size was smaller for the latter finding.

Finding that the course of depression in diabetics may be more recurrent and persistent is evidence that this comorbid condition needs to be treated as early as it is detected to prevent worsening health outcomes.

A number of studies done on treatment of depression in diabetes, show that treatment improves the depression and may even improve glycaemic control. Professor Lustman conducted four such studies on different types of pharmacotherapy commonly used in depression to investigate their effects on diabetics. Initially, he studied the use of the antidepressant nortriptyline to treat depression in diabetics and found that whilst nortriptyline on its own was associated with worsening glycaemic control, improvement in depressive symptoms led to reduced levels of HbA1C.[46] Nortriptyline, being a tricyclic antidepressant, is also associated with weight gain and arrhythmias and as such is not a drug of choice for use in comorbid depression and diabetes. This work, however showed that improved depressive symptoms can lead to improved glycaemic control and thus paved the way for further study into alternative treatment regimes.

His randomized controlled trial in 2000 using fluoxetine, showed improvement in depressive symptoms in only 8 weeks but did not show a significant impact on glycaemic control between treatment and placebo groups.[47]

In 2006, he conducted another randomized control trial to evaluate the efficacy of sertraline, a selective serotonin reuptake inhibitor (SSRI) on depression remission and HbA1C levels in diabetic patients with depression.[48] He evaluated subjects at baseline and treated all depressed patients with sertraline to induce a remission of their symptoms initially. After the initial treatment phase, patients' HbA1Cs were decreased and continued to remain reduced whilst their depression symptoms were abated. Once the initial treatment phase was completed he randomized the patients and found that those who remained on sertraline had a much longer remission time for depression compared to placebo. The time for major depression to recur was almost four times longer in the sertraline group.

In 2007 Lustman again conducted a two-phased depression treatment trial to investigate the effect of the drug Bupropion. In addition to its impact on depression remission and resultant diabetic control, he also evaluated patients' BMI, body fat percentage and diabetes self-care.[49] Similar to the previous studies, this study showed that improvement in depressive symptoms has a positive effect on glycaemic control. They were also able to show that this effect was independent of weight reduction and unrelated to improved diabetes self-care due to enhanced mood. This can be interpreted as further support of the previously mentioned Mussleman's findings that there exist biologic pathways that lead to diabetes in the depressed. In addition to these findings, Bupropion, like sertraline, was also found to be an effective means of reducing depression remission. They concluded that Bupropion was effective in both inducing remission of depressive symptoms and also in preventing recurrence of these symptoms amongst diabetics. These improvements in depressive symptoms also resulted in improved BMI, body fat percentage, diabetes self-care and control of diabetes.

The effect of psychological intervention on depression in diabetes has also been widely studied. A meta-analysis in 2004 by Ismail et al pooled the findings of randomised controlled trials that evaluated the effect of a psychological therapy on type 2 diabetics

with respect to diabetic control.[50] In addition to HbA1C, they measured blood glucose concentration, weight, and psychological distress. They found that the mean percentage HbA1C was lower in the intervention group vs the control group. (MD -0.32 95% CI −0·57 to −0·07). Psychological distress was also lower in the treatment group but blood glucose concentration and weight gain were not significantly different between groups.

Overall, the studies done on treatment of depression in diabetes have shown that improved depressive symptoms can improve glycaemic control and that this improvement may not be entirely due to improvement in mood, weight or diabetes self-care. This lends evidence to the aforementioned bidirectional relationship of depression and diabetes. It also stresses the need for screening, treatment and follow up of this population for prevention of poor health outcomes.

For diabetics to be treated for depression, however, the depression must first be detected. In 1987 Lustman and Harper assessed physicians' identification and treatment of depression in diabetic patients who were enrolled in a study about diabetic care.[51] They noted that whilst physicians noted abnormal psychological findings in most (68%) depressed patients, only about half of these were assigned a clinical diagnosis of depression and only half diagnosed as depression were treated with medication. These findings suggest that the physicians correctly identified features of depression in patients with diabetes, however, recording and treatment of the diagnosis of depression still fell short. The study was limited in its small numbers and it was conducted in 1987 before much of the awareness of the relationship between diabetes and depression.

There has been much debate about GP's ability to detect and treat depression. In terms of diagnosis a meta-analysis published in 2009 which examined 41 studies and assessed the diagnostic capabilities of GP's for depression in primary care.[52] They found a diagnostic sensitivity (true positive rate) of ≈50% and a specificity (true negative rate) of ≈80%. However, only a third of depressed persons had documentation of depression in their

medical notes. This meta-analysis was not specific to diabetes or chronic diseases but it can be argued that since many chronic disease patients are managed in primary care, that the findings would be similar for detection of depression in diabetes.

Aside from the aforementioned 1987 study we did not come across any further investigation into the detection of depression specifically in diabetic patients.

The immense amount of research and knowledge gathered in this field has led to the development of guidelines for screening for depression amongst diabetics.

In the UK, guidelines from the National Institute for Health and Clinical Excellence (NICE) suggest "targeted screening for patients at increased risk of depression, including those with a history of depression, diabetes or coronary heart disease, disability due to physical illness, or dementia."[53] They recommend using the two questions from the PHQ-2 (Patient Health Questionnaire – 2) for individuals who may be depressed.

The PHQ-2 (Appendix A) is a two-question screening tool that was developed based on the criteria used for diagnosis of depression – the DSM-IV (Diagnostic and Statistical Manual for Mental Disorders -IV).[54] According to the DSM, for a person to be diagnosed as having depression, their symptoms must be present for a minimum of two weeks and the symptoms must include either depressed feelings or anhedonia. The two questions ask about these two symptoms and their frequency from 0 (none at all) to 3 (nearly every day). The score ranges therefore, from 0-6. Manea et al conducted a meta-analysis of the literature which looked at use of PHQ-2 as a screening tool for depression. It was found that this tool has a high sensitivity (91%) if the cut-off point of ≥ 2 is used rather than the previously accepted cut off point of ≥ 3. This however lessens the specificity.[55]

The PHQ -9 (Appendix B) is an extension of PHQ-2 and contains questions about the specific symptoms of major depression. These questions arose directly out of the DSM-IV criteria for the diagnosis of depression. The PHQ-9 is scored 0 to 27, with scores 5-9 indicating minor depression, 10-14 moderate, 14-19 moderate severe and >20 severe. It also includes a question to assess whether depressive symptoms are impairing function, a key criterion to establish a DSM-based diagnosis. Its use in primary care has been well-validated for detection and monitoring of depression.[52] It has a high specificity (90%) for detecting depressive symptoms in primary care[56] and as such can be utilized as a more specific tool for depression if the initial screening with PHQ-2 is positive. This would reduce the number of false positives detected by the PHQ-2. For purposes of this study we will define 'presence of depression' as a score of ≥5. This was chosen following a diagnostic study done by Janssen et al which evaluated the use of PHQ-9 in detecting depression amongst diabetic patients.[57] They concluded that a cut-off of 5 was found to better distinguish between diabetic patients with and without depression. The brevity of the PHQ-9 as well as its validity as a screening tool for depressive symptoms and its use of the DSM criteria enable it to be a useful tool for primary care clinics which are often busy and pressed for time.

In summary, diabetes itself impacts negatively on finances and quality of life. It can affect employment and productivity at work.[58] It causes both macrovascular disease and microvascular disease which in turn leads to long term complications. These long-term complications significantly contribute to the burden of this disease, increasing the financial costs and negatively affecting quality of life.[25] Depression, also has a negative impact on health status, and has not only been shown to be prevalent in diabetics, but also to be a potential cause of diabetes as well as to worsen diabetic outcomes. As such, further study into the prevalence and nature of this relationship in Trinidad is necessary. The aim of this research is to look at not just the prevalence but the associated factors of this important comorbidity. It hopes to provide primary care physicians and policymakers with information that will allow them to recognize the importance of diagnosing and treating depression in patients with diabetes.

Methodology

This study took the form of a cross-sectional study with data collected via a researcher administered questionnaire. A sample of diabetic patients at St Joseph Enhanced Health Centre was used. This health centre has a well-established chronic disease clinic with 639 diabetic patients enrolled in the clinic for 2017. It is referred to as "enhanced" due to the availability of specialty services (ophthalmology, dermatology, pediatric asthma, minor surgical and psychiatry) as well as point of care testing (to determine Complete Blood Count, HbA1C and Microalbuminuria). These facilities result in a higher uptake of HbA1C monitoring and diabetic retinopathy screening than in any of the other health facilities in the North Central Regional Health Authority. In addition to the increased accessibility of clinical services with enhanced diagnostic capabilities, the clinic is adequately staffed to facilitate this research.

The sample size was calculated using the estimated prevalence from a study done by Maharaj et al in 2005.[23] This study was chosen as its selected population also comprised of chronic disease patients attending local health centres. In this study 342 diabetic patients were screened and 100 were found to be depressed. This gives an estimated prevalence of 29.2% for depression in diabetics (p=0.29).

The Type I error (α) would be 0.05 while the Confidence Level of this study will be 95% with a margin of error (d) of 0.05.

The formula used for determination of sample size (n) for the prevalence estimates (same as used for a cross-sectional study) is as follows[59] :

$$n = [Z_{\alpha}^2 \, p \, (1-p)] / d^2$$

$$\approx 317 \text{ respondents}$$

We estimated that at least 80% of the sampled population may be willing to participate and have their information collected. The expected 'dropout' rate was therefore 0.20. Thus the corrected sample size was determined by the following:

Formula for Correction of Sample Size due to expected Dropout Rate:

$= n \times [1 \div (1 - \text{dropout rate})]$

$= 317 \times [1 \div (1 - 0.20)]$

$= 396.25$ therefore 396 subjects are needed

Because this sample size represents a significant (over 50%) proportion of the study population, we applied a finite population correction factor.[60] The formula for this is:

$n_a = n_r / (1 + ((n_r - 1) / N))$

$= 396 / (1 + ((396 - 1) / 600))$

$= 396 / 1.62$

$= 238.8$

= 239 patients

Where n_a = the adjusted sample size, n_r = the original required sample size and N = population size.

The subjects were chosen by a consecutive sampling method whereby the date of starting data collection was chosen and the diabetic patients who attended clinic on that date, and consented to participate, were surveyed. Patients attending clinics on particular dates represent a selection of patients from the population that is pre-determined. There are no

determining factors that dictate which patients attend clinic on given days and patients attending clinic on the same day should not have any deliberately similar characteristics.

Inclusion criteria for this study entailed diabetics attending the St Joseph Health Centre chronic disease clinic who have been registered to the clinic and receiving treatment for a minimum of three months. (Three months is the approximate maximum time needed to achieve differences in HbA1C levels)

Patients who were new to the clinic (under three months) were excluded as they may not have been treated previously and their glycaemic level not reflective of the diabetic control. Also to be excluded, will be those for whom it would be difficult to respond to questions for data needed. For example, the PHQ-9 requires the patient to understand questions worded in English and respond appropriately. It was therefore not possible to collect this data on patients who had dementia/diminished mental capacity or who did not understand English.

We attained approval from the University of the West Indies Ethics Committee on August 8th 2017 (Appendix C) and approval from the North Central Regional Health Authority Ethics Committee on 13th September 2017. (Appendix D)

Pilot testing was done on the 14th September at the St Joseph Health Centre. A total of 10 patients' data was collected on this day and 5 met the criteria for depressive symptoms. Fifteen additional patients were seen by the researcher who did not meet the criteria for the study. These 10 patients' files were then marked as excluded from the final study.

During this pilot study, it was found that information on patient's long-term complications was not sufficiently recorded in the notes in 5 of these patients and

examination of the patients for neuropathy as well as attempting to locate the relevant information proved to be time consuming (increasing interview time by >5 minutes). As such, collection of data for the presence of long-term complications was eliminated from the final questionnaire.

The total time to interview a patient without the long-term complications amounted to an average of 10 minutes. The majority of the time was spent administering the PHQ-9. Usually the PHQ-9 can be self-administered but 4 patients reported difficulty seeing or reading the questions and thus needed to be interviewed. It was decided then that it will be administered via interview for all patients for uniformity of data collection.

The average time for a chronic disease consult by the researcher was approximately 8 minutes. A shift for a physician comprises of 7 working hours with a one-hour break. On average, each physician sees 25 chronic disease clients per clinic. This amounts to 200 minutes. If data is collected from 20 patients as well, this will add an additional 200 minutes to the clinic time amounting to a total time of 6.7 hours. Therefore, the aim was to collect data from 20 persons per clinic date to complete collection from 239 subjects in 12 weeks (chronic disease clinics are once per week). Data collection was completed on 30th November 2017 (before projected time).

The survey was conducted by the researcher only. The researcher was present and working at the clinic on the chosen dates and as such, the patients who were to be seen by the researcher for their chronic disease appointments as well, were interviewed before the visit. The patients seen by other doctors were interviewed after the clinic visits. The PHQ-2 and PHQ-9 were administered before the rest of data was collected and without knowledge of the patient's HbA1C. This was to prevent possible information bias. The data collected was quantitative.

The questionnaire (Appendix E) is divided into two parts. The first part comprised the patient's demographic and contact information. We also included the patient's social and family history as well as any personal or family history pertaining to mental health.

The second section of the form contained additional data which was collected from each patient with respect to their diabetic control and health parameters. This included measurements of current health status such as BMI (Kg/m^2) and Blood Pressure (mmHg) – these were measured directly by nurse in assessment area and recorded in notes as part of patients' routine chronic disease clinic entry. BMI Categories were determined as follows: 0-18.49 – Underweight, 18.5-24.9 – Normal Weight, ≥25 – Overweight and ≥30 – Obese.[61] BP was categorized as high or normal as based on the recommendations of the Eight Joint National Committee (JNC8).[62] This was measured by the nurse in assessment on the day of clinic. No special protocol for measurement was put in place for this purpose. Haemoglobin was attained from blood test results within the last three months. For patients who did not have a result in the file, we performed a STAT Complete Blood Count using the point of care machine at St Joseph Health Centre. A cut off of Hb <13g/dl for males and <12g/dl for females was used to define anaemia as per the Centres for Disease Control and Prevention guides for adults >18years.[63]

We also noted the patients' most recent creatinine. A point of care device was used for those patients without recent (within 6 months) bloodwork. Estimated Glomerular Filtration Rates (eGFR) were calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula via the online application Q_x Calculate.[64] This formula was chosen as it has been shown to have better accuracy than Modification of Diet in Renal Disease Study equation (MDRD) for determining eGFR. Categories used for determining CKD Stage were as follows (eGFR in $mL/min/1.73m^2$): Stage 1 (eGFR >90), Stage 2 (eGFR 60-89), Stage 3a (eGFR 45-59), Stage 3b (eGFR 30-44) Stage 4 (eGFR 15-29) Stage 5 (eGFR <15).[65]

Patients' Hba1c, within last 3 months were collected - A point of care device was used for those patients without recent bloodwork. A cut-off of <7.0 was used to define diabetic control in this population.[29,30] We recorded the number (#) and type of medications (Oral/Insulin) which were taken from file and whether there was compliance with medication (yes/no) as stated by patients when asked.

Most variables above can be obtained by interview of patients or should already be included in the patient's file. Additional tools used were:

Screening for depressive symptoms - Patients were screened for depressive symptoms using PHQ 2. The PHQ-2 has the advantage of easy verbal administration. To reduce the number of false positives, patients who tested positive using PHQ – 2 with a cut-off of ≥ 1 were then screened using PHQ – 9. The scores for both tests were recorded on the data sheet. A copy pf PHQ-2 and PHQ-9 was available to ease recall of questions required and to ensure accurate assessment and use of these tools.

Presence of depressive symptoms was defined as having a PHQ 9 score of ≥5 as was determined by the Maastricht Study by Janssen et al to be the ideal cut off when screening for depression amongst Individuals with Type 2 Diabetes[57]

Patients assessed as having depressive symptoms were treated according to normal protocol according to the severity of their symptoms. Severe depressive symptoms are usually referred to the psychiatric clinic at the same health centre. Mild to moderate symptoms may be attended to by the physician depending on their individual choices.

Once data was collected and entered, it was analyzed using SPSS version 24. The socio-economic and demographic data was analyzed and reported as well as descriptive

statistics for the parameters of patients' general health. The variables are reported under three headings: Socio-demographics, general health parameters and medical history.

Two main outcomes of the study: Diabetic Control and Presence of Depression were both defined as previously mentioned and analyzed for associated factors with the previously mentioned variables. We used the Pearson's chi-square test for this purpose. For those variables which were significantly associated, the odds ratios and accompanying 95% confidence intervals were also calculated to determine the direction and size of the effect on the dependent variables as well as the statistical significance of these odds (p value). This was done using logistic regression. Both bivariate and multivariate analyses were done.

We also attempted to use the independent-samples t-test was used to determine the difference in mean HbA1C levels with depressed and non-depressed diabetics, and its statistical significance. One of the assumptions for the t-test is normality of data of the dependent variable.[66] Tests for normality showed that HbA1C was not normally distributed and various attempts at transformations did not produce any change. As such, we used the non-parametric Mann-Whitney U test to test for differences in the median and variance of HbA1C of the two groups.

Results

Characteristics of Population

Socio-demographic and economic factors

Data was collected from 239 persons who met the inclusion criteria for the study. The population was predominately female (70.3% vs 29.7% males). The main ethnicity was East Indian (59.8%) with 25.1% African and 15.1% Mixed descent and the subjects were generally older, with 87.9% over the age of 50 and the largest percentage between the ages 60-69 years (33.9%). The majority of patients were either married or in a common-law union (54.8%) and had completed only up to primary school education (60.7%) whilst only 25.1% were employed and the largest percentage (46.4%) retired. Most (90.8%) had a household income of less than 10000 TT Dollars per month with 47.3% earning less than 5000 TTD per month.

Several of the patients' social demographics were examined and it was found that most lived with several family members (56.5%) compared to living alone or with one other person. The majority had children (83.7%) and many (66.9%) interacted with their children daily. With respect to regular religious activity/participation, 69.5% responded "no". Exercise participation was poor with most participants not engaging in any exercise (45.2%) and just 39.4% exercising 3 or more times per week.

Table 1: Sociodemographic and economic factors of the population sampled

Variables		**Number (%of total population)**
Gender	Male	71(29.7)
	Female	168(70.3)
Ethnicity	Afro-Trinidadian	60(25.1)
	Indo-Trinidadian	143(59.8)
	Mixed	36(15.1)
Age Group (yrs)	29 and under	1(0.4)
	30-39	8(3.3)
	40-49	20(8.4)
	50-59	63(26.4)
	60-69	81(33.9)
	70-79	56(23.4)
	80-89	10(4.2)
Marital Status	Married	91(38.1)
	Common-Law Union	16(16.7)
	Divorced	17(7.1)
	Separated	17(7.1)
	Widowed	49(20.5)
	Single	49(20.5)
Highest Level of Education Attained	Primary	145(60.7)
	Secondary	72(30.1)
	Tertiary or other Post Secondary	21(8.8)
Employment Status	Full Time	43(18)
	Part Time	17(7.1)
	Housewife	31(13)
	Retired	111(46.4)
	Student	1(0.4)
	Unemployed	36(15.1)

Variables		Number (%of total population)
Number of Household Occupants	Single	34(14.2)
	2 Persons	70 (29.3)
	3-5 Persons	104(43.5)
	5-10 Persons	26(10.9)
	>10 Persons	5(2.1)
Household Income (TTD/Month)	<5000	113(47.3)
	5000-10000	104(43.5)
	>10000	22(9.2)
Children	Yes	200 (83.7)
	No	39(16.3)
Interaction with Children	Daily	160(66.9)
	At least once a week but not daily	24(10)
	At least twice a month but not weekly	4(1.7)
	At least once a month	8(3.3)
	Less than above	5(2.1)
Exercise	Everyday	52(21.8)
	>3 times a week but not daily	5(2.1)
	3 times a week	37(15.5)
	2 times a week	37(15.5)
	None	108(45.2)
Religious Participation	Yes	73(30.5)
	No	166(69.5)

General Health Parameters

In terms of the general health status of the population, 52.3% of patients were found to have blood pressure readings that fell into the normal range for diabetics. However more than half the population were overweight (43.5%) or obese (31.4%). The majority of patients maintained an eGFR >60 mL/min/1.73m^2 (81.1%) with 48.5% having an eGFR >90 mL/min/1.73m^2. Anaemia was present in 30.4% of males and 35.8% of females with a total prevalence of 34.2% in the population. This figure was unusually high, so in an effort to explain the presence, we ran Chi Squared analyses and found a significant association between anaemia and CKD Stage 3 and above. (χ^2 15.88 p<0.000) As the HbA1C is a factor that is dependent on haemoglobin, Chi Squared test was also done to assess any association between anaemia and abnormal HbA1C levels. The resulting p value of 0.89 was not significant so it was assumed that the high levels of anaemia did not impact on the prevalence of uncontrolled diabetes as determined by the HbA1C.

Table 2: General Health Parameters of the population

Variables		**Total Number (% within poplation)**
Blood Pressure	Elevated	114(47.7)
BMI Category	Underweight	1(0.4)
	Normal	58(24.3)
	Overweight	104(43.5)
	Obese	75(31.4)
Haemoglobin	Anaemia	79(33.1)
CKD Category	Stage 1	116(48.5)
	Stage 2	78(32.6)
	Stage 3a	25(10.5)
	Stage 3b	10(4.2)
	Stage 4	7(2.9)
	Stage 5	1(0.4)

Medical History

With respect to medical management of this diabetic population, 28% had insulin as part of their treatment regime with 5.9% using insulin as the only pharmaceutical intervention for diabetes. A large proportion (90%) of patients were prescribed 4 or more medications with the average number of medications being 5.6 (SD ± 1.9). Self-reported compliance with medication was 79.1%. The prevalence of comorbid conditions was high with 91.2% of patients being treated for another medical condition other than diabetes. However, only 17 persons (7.1%) reported a previous history of depression. There was no association between a previous history of depression and current presence of depression. (χ^2 3.21 p = 0.07).

Table 3: Medical History of sampled population

Variable		**N (% within population)**
Type of Treatment	Insulin Only	14(5.9)
	Oral Only	172(72)
	Insulin and Oral	53(22)
Number of Prescribed Medications	>4	215(90)
Presence of Comorbid Conditions	Yes	218(91.2)
Compliance with Prescribed Medication	Yes	189(79.1)
Previous History of Depression	Yes	12(7.1)

Gender Differences

Due to the large proportion of females in the population, Chi Squared testing was applied to determine if there were significant differences between genders for the above-mentioned variables. There were significant associations between gender and daily interaction with children (χ^2 9.42 p=0.002), BMI Category (χ^2 14.9 p=0.002), compliance with medication (χ^2 6.19 p=0.013) and CKD Class ($\chi^2$13.62 p=0.018). Compared to males, females were more likely to be obese (OR 3.8 95% CI 1.8-3.0 p <0.000) but less likely to be overweight (OR 0.52 95% CI 0.30-0.91 p =0.022). They were more likely to have daily interaction with children (OR 2.4 95% CI 1.4-4.3 p = 0.002), to be compliant with medication (OR 2.3 95%CI 1.2-4.3 p=0.014) and less likely to have their eGFR fall into CKD category 3 or higher (OR 0.456 95%CI 0.23-0.90 p =0.024).

Diabetic Control and Associated Factors

All patients included in the study had an HbA1C done within the last three months, either via the main laboratory at Eric Williams Medical Sciences Complex or the point of care device at St Joseph Enhanced Health Centre. As previously mentioned, diabetic control was determined by use of the HbA1C. The value <7.0 % was used as the cut-off for diabetic control.[27] The median HbA1C of the population was 7.6 with an interquartile range ± 2.6%. Only 97 patients (or 40.6% of the population) met the criteria for diabetic control. To determine which variables were associated with diabetic control, the HbA1C continuous variable was converted to a dichotomous dependent variable; controlled and uncontrolled diabetes, with the aforementioned cut point. Pearson's Chi Squared Test for Independence with diabetic control as the dependent variable against all the variables listed in the tables above, was used to determine which factors were associated with diabetic control. Significant associations (p value <0.05) were found with three variables: employment status (χ^2 8.454 p0.038), treatment with insulin ($\chi^2$31.681 p < 0.001) and compliance with medication (χ^2 39.039 p <0.001). Using logistic regression with uncontrolled diabetes as the dependent variable, the odds ratio for the associations was determined. Using bivariate analysis, persons who were single had decreased odds for having uncontrolled diabetes as compared to non-single persons (OR 0.43 95% CI 0.226 – 0.810 p=0.009) whilst housewives had 3.2 increased odds compared to all other categories of employment status (95% CI 1.276-8.232 p 0.013). Using multivariate analysis, the findings for housewives remained significant (OR 3.4 95% CI 1.2-9.5 p = 0.02) as did the findings for single marital status (OR 0.43 95% CI 0.2-0.9 p = 0.02).

As expected, being compliant with medication resulted in reduced odds for having uncontrolled diabetes vs non-compliance. (OR 0.020 (95% CI 0.003-0.15 p 0.000)). For patients treated with insulin, there were approximately 8X higher odds of uncontrolled diabetes vs those who did not have insulin as part of their treatment regimen (OR 7.9 (95% CI 3.5-17.5 p <0.000)). Adjusting ORs for age and gender did not produce a significant change for the relationship of insulin use (OR 7.8 95%CI 3.5-17.4 p<0.000) or

compliance with medications (OR 0.017 95% CI 0.002-0.13 p <0.000) with uncontrolled diabetes.

Table 4: Frequencies of variables for controlled and uncontrolled groups and resultant p value

Variable	Uncontrolled DM: Number (% within Variable)	Controlled DM: Number (% within Variable)	P value
Gender			0.359
Male	39(27.5)	32(33)	
Female	103(72.5)	65(67)	
Age Group			0.149
<40	7(4.9)	2(2.1)	0.253
40-49	13(9.2)	7(7.2)	0.595
50-59	44(31)	19(19.6)	0.051
60-69	45(31.7)	36(37.1)	0.384
>70	33(22.2)	33(34)	0.067
Ethnicity			0.325
Indo-Trinidadian	90(63.4)	53(54.6)	0.176
Afro-Trinidadian	31(21.8)	29(29.9)	0.158
Mixed	21(14.8)	15(15.5)	0.886
Level of Education			0.573
Primary	90(63.4)	55(56.7)	0.299
Secondary	40(28.2)	33(34)	0.335
Tertiary	12(8.5)	9(9.3)	0.824
Employment Status			0.108
Retired	59(41.5)	52(53.6)	0.066
Unemployed	23(16.2)	13(13.4)	0.553
Housewife	*25(17.6)*	*6(6.2)*	*0.010*
Marital Status			0.062
Single	*21(14.8)*	*28(28.9)*	*0.008*

Variable	Uncontrolled DM: Number (% within Variable)	Controlled DM: Number (% within Variable)	P value
Married	58(40.8)	33(34)	0.286
Widowed	27(19)	22(22.7)	0.491
Divorced	11(7.7)	6(6.2)	0.645
Common-law	12(8.5)	4(4.1)	0.189
Household Income			0.481
<5000 vs other	70(51.5)	41(43.2)	0.285
5000-10000 vs other	57(41.9)	43(45.3)	0.519
>10000 vs other	9(6.6)	11(11.5)	0.170
No. of Persons in Household (Grouped)			0.217
Children			0.065
Has Children	124(87.3)	76(78.4)	
No Children	18(12.7)	21(21.6)	
Religious Participation (Yes)	38(26.8)	35(36.1)	0.124
Exercise (Grouped)			0.466
Blood Pressure Contolled	70(49.3)	55(56.7)	0.260
BMI Category			0.364
Insulin Treatment (Yes)	*59(41.5)*	*8(8.2)*	*0.000*
Compliance with Medication (No)	*49(34.5)*	*1(1)*	*0.000*
Comorbid Condition (Yes)	128(90.1)	90(92.8)	0.479
Polypharmacy (Use of 4 or more medications)	13(9.2)	11(11.3)	0.581
CKD Class (Grouped)			0.372
Anaemia (Present)	46(33.8)	33(34.7)	0.886
Previous History of Depression	13(9.2)	4(4.1)	0.137

Depression and its Associated Factors

All patients were screened using PHQ-2 initially (n=239). The two questions comprising the PHQ-2 ask specifically about the presence of sadness/hopelessness and anhedonia. Persons scoring positive for either question on PHQ-2 (or a score of 1 or more) were then screened using PHQ-9. (n=90). Persons who scored zero for both questions in PHQ-2 were classified as not being depressed. This assumption was based on the criteria for the diagnosis of depression as outlined by the DSM-IV which requires that either depressed/hopeless feelings or anhedonia must be present for depression to be diagnosed.

Using a cut-off of ≥5 on the PHQ-9 scale to determine presence of depressive symptoms, 56 patients met these criteria, giving a prevalence of 23.4% for depression in this population. Depression symptoms were mostly mild with only 5% of patients having a PHQ-9 score ≥10 and only 3 persons scoring 15 and above. The highest score was 16.

Chi Squared analysis using presence of depressive symptoms as the dependent variable found significant ($p < 0.05$) associations between gender (χ^2 10.370, p 0.001), employment status ($\chi^2$26.662, $p < 0.000$), religious participation (χ^2 7.221 p 0.007), exercise (χ^2 4,220 p 0.40), insulin therapy (χ^2 7.966 p 0.005) and compliance with medication (χ^2 12.152 p 0.000).

Using logistic regression, with presence of depression as the dichotomous dependent variable (presence and absence of depression), the direction and strength of the associations were determined using odds ratios. (Table 5) Increasing the odds for depression were: female gender (OR 3.8 (95% CI 1.6-8.9 p 0.002)), unemployment (OR 3.8 (95% CI 1.8-7.9 $p < 0.000$)), housewives (OR 2.4 95% CI 1.1-5.2 p 0.035)), no exercise (OR 1.9 (95% CI 1.02 -3.4 p 0.041)), age group 50-59 (OR 2.2 (95% CI 1.2-4.3 p 0.013)) and insulin use (OR 2.4 (95% CI 1.3-4.6 p 0.005)).

Reducing the odds for presence of depression were: Afro-Trinidadian ethnicity (OR 0.41 (95% CI 0.18-0.93 p=0.037)), religious participation (OR 0.36 (95% CI 0.2 – 0.8 p 0.009)), exercising 3 or more times a week (OR 0.4 (95% CI 0.2-0.8 p 0.014)), being retired (OR 0.3 (95% CI 0.1-0.5 p <0.000)), single status (OR 0.391 (95% CI 0.2-0.97 p 0.044)) and compliance with medication (OR 0.3 (95% CI 0.2-0.6)).

Adjusting ORs for age and gender in non socio-demographic variables did not result in any changes to the significance of the findings (See Table 6)

Some notable findings were that age group, marital status and ethnicity as variables did not produce statistically significant associations (χ^2 12.32 p=0.055, χ^2 10.5 p=0.062 and $\chi^2$4.576 p=0.101 respectively), however when sub groups of these were analyzed individually via bivariate analysis, the groups Afro-Trinidadian, age group 50-59 and single marital status produced significant associations.

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Using multivariate analysis, however, the findings for single marital status and age group 50-59 no longer were significant (p= 0.098 and p= 0.15) but the association with Afro-Trinidadian ethnicity were mostly unchanged (p= 0.04 OR 0.42 95% CI 0.19-0.98). Looking at employment status via multivariate analysis, the results for housewives (p= 0.11) and retired persons (p = 0.07) were no longer significant but the findings for unemployment were still significant albeit a bit reduced (p = 0.02 OR 2.9 95% CI 1.2-7.1).

As mentioned above, only 12 persons (5%) scored ≥10 on the PHQ-9. This range of score, which indicates moderate to severe depression, was associated with unemployment (OR 9.6 95% CI 2.9-32.1 p<0.000) and Insulin use (OR 3.9 95% CI 1.2-12.8 p=0.024).

Table 5: Unadjusted Odds Ratios for Presence of Depression with Associated Significance Levels

Variable		**Odds Ratio for Presence of Depression**	**95% CI**	**P Value**
Gender	*Female vs Male*	*3.765*	*1.612 – 8.792*	*0.002*
Ethnicity	Indo-Trinidadian	0.638	0.339-1.201	0.163
	Afro-Trinidadian	*0.420*	*0.186-0.948*	*0.037*
	Mixed	0.762	0.342-1.695	0.505
Age Group	<40	2.514	0.308-20.549	0.390
	40-49	2.375	0.918-6.142	0.074
	50-59	*2.24*	*1.18-4.25*	*0.013*
	60-69	1.542	0.794-2.995	0.201
	>70	2.208	0.956-4.305	0.066
Marital Status	*Single*	*0.391*	*0.157-0.974*	*0.044*
	Married	1.069	0.570-1.975	0.831
	Widow/Widower	0.933	.0441-1.974	0.856
	Divorced	1.464	0.405-5.288	0.561
	Common Law	2.762	0.979-7.793	.055
Employment Status	*Retired*	*0.262*	*0.132-0.520*	*0.000*
	Unemployed	*3.762*	*1.792-7.899*	*0.000*
	Housewife	*2.354*	*1.062-5.216*	*0.035*
	Employed	0.927	0.458-1.878	0.834
Religious Partcipation	*Religious Participation (yes)*	*0.356*	*0.164-0.773*	*0.009*
Exercise	*Exercise(no)*	*1.877*	*1.025-3.439*	*0.041*
	Frequent Exercise (3 or more times a week)	*0.429*	*0.219-0.840*	*0.014*

Variable		Odds Ratio for Presence of Depression	95% CI	P Value
Household Income per month (TTD)	5000 and less	0.570	0.311-1.043	0.570
	5000-10000	1.266	0.684-2.342	0.452
	>10000	1.809	0.510-6.415	0.359
Children	Has Children	0.545	0.216-1.378	0.200
	Daily Interaction with children	0.744	0.387-1.431	0.375
	Interaction once a week at least	1.404	0.463-4.257	0.549
Blood Pressure Reading	High (>140/90)	1.360	0.746-2.479	0.316
BMI Category	Overweight or Obese Vs Other	1.267	0.617-2.601	0.519
Haemoglobin	Anaemia present	0.679	0.348-1.327	0.257
Polypharmacy	4 or more medications	1.595	0.521-4.879	0.413
Insulin Use	*Insulin Yes vs No*	*2.442*	*1.301-4.585*	*0.005*
Presence of Comorbid Condition	Yes	1.927	0.546-6.80	0.308
Compliance with Prescribed Medication	*Yes*	*0.314*	*0.160-0.614*	*0.001*
Previous History of Depression	Yes	2.471	0.894-6.831	0.081

Table 6: Odds Ratios for presence of depression adjusted for age and gender

Variable	Odds Ratio for presence of depression adjusted for age and gender (95% CI)	P value
Religious Participation	0.29(0.1-0.7)	0.004
No Exercise	1.98(1.0-3.8)	0.038
Frequent Exercise	0.42(0.2-0.9)	0.017
Insulin Use	2.5(1.3-4.9)	0.006
Compliance with medications	0.19(0.09-0.4)	0.000

Depression and its association with diabetic control

To answer our main objective on whether depression was associated with control of diabetes, we first conducted chi squared analysis. This produced a strong association between the two variables (χ^2 27.064, p < 0.000).

To evaluate the strength of the association, we first calculated the relative risk for uncontrolled diabetes for patients who had depression. This was found to be 1.78 (95% CI 1.498-2.106) suggesting an increased risk of uncontrolled diabetes in depressed patients. Using logistic regression, the odds of uncontrolled diabetes amongst patients with depression were >8X more than patients without depression (OR 8.24 (95%CI 3.37-20.17 p <0.000)). These odds were approximately the same when adjusted for gender and age (Adjusted OR 7.98 (95% CI 3.1-19.9 p<0.000)).

To further investigate the relationship between depression and diabetic control we conducted the Mann-Whitney U Test for independent Samples to compare HbA1C between the depressed and non-depressed groups with the null hypotheses(H_0): The distribution and median of the HbA1C is the same across categories of: Presence of Depression. The resulting p value of <0.00 was significant therefore we can reject the null hypothesis and assume differences were statistically significant between groups. In other words, there were significant differences in both the median HbA1C and the distributions of HbA1C between depressed and non-depressed persons. The median HbA1C for the depressed group was 9.0% (IQ Range ± 2.0) and for the non-depressed group was 7.1% (IQ Range ± 2.2).

Further to the above analyses, the cut-off for HbA1C was also adjusted using an upper limit 8% for diabetic control. This was done to acknowledge the possibility of mis-classification of patients as a study done in 2018 suggested utilizing a slightly higher cut-off of 7 to 8% for diabetic control[83]. This reclassification however did not produce any

significant changes to the association between diabetic control and depression (χ^2 42.4 p < 0.00) and the resultant odds of depression amongst persons with uncontrolled diabetes (OR 9.0 95%CI 4.4-18.7). The current NICE and ADA guidelines however, still maintain a cut-off of 7% for non-pregnant adults[30,31] and thus, this is the cut-off we continued to utilize for the purposes of this study.

Summary

See Table 7 for a summary of findings grouped according to research objectives

Table 7: Summary of Findings

Objective	**Findings**	
Prevalence of Uncontrolled Diabetes	59.4% of patients have HbA1c >7.0%	
Factors associated with Uncontrolled Diabetes	Increased odds of uncontrolled diabetes: ➢ Employment status "Housewife" ➢ Insulin Use	Decreased odds for uncontrolled diabetes: ➢ Marital Status "single" ➢ Compliance with medication
Prevalence of Depression	23.4% patients have PHQ score ≥5	
Factors associated with Depression	Increased odds for depression: ➢ Female gender ➢ Employment status "unemployed" ➢ No Exercise ➢ Insulin Use	Decreased odds for depression ➢ Religious Participation ➢ Exercise 3 or more times a week ➢ Compliance with medication ➢ Ethnicity Afro-Trinidadian
The relationship between depression and diabetic control	➢ There was an association between the presence of depressive symptoms and uncontrolled DM (OR 8.24 95%CI 3.37-20.17 p <0.000) ➢ Median and variance in HbA1C levels were significantly different in depressed and non-depressed groups	

Discussion

Our study had three objectives. We aimed to examine diabetic control and depression, their individual associated factors and the relationship between them. We concluded that the prevalence of uncontrolled diabetes and depression amongst the population were 59.4% and 23.4% respectively. We determined that treatment with insulin resulted in increased odds of both uncontrolled diabetes and depression, whilst compliance with medications were associated with decreased odds for both. Also associated with increased odds for depression were females and unemployment, whilst self-reported religious participation and Afro-Trinidadians were found to have lowered odds for depression. Exercise was associated with depression as well, with persons reporting no exercise having increased odds of depression and those who exercised 3 or more times a week decreasing their depression odds. In terms of the relationship between diabetic control and depression, there was a strong association between the two outcomes with the presence of depression associated with 8X increased odds for uncontrolled diabetes as well as significant differences in median HbA1C between depressed and non-depressed groups.

The population studied had some interesting characteristics. There was a predominance of females, persons of East Indian descent and older persons (>50 years). The finding of a larger proportion of females was not surprising. The diabetic population of the St Joseph Clinic in 2017 was 64.6% female. Other studies conducted in different primary care settings in Trinidad on diabetic patients also showed larger proportion of females, with a study in Carenage Health Centre reporting 55.8% females and one at Penal Health Centre having 62.7% females. [28,68] Maharaj et al studied four primary care clinics in south-west Trinidad and found 72.3% females.[23] According to latest WHO figures the diabetic population of Trinidad is 56% female[69]. This implies that a larger population of females attend clinic for diabetes than males despite an almost even prevalence of diabetes between the sexes. This echoes the findings of a previous local study by Babwah et al, which showed that more women attended diabetic clinics than men.[70] They also noted

that women tended to be more compliant with treatment regimens, which was also found in this study.

Globally, depression rates for the general population are higher amongst females[71] and in Trinidad and Tobago the estimated prevalence of depression for females is 3.7% compared to 2.5% of males[72]. Therefore, the prevalence of depression in this population may have been overestimated due to the substantially larger female population. For this reason and also due to the associations between gender and many variables, including a strong association with the presence of depression, we adjusted odds ratios for gender.

With respect to ethnicity, the finding of a predominant East Indian population may have been due to geographic location of the St Joseph Health Centre. This has been shown by comparing other studies on diabetics at health centres in Trinidad with Carenage Health Centre reporting a prevalence of 7% for this this ethnic group as opposed to 93.5% reported at Penal Health Centre.[28,68] East Indians in Trinidad have higher prevalence rates of diabetes. A study on associations with Type 2 Diabetes Mellitus in Trinidad found that a higher percentage of Indo-Trinidadians were diabetics compared to Afro-Trinidadians and persons of Mixed descent.[73] Due to this finding of larger proportions of East Indians with diabetes as compared to other ethnicities, we concluded that our population sample, with 59.8% East Indians, resembles that of the general diabetic population. Also, there was no significant associations between East-Indian ethnicity and the two main outcomes, so we did not adjust for ethnicity.

The mean age of our population was 61 years with the vast majority over the age of 50. This is not surprising given that the risk of type 2 diabetes increases with age. This finding was the same across other studies done with Penal and Carenage Health Centres reporting average ages as 59 and 64 years respectively[28,68]. Maharaj reported 76.4% patients were over 50 and Frederick reported 79.7% over 50.[23,27] Given the wide range of ages (21-87) in the population however, we adjusted our odds ratios for age.

Moving on to the findings of the study, we determined that nearly 60% of the patients did not achieve glycaemic control with a median HbA1C of 7.6%. We found that persons who were housewives or who were treated with insulin were more likely to be uncontrolled and those who were single or compliant with medication less likely to be uncontrolled. A European study including data from patients in 9 countries found a prevalence of uncontrolled diabetes of 37%.[74] They found that persons who were younger, unemployed, less educated, female and who were more overweight had higher odds of being uncontrolled. The only similar association with our study was the finding that persons who had more complex treatment regimens (including those on insulin) had higher odds of uncontrolled diabetes. Another study done in Jordan found a prevalence of uncontrolled diabetes of 65%.[75] They also concurred with the European study in that this was found to be associated with lower educational status and higher BMI. The association with poorer diabetic control and insulin use was again noted. Locally, a study by Ezenwaka et al also used the clinical target of HbA1C <7.0% for diabetic control and reported a prevalence of uncontrolled diabetes of 85%.[76] This study, done in 2000, included data from 191 patients attending Chaguanas and Arima Health Centres and did not include information regarding associated factors. The Penal Health Centre study reported 79% of patients were not meeting the clinical target for HbA1C but they used a lower cut-off of 6.5%.[28]

Clearly, there exists large differences in rates of glycaemic control amongst different populations. Universally, however, there is an association between treatment with insulin and poorer diabetic control. As a result of our study being cross-sectional, we cannot conclude the directional nature of this relationship. In Trinidad however, many diabetics are started on insulin as a "last resort" due to the general fears and stigma associated with use of needles and self-administration. This may result in these individuals failing to achieve control due to poor compliance as well as having high HbA1C's as a result of prior poor attempts at control by other means with the intent of avoiding being put on insulin.

Housewives were found to have higher odds for uncontrolled diabetes. We explored the possibility that the role of housewives in caring for others results in their having lower levels of self-care which results in a higher likelihood of uncontrolled diabetes. However, we did not find an association between housewives and any parameter of self-care such as exercise or compliance with medication. Perhaps this association is due to other parameters of self-care that were not measured such as dietary adjustments.

With more than half the patients exhibiting uncontrolled diabetes in this clinic however, emphasis needs to be placed on the impact of uncontrolled diabetes, particularly on the importance of achieving HbA1C goals. Blood pressure control was achieved in more than half of the population of this study. According to Palmer et al[77], a 10% reduction in HbA1C, when compared to improvements in blood pressure and lipids, was associated with the largest improvements in life expectancy and savings in cost associated with long term outcomes (cardiovascular, nephropathy, retinopathy and neuropathy).

The prevalence of depression amongst diabetics was found to be 23.4%. Our study utilized the PHQ-9 as the screening tool for depression. As mentioned in the literature review, the PHQ-9 is a brief and valid form of screening for depression and has been shown to be useful in detecting depression amongst diabetics when using a cut-off of ≥ 5.[56,57] The use of this screening tool made our study different from previous research done locally. A study done in Penal Health Centre, found a prevalence of depressive symptoms to be 49%. This study used the PHQ-8 which does not include the last question in the PHQ-9 that asks about suicidal thoughts or ideas. As such, its total score is 24, not 27. However, they also used a cut off of ≥ 5 for depressive symptoms and reported that 18% of patients in this health centre had scores ≥10.[28] These numbers were significantly higher than our study, with only 5% of our patients having a score ≥10. Geographically, Penal is considered a rural area of Trinidad. A study done in northern India showed a significant

association between living in a rural area and depression amongst diabetics.[78] They postulated that the association had to do with the lower economic status of persons living in rural areas and the associated struggles to provide for their families leading to a greater overall burden on persons afflicted with diabetes.

Aside from a geographical difference amongst the Penal and St Joseph Health Centres, there were some significant differences amongst the sociodemographic characteristics found in the two studies. Penal Health Centre had a significantly higher prevalence of persons of East Indian ethnicity and lowered prevalence of single persons. Neither of these demographics were associated with depression in our study so it unclear whether the differences may have impacted on the variance of estimated depression prevalence between the two studies.

Two other studies done locally to estimate prevalence of depression in diabetes used the Zung scale as the screening tool for depression. Maharaj et al utilized a modified version of the Zung and determined a slightly higher prevalence of depression of 29.2% amongst diabetics and 28.3% amongst all chronic disease clinic attendants.[23] This study was done amongst four clinics in Southwest Trinidad. The socio-demographic background of the subjects in this study was similar to ours in gender, age group and ethnicity. However, the geographic location was again different with two of the four health centres falling into the category of rural settings (Debe and La Brea).

The other study done by Frederick et al, reported a prevalence of 17.9%, however as previously mentioned in the review, this study differed in its use of patients attending tertiary care clinics.[27]

Internationally, rates of depression amongst diabetics vary, with a meta-analysis in 2001 concluding that 31% of diabetics had increased depressive symptoms and 11% had major depressive disorder symptoms.[19] This systematic review included studies on both Type 1

and Type 2 diabetics. Another study combined studies done on Type 2 diabetes separately and found a prevalence of 17.6%.[20]

From the findings of previous work and our study, it can be seen that depression affects 20-30% of persons with diabetes. However, these figures may be higher in some settings as was seen in the study done in India which reported a prevalence of 41%.[78] This evidence lends much to the notion that there is much need for primary care physicians to be aware of and screen for this important comorbidity.

We next looked at the factors associated with depression in comparison to other studies. Of the factors we found associated with depression in this study, none were similar to the findings of Maharaj's family practice study[26] who noted persons not currently in a relationship (single) were more likely to be depressed and those 50 years and over and with higher levels of education, less likely to be depressed. We did not find any association with level of education, age group or single marital status. As mentioned in the literature review, this study greatly differed from ours in that it was a study on persons attending a fee for service GP clinic for various complaints as opposed to our population of diabetic patients attending a public health centre. The prevalence of depression (12.8%) was also much less than our study.

Compared to the other study done by Maharaj et al at chronic disease clinics in Trinidad[23], our findings of higher odds of depression amongst females, and unemployed persons were consistent. However, they again found an association with depression and education level, with persons attaining a secondary education or higher having lower odds of depression. They also found higher odds of depression in persons with other chronic diseases but our analysis did not show a significant association. This study found that persons >50 years were more likely to be depressed which was the opposite of the findings from the family practice study.[26] The associations found in this study, however,

were for depression amongst persons attending chronic disease clinics and not specific to diabetes.

Also finding an association with the presence of comorbid conditions and depression amongst diabetics was Frederick et al who, using the mean score from the Zung depression scale and the dependent variable in an independent samples t test, showed higher mean scores in those with comorbid conditions.[27] In keeping with our findings though, they also reported increased scores amongst females.

Internationally, two studies also reported association with lower educational status and depression amongst diabetics.[32,33] The associations with marital status found by Maharaj's family practice study[26] were consistent with these studies, with Katon reporting increased odds amongst unmarried persons and Habtewold reporting increased odds amongst divorced persons. Both also found that female diabetics were at increased odds of depression. Our findings of increased odds for depression amongst persons treated with insulin were consistent with findings of these studies. In addition, the study done by Habtewold et al also found that regular exercise reduced odds for presence of depression.

The finding of increased odds for depression amongst female diabetics was consistent amongst all reviewed studies. This, however, is not unexpected given that females also have higher rates of depression in the general population.

With respect to unemployment, unemployed persons may face hardships such as reduced social interactions, financial strain and feelings of inadequacy and as such may be expected to exhibit symptoms of depression. This was further demonstrated by the association between unemployment and a PHQ-9 score of ≥10.

Our findings in relation to marital status were unusual, with single persons less likely to have uncontrolled diabetes. As mentioned, most findings suggest that being unmarried or not in a relationship would increase a person's chances of being depressed as well as having uncontrolled diabetes. This is logical, given that persons who are single would presumably lack the social and emotional support of a spouse. Interestingly, our findings also suggest that single persons were less likely to have children in this population ($p<0.000$) Perhaps, in light of recent economic downturns seen in Trinidad, the lack of financial dependents has led to less burden amongst these individuals, and the absence of other persons for whom care and attention is required, leads to improved self-care with resultant improved glycaemic control.

As with unemployment, insulin use was also found to increase odds of depression as well as the odds of moderate to severe symptoms. As discussed earlier with respect to diabetic control, insulin is often prescribed to persons after failure of response to oral hypoglycaemics. The practice of prescribing insulin as the last resort may give patients the belief that their diabetes has now worsened to such a degree, that there is little hope of gaining control and may increase feelings of hopelessness and depression. The fears and social stigma associated with the use of needles may also add to these feelings. Also, as was shown above, insulin use is strongly associated with uncontrolled diabetes which, as we will discuss further on, increases odds of depression.

With respect to age group, there has not been any consensus on the association with age and depression amongst diabetics. As mentioned above, Maharaj's two studies[23,26] found opposing findings and Frederick reported no association with age.[27] Internationally, Katon found increased odds for depression amongst younger diabetics whilst Habtewold found no association.[32,33]

Other interesting associations we found were the reduced odds for depression amongst persons who reported active religious participation and those who were compliant with

medication. Persons who take part in regular religious activity often have more social interactions which may lead to improved mood and their spiritual beliefs may lead to less feelings of hopelessness. A meta-analysis published in 1999 on religion and depression found that persons who were involved in organized religious practices and those who value their faith were less likely to be depressed.[79] With respect to compliance with medication, this may be a case where the direction of the relationship needs to be explored as persons with depression may be less likely to be compliant due to feelings of hopelessness and persons who are non-compliant, more likely to feel guilty and depressed.

Another notable relationship that may be bidirectional is that of exercise and depression. Persons who are depressed may be less motivated to exercise and those who exercise may be less likely to be depressed. This was shown by a meta-analysis done in 2012 which concluded that exercise resulted in reduced symptoms of depression in persons with chronic diseases.[80] Exercise was found to be associated with lowered odds for depression amongst diabetics by both Habtewold and Katon[32,33]

Our final and main objective for the study was to investigate the relationship between depression and diabetic control. We determined that the presence of depressive symptoms is associated with diabetic control. This was demonstrated by the increased odds of uncontrolled diabetes in persons with depression (OR 8.24 95%CI 3.37-20.17 p <0.000) as well as the differences in the median and variance of HbA1C between the depressed and non-depressed group as demonstrated by the Mann-Whitney U test. Our confidence in this finding was further compounded by the discovery that adjusting the HbA1C to a higher cut-off (8%) for uncontrolled diabetes continued to produce a significant association and similar odds to the lower, more stringent cut-off of 7%.

This association is in keeping with the combined findings of the studies evaluated by the meta-analysis done by Lustman et al in 2000[40]. This is interesting, given our use of the PHQ-9 as a screening tool for depression in our study, as none of those included used this form of screening. The PHQ-9 was developed in 1999 so would not have been in widespread use at the time of the meta-analysis.[54]

The only local study which attempted to explore the possibility of this association was Frederick et al,[27] who concluded that glucose control was not associated with depression (p=0.28). This study, however, used patients' clinic random blood glucose measurements as a means of determining blood glucose control, which is prone to bias as many patients may attempt to be more controlled in days leading up to clinic appointments.

This important finding may have more than one explanation, as discussed in the literature, that may be applicable to the study population. The so called "burden of disease" theory implies that those afflicted with diabetes have increased rates of depression as a result of the difficulties associated with a chronic disease. This could be shown by the increased odds of depression amongst those patients using insulin. As mentioned earlier, insulin use is usually initiated as a last resort and patients using insulin often are weary of the more complicated process of handling needles and self-administration, which may lead to increased feelings of burden. Also, as shown in previous literature, lower socio-economic status has been shown to be associated with higher rates of depression, which also conforms with the burden of illness theory as persons with financial difficulties would have additional burdens to bear. We did not find an association with income level, but our finding that unemployment is associated with increased odds of depression as well as more severe depression symptoms also adds to this theory.

An alternative explanation for this finding, however, may be that the presence of depression is the cause of the uncontrolled diabetes. This is supported by our findings of

higher odds for depression amongst patients who were non-compliant and those who did not exercise. Depressed patients often lack the motivation to exercise or to comply with treatment regimens along with other forms of self-care. This in turn may lead to higher rates of uncontrolled diabetes.

As discussed in the literature, diabetes and depression may have a bidirectional relationship. Perhaps this may also be the case for depression and diabetic control.

The difference between the median HbA1C between the depressed and non-depressed group was 1.9% which represents a 21% difference in HbA1C between groups. According to the study by Palmer et al, this difference would impact significantly on outcomes associated with diabetes resulting in increased cost of diabetes related outcomes and reduced life expectancy.[77] In addition, the UK Prospective Diabetes Study (UKPDS) has found that every 1% drop in HbA1C was associated with improved diabetic outcomes and that there was no threshold for this effect.[81]

Based on our findings and those of previous studies, it has been shown that between 2-3 out of every ten diabetic patients seen in primary care may have depressive symptoms. In this study, of the persons found to have depressive symptoms, 89% had uncontrolled diabetes. The association between depression and diabetic control and the resultant impact that uncontrolled diabetes has on outcomes is of major importance and should always be considered in the mind of any primary care physician who is attending to diabetic patients.

The findings of this study are profound as it is the first of its kind to show a significant association between diabetic control and depression in Trinidad. This is in keeping with findings of international studies and implies that diabetics in Trinidad may also fall victim to the worsening health outcomes associated with the comorbidity. This would hopefully impact on health care workers and policymakers and encourage more attention to be placed on mental health and wellness amongst diabetics.

Recommendations

The most important recommendation to come out of this research would be to initiate screening for the presence of depressive symptoms amongst diabetics in Trinidad. In the UK, screening is recommended for all high-risk patients, including diabetics[53] and in the US, screening is recommended for all adults once adequate support services are available.[82] In Trinidad, each of the Regional Health Authorities are equipped with both tertiary and primary care mental health/psychiatric outpatient clinics. At St Joseph Health Centre there was recent introduction of a psychiatry clinic which serves to integrate psychiatry and primary care as per the WHO Mental Health Gap Action Programme (mhGAP). This programme aims to increase availability of mental health services in lower to middle-income countries. The availability of these services proves that Trinidad has the required support services for mental health, and as such, global screening should be initiated in this high-risk group.

The recommended screening tool would be the PHQ-9. As discussed previously, the tool is brief and valid and provides busy physicians with a reliable form of detecting the presence of depressive symptoms in diabetics, whom may either be referred for further evaluation or managed according to severity. It usually takes less than 5 minutes if being administered to the patient. Other tools used for detection of depression such as the Zung scale and Beck's Depression Inventory (BDI) provide useful information for the diagnosis of major depressive disorder as well as the nature of depressive symptoms. They, however, are lengthy and as such may be unappealing to both the physicians working at the diabetic outpatient clinics and the patients. The PHQ-9 can be printed on one page and added to the patients' files to encourage health care workers to remember to administer and record findings. It can also be filled out by patients themselves, whilst they are awaiting to be attended to at the clinics once they are capable of reading and interpreting the questions on their own. The ease of administration and validity of this tool justifies its use for universal screening amongst all high-risk groups including diabetics. Whilst our evidence shows increased rates of depression amongst uncontrolled

diabetics, there is still potential for depression to exist amongst diabetics who are well controlled and as such, screening all persons would be recommended, particularly as the bidirectional relationship of this association may mean that presence of depression may lead to poorer diabetic control in the future.

In order for there to be universal screening for depression in diabetics, however, health care providers must first be aware of the importance of the comorbidity. Continuing Medical Education (CME) detailing the prevalence as found by this and other studies done in Trinidad plus the strong association found between depression and gylcaemic control, as evidenced in our findings, would be key points to enlighten persons about the impact of depression on diabetes locally. Further important points to highlight would be the impact of presence of depression on long term outcomes of diabetes and how treatment of depression in diabetics can improve outcomes. These are findings that are based in international evidence and may also stimulate local and regional researchers to investigate in our population.

Further research may also be done regionally to look at the longitudinal relationship of depression and diabetes. Approvals were obtained and subjects in this study were consented for possible follow up and their contact information collected. We were unable to collect follow up data as the time period for submission for the DM program was too short to permit, but the intention is to collect further data on the subjects at 6 months following the original data collection point. This is to determine the prevalence of persistent depressive symptoms (symptoms present initially and 6 months follow up). We would also be able to determine the incidence of depression (newly diagnosed with depressive symptoms at 6 months follow up) and the factors associated with persistent and incident depression amongst diabetics.

Interventional studies regionally are also required as our literature review included international studies that showed both psychological and pharmaceutical interventions

leading to improvement in glycaemic control. This would encourage local physicians to not just diagnose, but to attempt treatment of depressive symptoms in the interest of improved diabetic outcomes.

Limitations

The finding of association between depression and diabetic control and the conclusion that the presence of depressive symptoms is associated with worsened control of diabetes is significant but due to the cross-sectional nature of this study, we cannot make any conclusions about causation. We therefore cannot make any assumptions about whether depression precedes or is as a result of uncontrolled diabetes. Longitudinal studies in the past have shown a bidirectional relationship between diabetes and depression, thus our findings lend support to the theory that a similar relationship may exist between depression and diabetic control.

For the purposes of completing the study in time for submission for the deadline of the DM, we were only able to conduct the study in one health centre. This greatly limits the study's generalizability to the general diabetic population of Trinidad and Tobago. The larger proportion of females (70.3%) is not reflective of the Trinidadian diabetic population (56% female). As stated previously, females in the general population have a higher prevalence of depression so this discrepancy may have led to an overestimation of the prevalence of depression in this population as compared to the general diabetic population. We adjusted odds ratios for gender in an attempt to reduce the bias associated.

In addition, the St Joseph Enhanced Health Centre has readily available specialty services and point of care testing devices. It is also well staffed and in close proximity to tertiary care services. These features are not typical of all primary care facilities in Trinidad and as such also limits the study's generalizability.

Aside from the difference in socio-demographics, the population of diabetics in the general community of St Joseph may differ in other ways to the population of persons who attend the health centre. For instance, persons attending free public health facilities

such as this are more likely to fall in to lower income brackets than those who attend fee for service private institutions. Previous studies show that lower socio-economic status is associated with higher rates of depression[82] and thus there may have been an overestimation of the prevalence of depression amongst diabetics using this population. Conversely, there is also a population of persons who do not seek medical attention for diabetes at any institution and of whom depression may play a part in their reluctance to seek help. These may therefore have higher rates of depression than those surveyed.

Another possible limitation to this study was the administration of the questionnaire by the researcher, who also was the attending physician to the patients on their clinic dates. This method was chosen in the interest of time and also to assure uniformity, adequate completion and accuracy of data collection. It could have led to possible response bias as patients may indicate responses to questions asked that they interpret the researcher/physician would prefer to hear. This potential threat however, would only have affected questions pertaining to issues such as compliance with medication which was self-reported by the patients as most of data collected was socio demographic or attained from measurements. The association found between non-compliance and uncontrolled diabetes, however adds strength to the belief that the prevalence of non-compliance was not underestimated by the method of data collection.

Ethical Considerations

This study required the use of patients' confidential data. As such, patients who chose to participate, were consented to involvement in the study. A consent form was devised for this purpose and was attached to each patient's data form (Appendix F). Patients may revoke consent at any time without regress. In addition, the data sheets were kept in a locked, fire-proof container for the duration of this research. All data will be kept strictly confidential.

All patients newly diagnosed with depressive symptoms as a result of screening utilized in data collection for this research were referred or treated according to normal protocol for these cases.

Approval from the ethics committees of the University of the West Indies and North Central Regional Health Authority were sought prior to commencing data collection.

Budget (TTD)

Photocopying of consent forms, questionnaires and Patient Health Questionnaires (PHQ-2 and PHQ-9) = $1000.00

Research assistant for data entry ($10/Questionnaire for 239 Questionnaires) = $2390.00

Total - $3390

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Appendix A: The Patient Health Questionnaire - 2 (PHQ-2)

Over the past two weeks, how often have you been bothered by any of the following problems?	
Little interest or pleasure in doing things?	0 = Not at all 1 = Several days 2 = More than half the days 3 = Nearly every day
Feeling down, depressed, or hopeless	0 = Not at all 1 = Several days 2 = More than half the days 3 = Nearly every day
Total point score:	

Score interpretation[1]:

PHQ-2 score	Probability of major depressive disorder (percent)	Probability of any depressive disorder (percent)
1	15.4	36.9
2	21.1	48.3
3	38.4	75.0
4	45.5	81.2
5	56.4	84.6
6	78.6	92.9

Appendix B: The Patient Health Questionnaire - 9 (PHQ-9)

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

Appendix C: Ethical Approval from The University of The West Indies

THE UNIVERSITY OF THE WEST INDIES
ST AUGUSTINE, TRINIDAD AND TOBAGO, WEST INDIES
CAMPUS ETHICS COMMITTEE
E-mail: campusethics@sta.uwi.edu

August 8, 2017

Rohan Maharaj (Shanaaz Ali et al)
Public Health unit, Department of Paraclinical Sciences
FMS, UWI
Email: Rohan.Maharaj@sta.uwi.edu; shanaazali@yahoo.com

Dear Dr. Maharaj,

Ref: CEC 245/07/17-Depression amongst Diabetics attending a chronic disease clinic in Trinidad: A prospective cohort trial

Further to our letter of August 4, 2017 and your amendments received dated August 7, 2017, I am pleased to advise that your application for research has been approved on behalf of Campus Ethics Committee.

Sincerely

Shivananda Nayak (Prof.)
Chairman
Campus Ethics Committee
Sn

Appendix D: Ethical Approval from North Central Regional Health Authority

NORTH CENTRAL REGIONAL HEALTH AUTHORITY

OFFICE OF THE CHIEF EXECUTIVE OFFICER

3rd Floor, Building 39, Eric Williams Medical Sciences Complex, Uriah Butler Highway, Champs Fleurs PBX: (868)-225-4673 Ext: 2490 / 3089 / 5091 D.L. (868)-662-5579 Fax: (868)-663-0671

September 13th, 2017

Dr. Shanaaz Ali
Student (UWI)
EWMSC
Mt. Hope.

Dear Dr. Ali,

Approval to Conduct Research Project in the NCRHA

Reference is made to the subject at caption.

Please be informed that approval has been granted for research entitled – **"Depression amongst Diabetics attending a chronic disease clinic in Trinidad: A prospective cohort trial."**

The commencement of this research indicates that you have understood and accepted the responsibility of maintaining the confidentiality of all data and information collected and processed.

The NCRHA wishes you every success in this undertaking, and looks forward to receiving a **HARD** and **SOFT** copy of your Project Report within two (2) weeks of completion.

Sincerely,

Davlin Thomas
Chief Executive Officer (Ag.)

x.c: ***Ms. Vernessar Cummings – Manager, Business Planning and Support (Ag.), NCRHA***
Public Health Observatory, NCRHA

Board Members: Mr. Steve De Las (Chairperson), Mr. Elvin Edwards (Deputy Chairperson), Mr. Randolph Clouden, Ms. Wendy Ali, Ms. Yvonne Bullen-Smith, Ms. Marie Ayoung-Chee, Mr.Stewart Smith, Dr. Maria Bartholomew

Appendix E: Final Questionnaire Used for Data Collection

Patient Data Form

Please ensure consent form is filled out prior to beginning

All Items to be completed by Primary Care Physician at initial consult with patient during Stage 1 of data collection. Instructions on techniques of collection can be obtained from Dr Shanaaz Ali. (Contact # 369-4418)

Section 1

1) **Contact Info**

Contact Number (2)	
ID	

2) **Demographics**

a) Date of Birth: _____

b) Ethnicity:
   a. African
   b. East – Indian
   c. Mixed- Afro-Indian
   d. Mixed- Other- Specify_____
   e. Other

      Please Specify: _____

c)Employment Status:

a. Employed- Full time
b. Employed- Part time
c. Retired
d. Unemployed
e. Housewife
f. Student
g. Other- Specify_____

d)Gender:

a. Male

b. Female

e) Highest Level of Education attained:

a. Primary

b. Secondary

c. Tertiary

d. Post Graduate

3) **<u>Social and Family History</u>**

a) No. of persons living in household: _____

b) Household Income (in TT Dollars per month). This includes any disability, public assistance or pension payments:
   a. <5000

b. 5000-10000
c. 10000-20000
d. 20000-30000
e. >30000

c) Marital Status:

a. Single
b. Married
c. Common-Law Union
d. Divorced
e. Widow/Widower
f. Separated
g. In a relationship

d) Children

a. Yes
b. No

If Yes, How often are u in contact with your children

a. Daily
b. At least once a week
c. At least twice a month
d. At least once a month
e. Less than above

e) Do you partake in community religious activities (e.g. attend church, mosque, temple or other)?

a. Yes
b. No

f) How many days do you exercise per week?

a. None

b. Everyday

c. 2 times a week

d. 3 times a week

e. >3 times but not everyday

g) Family History of Depression

a. Yes

b. No

h) Current depression status/treatment

a) Previously diagnosed with depression (yes/no)	
b) If yes: was diagnosis made by primary care physician (yes/no)	
c)If yes: is person undergoing treatment for depression (this includes counselling/medical treatment) (yes/no)	

Section 2

1. **Current Health Status (all values must be within last 3 months)**

	Value
Blood Pressure	
Pulse	
Weight	

Height	
BMI	
Haemoglobin	
HbA1c	
Random Blood Sugar	
Renal Function: Creatinine eGFR	
Presence of other medical conditions (Yes/No)	

2. Medications and Diabetic Control (all values within last 6 weeks)

	Value
HbA1c	

Type of Diabetic Medication(s) – Please indicate a-c: a. Oral only b. Oral and Insulin c. Insulin only	
Compliance with diabetic medication (Yes/No)	
In all, how much prescribed medication does patient take per day? (state #)	

3. Depression Screening (PHQ-9 only needs to be administered if PHQ -2 is positive). Please also state the score achieved.

	Score
PHQ-2	
PHQ-9	

Appendix F: Consent Form Used For Data Collection

THE UNIVERSITY OF THE WEST INDIES

ST. AUGUSTINE, TRINIDAD AND TOBAGO, WEST INDIES

CAMPUS ETHICS COMMITTEE

CONSENT TO PARTICIPATE IN RESEARCH

Phone: 645-3232 Ext: 5021 Email: campusethics@sta.uwi.edu

Complete Protocol Title	Depression amongst diabetics attending a chronic disease clinic in Trinidad: A prospective cohort trial
Principal Investigator	Dr Rohan Maharaj
Co-Investigators	Dr Shanaaz Ali
Research Site(s)	St Joseph Enhanced Health Centre
Sponsors	Nil

Why is this research being done?

The researcher, Dr. Shanaaz Ali is a student of the University of the West Indies, currently enrolled in the Doctorate in Medicine (DM) Family Medicine. She is conducting research about depressive symptoms amongst diabetics attending chronic disease clinic at St Joseph Enhanced Health Centre.

What is the duration of taking part in the study (for each subject)?

5 months

What will happen to me?

You will be seen at you clinic appointments as usual five months apart. Some additional data will be collected from you regarding symptoms of depression, if present and your socio-economic back ground. Clinical data regarding your diabetes management will aslo be collected. This includes the medication you are taking and results of your most recent blood tests. No additional bloodwork will be required other than those already done as part of your routine clinic follow up.

What is in in for me?

Diabetic patients have a high prevalence of depression. Screening is not usually part of the assessment of diabetics. By participating you will be screened for depression and treated if necessary. This can lead to better health outcomes.

EXPERIMENTAL SUBJECT'S RIGHTS

If I am asked to consent to participate as a subject in a research study involving a medical experiment, or if I am asked to consent for someone else, I have the right to:

1. *Learn the nature and purpose of the experiment (also called "study" or "clinical trial").*
2. *Receive an explanation of the procedures to be followed in the study, and any drug or device used.*
3. *Receive a description of any discomforts and risks that I could experience from the study.*
4. *Receive an explanation of any benefits I might expect form the study.*
5. *Learn about the risks and benefits of any other available procedures, drugs or devices that might be helpful to me.*
6. *Learn what medical treatment will be made available to me if I should be injured as a result of this study.*
7. *Ask any questions about the study or the procedures involved.*
8. *Quit the study at any time, and my decision will not be used as an excuse to withhold necessary medical treatment.*
9. *Receive a copy of the signed and dated consent form.*
10. *Decide to consent or not to consent to a study without feeling forced or obligated.*

If I have questions about a research study, I can call the contact person listed on the consent form. If I have concerns about the research staff, or need more information about my rights as a subject, I can contact the Principal Investigator, The University of the West Indies at:

By signing this document, I agree that I have ready and received a copy of this document.

Signature of Subject or Legal Representative **Date**

REQUEST FOR PERMISSION TO USE AN INDIVIDUAL'S PRIVATE HEALTH INFORMATION

Name of Study:

Depression amongst diabetics attending a chronic disease clinic in Trinidad: A prospective cohort trial

Investigators:

Dr Rohan Maharaj, Dr Shanaaz Ali

What is private health information?

Private health information is any information that can be traced back to you. We need your permission to use your private health information in this research study. The type of private health information that will be used and shared for this study includes:
- Your past and present physical and mental health information
- Information that can be used to contact you
- Results of your medical tests and DNA
- Questionnaires and information on your drug/alcohol usage and that of your family.

Who else will see my information?

Investigators only will see data collection sheet

How long will the investigators use and share my information?

for the duration of the study which is scheduled to be completed by May 2018

What will happen if I drop out of the study early?

Nothing, participation is voluntary and dropping out of the study can be done at any time without regress

What are my responsibilities if I join and what about confidentiality?

You are responsible for providing accurate background information and to appear for follow up at your next clinic appointment 5 months later.

What if I get hurt in the study?

No additional testing or investigation is being done and as such there is no risk for harm with participation

CONSENT

I have read and understood this explanation. The researcher has also explained the study to me. I have had a chance to ask questions and have them answered to my satisfaction. I agree to take part in this study. I have not been forced or made to feel like I had to take part.

I have read the attached experimental Subject's Rights, which contain some important information about research studies. I have also read the Authorisation to use my Private Health Information. **I must sign this Consent Form, the Experimental Subject's Rights and the Authorisation to use my Private Health Information. I will be given a signed copy of each to keep.**

Print Name of Subject	Signature of Subject	Date

Signature of Person conducting the informed consent discussion	Date

Role of person named above in the research project

Signature of Second Witness	Date

This document was approved by Campus Ethics Committee on:

4th August 2017

By Chairman: (Prof S Nayak)

This document expires on:

4th July 2018

..

What if I change my mind about sharing my research information?

Data collection sheet will be destroyed

Do I have the right to see and copy my research information?

Yes

If you agree to share your information, you should sign this form below. You will receive a copy of this form.

I agree to share my information as described in this form

Print Name	**Signature**	**Date**

If you have questions or concerns about your privacy and the use of your personal medical information, please contact the investigator at the telephone number listed in the consent form.