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Efficacy of Formal Screening for Depression in Pediatric Type 1 Diabetes Clinic

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Efficacy of Formal Screening for Depression in Pediatric Type 1 Diabetes Clinic

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ABSTRACT

EFFICACY OF FORMAL SCREENING FOR DEPRESSION IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES. Jeffrey Craig Winer, Natalie Hale, Sylvia Lavietes, and William J. Tamborlane. Section of Endocrinology, Department of Pediatrics, Yale University, School of Medicine, New Haven, CT.

This study was undertaken to examine the efficacy of screening for depression in a pediatric diabetes clinic and how the yield of such screening compares with established screening protocols aimed at identifying early microvascular complications and associated autoimmune diseases. Two-hundred-fifteen children and adolescents 8-18 years old in the Yale Pediatric Diabetes Center were screened for depression using the Children's Depression Inventory (CDI), with information including gender, age, duration of diabetes, HbA1C, and results of other screening protocols compiled.

A total of 8.4% of our cohort had CDI scores ≥13 indicative of clinically-significant depressive symptoms, with a range of 0-34. Depression scores were not associated with gender, age, or HbA1C. However, duration of diabetes showed a trend toward statistical significance (adjusted p=.068). Screening for depression using the CDI with a cutoff of ≥13 had similar positive testing rates as screening for microalbuminuria, hypercholesterolemia, thyroid dysfunction, and celiac sprue; in contrast, none of the clinic patients had evidence of retinopathy at their last ophthalmologic examination. These findings indicate that screening for depression in a pediatric diabetes clinic identifies a substantial number of youngsters with high levels of depressive symptoms and has a yield that is equal to or greater than other standard screening tests and examinations. Thus, screening appears to be warranted.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a chronic disease that affects over one million Americans. The fundamental dysfunction in T1DM is autoimmune destruction of the beta cells of the endocrine pancreas, which produce insulin. Insulin is used by the body to regulate blood glucose concentrations by promoting glucose transport into muscle and fat cells in the fed state and by regulating the production of glucose by the liver during fasting. In the absence of insulin, breakdown of fat is accelerated, leading to ketone formation and eventually diabetic ketoacidosis, a life threatening condition. On the other hand, the administration of too much insulin can cause hypoglycemia, leading to change in mental status and eventually syncope and seizure.

T1DM markedly increases the risk for the development of vascular and neuropathic complications. These complications include microvascular disease involving the retina and kidney, peripheral neuropathy, and macrovascular changes leading to peripheral vascular insufficiency, ischemic heart disease and stroke. The Diabetes Control and Complications Trial (DCCT) *(1)* showed that the microvascular and neuropathic changes seen in T1DM are directly related to higher HbA1C, a measure of long-term glycemic control.

Other conditions related to T1DM include an increased risk for other organ-specific autoimmune diseases and for adverse psychosocial outcomes. Associated autoimmune diseases of note include thyroid dysfunction and celiac sprue, whereas psychosocial associations include a higher rate of major depressive disorder *(2-18)*, eating disorders *(19-21)*, and suicidality *(16)* than age matched non-diabetic cohorts.

Standards of care for patients with T1DM include routine screening for early-onset microvascular changes as well as associated autoimmune diseases annually, including ophthalmologic examination for retinopathy and biochemical measurements of urinary albumin excretion, thyroid function tests and celiac-related autoantibodies *(22)*. However, clinicians have traditionally relied on their clinical acumen to identify those patients who are suffering from or at risk for depression and related psychiatric diseases *(3)*.

Recently, groups including the American Diabetes Association (ADA) *(22)* have recommended formal and regular screening for depression in addition to the screening already done for other associated diseases in diabetes clinics. The International Society for Pediatric and Adolescent Diabetes *(3)* also recognizes this problem, stating that "identification of psychosocial adjustment problems, depression, eating disorders, and other psychiatric disorders should be conducted at planned intervals by mental health professionals" using clinical interview for diagnosis.

The rationale for screening for depression in children and adolescents with T1DM includes the higher prevalence of depression among youngsters with, versus those without, diabetes and improvements in diabetes self-care, as well as emotional well-being, after identification and treatment of comorbid depression. However, the majority of investigations in this area have been short term studies carried out outside of the clinical environment. In fact, a search of the MEDLINE database for "Type 1 Diabetes Mellitus" and "Depression" limited to 1-18 year-olds and English articles returns no articles specifically investigating the efficacy of screening for depression within the clinic environment.

It is important to study screening for depression within the clinic environment per se when discussing the efficacy of such screening. Many differences exist between screening patients who have voluntarily enrolled in a study and screening those who have come to a scheduled clinic visit. In the case of a research study population, patients are offered the opportunity to participate in a study and they must formally consent to do so. Since routine screening for depression has been recommended for children with T1DM, this project was instituted to field test the usefulness of the depression screening in our diabetes clinic using the Children's Depression Inventory (CDI). While the patients and parents are entitled to refuse any part of or the entire screening test, the test was administered as part of their regular diabetes care. This change may lead to differences in the reliability of the screening tool, and therefore lead to different epidemiologic statistics, including sensitivity and specificity, when compared to prior studies.

In this report, we discuss a) the difficulties that we encountered in implementing screening in the clinic environment and our solutions to these obstacles, b) how our results compare to those of previous research protocol trials and discuss possible reasons for different epidemiologic statistics, c) the efficacy of depression screening as compared to established screening protocols for other associated diseases, and d) future work necessary to determine the cost effectiveness of long term screening for depression in T1DM.

EPIDEMIOLOGY OF DEPRESSION IN T1DM

The prevalence of depression among youth with T1DM has been reported to be 2-3 times that of non-diabetic age matched children in a number of studies *(18, 23)*. The

trials are difficult to compare, however, because the clinical cutoff for depression and the screening measures used are different between the studies. Therefore, the true prevalence of depression is difficult to estimate. In Blanz' study, a 33.3% rate of moderate or severe psychiatric disturbance was reported among patients with TIDM based on clinical interview as compared to a 9.7% rate among controls without T1DM. This paper also referenced eight prior studies using questionnaires to investigate whether patients with T1DM had increased rates of psychiatric symptoms. Four of these studies showed rates of depression as high as 35%. One study had equivocal results and three studies showed no increase in depressive symptoms as compared with non-diabetic controls *(2)*.

Kokkonen and Kokkonen published a 12% point prevalence of depression in children with T1DM and 18% in adolescents using unclear methodology *(18)*. Stewart et al published positive rates as high as 33% based on the Center for Epidemiological Studies Depression Scale (CES-D) *(23)*. Others, such as Lawrence, have estimated the point prevalence to be as low as 2-10% *(4)*.

Over the years, the Children's Depression Inventory (CDI) developed by Kovacs and colleagues has emerged as a standard screening tool to measure depressive symptoms in children and adolescents. Of interest to the current investigation, Hood et al found a 15.2% positive testing rate among children and adolescents measured with CDI $\geq$ 13 *(13)*. Grey showed a 12% positive testing rate among adolescents with diabetes using the same measurement *(24)*. Because these studies used the same screening tool as the current investigation they will be used for comparing research study protocol to our clinical screening results. In fact, Grey's study recruited patients from the Yale Pediatric Diabetes Center, and so the populations should have similar demographics.

Epidemiologic measurements of depression within T1DM other than point prevalence have also been studied. Gavard et al have reported that the lifetime incidence of depression is between 14.4% and 32.5% for both T1DM and type 2 diabetes mellitus *(18)*, with no significant difference based on type of diabetes. Cumulative incidence of depression before the age of 18 in T1DM is estimated to be up to 20% by Lawrence *(4)*. Over ten years follow-up from diagnosis, 26.1% of a cohort had at least one major depressive episode measured by clinical diagnosis *(6)*. Again, the criteria for diagnosis are different among these studies, and so they only provide a general idea of the scope of the problem.

Jacobsen et al, however, disputed higher rates of depression rates in T1DM. His group showed no significant difference in either the prevalence of depression during childhood or the incidence of depression during a ten year follow-up between children with and without diabetes. This study showed a prevalence of depression of 11% among subjects with diabetes and 10% among a control group using the Symptom Checklist-90R (SCL-90R). These authors criticized many of the previous epidemiologic studies for using prevalence of healthy cohorts in published data rather than control groups of children without diabetes. Thus, some question still remains about the magnitude, if any, of the increased rate of depression in children and adolescents with diabetes.

Even Jacobson's studies found lower psychosocial measurements in youth with diabetes, including lower self-perception of general competence, self-worth, sociability, physical appearance, ability to provide, and humor *(5, 8)*. He acknowledged that diabetes does increase psychosocial stress, and theoretically should be a risk factor for depression.

Despite the aforementioned psychosocial liability that T1DM brings, most children and adolescents with the disease are remarkably resilient. Psychosocial measures which have not been shown to change due to diabetes include self-perceived competency in school, social situations, athletics, and physical appearance *(15)*.

DEMOGRAPHIC AND CLINICAL ASSOCIATIONS WITH DEPRESSION

Although gender has not been associated with prevalence of depressive symptoms per se, girls tend to manifest their depression with more anxiety-related symptoms and boys tend more towards aggression and acting out. In addition, similar to the population at-large, girls with diabetes tend towards disordered eating behaviors much more commonly than boys *(17)*.

As in children without diabetes, one factor that previous work has associated with the rate of depression in diabetes is age. Adolescence is a tumultuous time in healthy children and the added stresses of diabetes coupled with the traditional "teenage angst" often leads to depressive symptoms and in many cases, frank clinical depression. This factor has also been found to have contradictory results between different studies. Insabella et al showed no linear association between age and prevalence of depressive symptoms (CDI > 13) when comparing <16 years old to 17-20 years old *(25)*. However, later work by the same group found that adolescents with T1DM have lower self-esteem, worse peer relations, and higher levels of depressive symptoms than preadolescents with T1DM *(26)*. It is also noteworthy that adolescence is a particularly difficult period to treat T1DM, although this is likely to be due to physiological in addition to known

psychological causes, because many of the hormones that increase during puberty have insulin-resistant properties *(25)*.

Another factor which has been shown to predict the rate of depression in children with T1DM is duration of diabetes. Grey et al have shown increased rate of depression in the months after diagnosis, improvements in depressive symptom scores at one year and a second wave of higher depressive symptom scores two years after diagnosis. The biphasic nature of this risk is postulated to be due to adjustment to new diagnosis at the outset and then subconscious realization of the permanent nature of diabetes contributing to the late phase *(15)*. The tedium of daily diabetes care can be daunting, and the stress can build over time. Of note, the two phases mentioned are strongly correlated. Those who have significant adjustment difficulties at the time of diagnosis are at increased risk for psychological disorders later, with increased risk continuing into adulthood *(25)*.

While it has been shown that depression is associated with higher HbA1C in diabetes, there has been no decrease in the estimated rates of depression among children and adolescents with T1DM as the treatment of T1DM has improved over the past twenty years. A study by Azar in 1999 *(27)* showed that transition to intensive insulin treatment does not change the rates of depression among pediatric diabetes patients. In addition, other studies have also shown no difference in rates of depression between patients treated with continuous subcutaneous insulin infusion (CSII) pump therapy and multiple daily injection regimens. While long term worries about complications may decrease as treatment of T1DM improves, this may be offset by increased burdens of therapy and worries about self-image and identity. The insulin pump may be more apparent to peers than the relatively private process of giving subcutaneous injections. The interplay of

these diabetes specific factors leading to depression among those with T1DM is discussed further below.

DIABETES-SPECIFIC FACTORS IN DEPRESSION

Depression is a significant problem even in healthy cohorts, with increased rates the context of chronic disease in pediatrics. However, the expectation of children and adolescents to quickly resume a "normal" life while simultaneously taking on certain aspects of fairly complicated treatment regimens makes T1DM somewhat unique among chronic diseases *(2)*. Because of the difficult, time consuming, and frustrating nature of T1DM care, many studies have investigated the relationship between disease-specific measurements and depressive symptomatology in children and adolescents with diabetes.

The Diabetes Adjustment Scale *(28)* was designed as a measure of psychosocial adjustment to T1DM in adolescent girls but it has been shown to be valid for children and adolescent of both genders and to correlate strongly with the Beck Depression Scale and self-esteem measurements *(10)*. Among the diabetes specific factors which have been associated with depression are illness centrality, illness negativity, diabetes adjustment, personal self-confidence in ability to treat oneself successfully and diabetes-based bullying.

The degree to which diabetes is a part of a patient's self-image, which is known as illness centrality, has a significant effect on risk for depression. The effect of illness centrality on rate of depression is confounded by negativity towards diabetes, as one might expect. Those for whom T1DM was more central to their lives had better self-care regimens and less depression when T1DM was seen in a less negative way. However, in

those who had a high level of negativity towards diabetes, lower illness centrality predicted a lower risk of depression. In addition, increased illness centrality was associated with worse metabolic control of diabetes. This effect is interesting, as one might expect those with increased illness centrality to have better self-care and therefore better glycemic control. However, it is likely that pediatric patients, especially adolescents, who have greater illness centrality may be more self-conscious in social situations and be more likely to forego both dietary control and blood checking behaviors during social situations with their peers *(29)*.

The effect of illness centrality on psychosocial adjustment to diabetes is in part mediated by gender. Females tend to define themselves more in terms of their diabetes than age-matched males, whereas males tend to have less anxiety even in cases of high illness centrality and high negativity than female counterparts. Helgeson and Novak *(29)* postulate that this may be due to the socialization of males in the U.S. to limit the effect of pain, leading to less integration of the sick role into their personality when faced with a chronic disease such as T1DM. With increasing age and longer duration of disease, illness centrality tended to decrease, and thus studies of adults with T1DM have lower relative risk of depression as compared with age-matched cohorts than adolescent studies *(29)*.

Work has also been performed investigating the relationship of depressive symptoms and feeling of control over metabolic outcomes in diabetes. The more that adolescents believe their behavior affects their metabolic outcomes, the better they tend to take care of themselves *(30)*. However, in patients with increased feelings of control, poor metabolic outcomes may lead to increased depression and anxiety, as they become

frustrated by their inability to manage their disease. When one believes that he or she controls metabolic outcomes, then failures may become more internalized.

Bullying based on diabetes has been shown to inversely affect self-esteem among youth with T1DM. Those who were bullied also tended to have worse diabetes self-care in social situations, often not adhering to proper dietary and blood glucose checking behaviors, likely to try to appear more "normal" *(31)*.

POSSIBLE PHYSIOLOGIC CAUSE OF DEPRESSION IN T1DM

In addition to the psychosocial impact of diabetes discussed above, recent work has postulated a physiologic mechanism for depression in the context of T1DM. It is known that approximately 50% of newly-diagnosed T1DM patients have positive titers of antibodies directed against the enzyme glutamic acid decarboxylase (GAD) *(32)*. In addition to peripheral functions, this enzyme controls the reaction transforming glutamate into gamma-aminobutyric acid (GABA) in the nervous system. Research by Sanacora et al has linked decreased plasma, cerebrospinal fluid, and brain concentrations of GABA to clinical depression and has shown increased GABA levels following successful treatment of depression with multiple modalities *(33)*. If the autoimmune response leading to production of anti-GAD antibodies and to T1DM is also expressed in the central nervous system, lowered conversion of glutamate into GABA could explain the increased risk of depression among patients with T1DM. Additional work needs to be done to investigate the relationship of GABA levels to diabetes in general and specifically in comorbid depression and diabetes.

EFFECT OF DEPRESSION ON DIABETES SELF CARE

While failure of treatment in T1DM can theoretically lead to depression, studies have also postulated that depression can also lead to worsening diabetes self-care and worse metabolic control of diabetes. Patients with diabetes in poorer metabolic control have a relative risk of 3.2 for depression relative to those in better metabolic control *(12)*. Those with worse glycemic control have higher rates of anxiety and depression *(34)*. Those who have depression scores above cutoff have a higher probability of hospitalization due to T1DM in the first year after diagnosis *(23)*.

It is difficult to investigate the causality of this association, however, because most of the studies on this topic were retrospective or prospective cohort studies, and not randomized control trials. However, response-to-treatment studies may begin to elucidate the relationship between metabolic control and depression. There exist studies showing that diabetes teaching lowers the rate of depressive symptoms *(35)* and that treatment of comorbid depression improves metabolic control of diabetes *(36)*. These studies together imply the cyclic causal relationship between depression and poor glycemic control, such that each of these two factors can feed each other, worsening both the physical and psychological well-being of the patient.

TREATMENT FOR DEPRESSION IN DIABETES

Treatment for depression in T1DM includes both pharmacologic and psychotherapeutic methods. In general, most of the pharmacologic treatment trials for depression have been performed on adults. However, recently, there has been increasing evidence of the efficacy of selective serotonin reuptake inhibitors (SSRIs) in children and

adolescents *(18)*. The added complication in terms of discussing treatment for depression in the context of T1DM is that some of the antidepressant medications have diabetes-specific side effects. For example, sertraline, an SSRI, has been shown to be associated with decreased sensitivity to symptoms of hypoglycemia *(37)*. In addition, tri-cyclic antidepressants such as nortriptyline have been observed in randomized placebo controlled trials to lead to hyperglycemia *(18)*.

The intervention that has been studied in children and adolescents with T1DM is psychosocial treatment including nondirective supportive treatment (NST), cognitive behavioral therapy (CBT), and interpersonal psychotherapy (IPT). Randomized studies have shown efficacy of initial supportive therapy for milder forms of depression among patients with diabetes. CBT methods and IPT have been shown to be effective in adolescents with depression, although no study specifically about diabetes exists *(18)*. One form of cognitive behavioral therapy, coping skills training, was investigated by Grey et al and found to reduce depressive symptoms significantly more than intensive diabetes education at the time when adolescents were transitioned to intensive therapy *(38)*. These methods likely all have benefits, and thus management should be individualized, including the possibility of combining methods of therapy.

DISORDERED EATING AND DIABETES

In addition to depression, many papers have addressed the topic of increased rates of disordered eating and eating disorders in youth with T1DM. In addition to the psychosocial aspects of diabetes affecting self-image, T1DM also unfortunately provides a unique and particularly unhealthy weight control mechanism: withholding insulin. This

behavior occurred in 2% of a cohort of adolescents with diabetes. In addition, 3% of subjects with diabetes, as opposed to .3% of non-diabetic patients, reported regular binge eating episodes, and 8% of diabetic as opposed to 1% of non-diabetic subjects reported two or more disturbed eating behaviors. Of these, the most prevalent behaviors were strict dieting and excessive exercising *(20)*. Another study by Rodin *(19)* quotes a 12% rate of bulimia by DSM-III criteria in a population of young adult women with T1DM, compared with 3% of the non-diabetic population. 39% reported under-dosing their insulin for the specific purpose of losing weight. 13% reported purging by some other means, mostly by excessive exercising. A study by Littlefield showed that history of binging behavior is associated with worse metabolic control of diabetes *(21)*. This association may be due to the nature of behavioral aspects of disordered behavior among patients with T1DM, the relatively large numbers that withhold insulin for weight loss, and the effect of psychological problems on self-care behavior as discussed above.

SUICIDALITY AND DIABETES

Perhaps the most worrisome concern in patients with T1DM and depression is the elevated risk of suicide. Diabetes is associated with high rates of depression and suicidal ideation and also provides children and adolescents to a relatively easy, painless means in which to hurt themselves: insulin overdose. Children and adolescents with T1DM have a 10 times greater risk of committing successful suicide than age matched non-diabetic cohorts *(16)*. The reports of increased risk of suicide in non-diabetic adolescents treated with paroxetine and other SSRI's has further complicated the treatment of comorbid depression and T1DM in teenagers.

OTHER ROUTINE SCREENING IN DIABETES CARE

Prior to this study, screening performed by the Yale Pediatric Diabetes Center included blood pressure and HbA1C measurements every three months at scheduled office visits in addition to annual cholesterol, urine albumin/creatinine ratio, thyroid function tests, and celiac antibody titer determinations. Eye exams by local ophthalmologists are recommended on annual basis for patients who are >10 years of age and have three or more years duration of diabetes.

The current guidelines for the above tests are based primarily on the results of the DCCT trial *(1)*. At the point when these data came out, the majority of diabetes care was conventional treatment, which meant that there was 7.8% per patient-year rate of development of retinopathy, 1.4% per patient-year development of microalbuminemia and the incidence of diabetic neuropathy was 16.1% after five years follow-up *(1)*. However, with intensive insulin therapy, and increased use of CSII pump therapy, mean HbA1C levels have been lowered from mean values of ~10% to the 7.5% range in the Yale Pediatric Diabetes Clinic. Recent studies have shown markedly lowered risk of vascular changes in children and adolescents with diabetes under this improved treatment, including a 0% prevalence of sustained retinopathy within the Yale Pediatric Diabetes Clinic population in a recent clinical outcomes study *(39)*.

Less likely to change with improved insulin therapy are the incidences of auto-immune diseases associated with T1DM. However, the literature suggests that these comorbid diseases are less prevalent in the T1DM population than depression. The estimate of the prevalence of Celiac disease in one T1DM population was 4.4% *(40)*.

Approximately 7.3% of patients with T1DM have thyroid dysfunction, although the majority of these were antibody titer negative thyroiditis *(41)*.

As will be discussed later, these numbers are not directly comparable to either cumulative incidence of depression or point prevalence of depression. This is because these diseases are chronic and permanent, whereas depression is a fluid syndrome. However, the cumulative incidences before the age of 18 of either disease still pale in comparison to the estimate of 20% incidence of depression, which is the lowest value from previous studies.

WORLD HEALTH ORGANIZATION'S PRICIPLES OF SCREENING

In 1968, the World Health Organization published principles of successful screening *(42)*. These principles apply equally to primary screening of the entire population, as well as secondary screening of select populations at increased risk for a disease, such as depression in diabetes, and tertiary screening for complications of disease.

These principles are:

1. *The condition should be an important health problem.*
2. *There should be a treatment for the condition.*
3. *Facilities for diagnosis and treatment should be available.*
4. *There should be a latent stage of the disease.*
5. *There should be a test or examination for the condition.*
6. *The test should be acceptable to the population.*
7. *The natural history of the disease should be adequately understood.*
8. *There should be an agreed policy on who to treat.*
9. *The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.*
10. *Case-finding should be a continuous process, not just a "once and for all" project.*

The application of the principles of screening to screening for depression will be discussed below.

STUDY AIMS AND HYPOTHESES

AIM 1.

To discuss the implementation of formal screening for depression in the clinical environment including difficulties encountered and solutions to those difficulties.

We anticipated that the greatest difficulties that would be encountered in implementing a depression screening program are the added burden that such a program puts on a busy clinical practice and resistance of some patients and parents to screening for depression. In order to minimize the added time that this process will take, we used the CDI as our screening instrument, since this form requires only about ten minutes to complete and administered the questionnaire while a patient waited for his or her appointment. We anticipated that the biggest resistance to the CDI would be from adolescents for whom psychiatric disease is stigmatized and from parents of relatively young children who often do not think of childhood as having psychological stress.

AIM 2.

To compare results of depression screening in research protocols to those in the clinical setting.

The difference between this study and the previous studies described above is that this study took place within the context of a clinical protocol in clinic. In screening a population as part of clinical protocol, we removed all selection bias that might have been present in research protocols. However, we also likely removed some of the patients'

subjective feeling of anonymity. Thus, it is possible that the prevalence of depression in our population may be different than in previous experimental populations.

Patients' responses to the CDI questionnaire might also be affected due to the knowledge that someone is scoring the test about them, rather for an anonymous study, and so even if the epidemiology of depression in this clinic is similar to previous studies, the test characteristics may change in terms of sensitivity and specificity.

AIM 3.

To compare the efficacy of formal depression screening using the CDI in clinic to other screening protocols already implemented in the clinic.

Assuming that the results of clinical screening are similar to previous research protocols, then depression screening in the clinic would be much more efficient than already established screening protocols based on published prevalence. Depression is likely more prevalent in a T1DM population than any of the other disease manifestations that are tested. The cost of screening for depression is minor in terms of both cost and time relative to lab testing and annual ophthalmologic examination, especially as the incidence of vascular changes decreases with improving metabolic control of diabetes: an ophthalmologic appointment is estimated to cost $175 *(39)*, as opposed to the employee salary for a 10 minute depression screen, <$10.

Clinical results consistent to previous work would help to argue for an effort to improve the efficacy of diabetes care by adding formal depression screening. In addition, further work would be necessary to reexamine current screening guidelines for these other diseases in terms of cost effectiveness, especially those vascular complications of poor glycemic control.

METHODS

STUDY OVERVIEW

Data were collected by the author (JCW) based on scheduled routine diabetes care appointments in the Yale Pediatric Diabetes Center during June 20 – August 24, 2005 and by an undergraduate student (NH) under the author's (JCW) direction from September 12 – December 10, 2005. A group of 20 patients was administered the CDI prior to data collection as a pilot group in order to optimize the presentation and administration thereof. Inclusion criteria included all patients with T1DM between 8-18 years of age. There were no exclusion criteria for primary analysis. However, for secondary analyses investigating the association of HbA1C, age and duration of diabetes to prevalence of depression and that comparing depression screening to other screening performed in clinic, patients were excluded if their HbA1Cs could not be found during the chart review phase of the study or if they did not have laboratory values taken within nine months of their appointment, respectively.

Patients were administered the CDI after a brief introduction to the purpose and procedure of the screening process. Additional clinical information was obtained by the author (JCW) by chart review of the screened cohort including age, duration of diabetes, HbA1C, most recent thyroid function tests, most recent cholesterol, most recent albumin/creatinine ratio, celiac titers, and history of any diabetes-associated complications. All statistical analysis was performed by the author (JCW).

This work was performed under Yale HIC protocol 3861, which allows the use of anonymous clinical data from the Yale Pediatric Diabetes Center for the purpose of clinical research.

CHILDREN'S DEPRESSION INVENTORY

Developed by Maria Kovacs, the Children's Depression Inventory (CDI) is a 27 item screening test used for research and clinical purposes to screen for depression in children and adolescents. It has the lowest reading level of any depression measure designed for children, and has been validated for children and adolescents 7-17 years of age. Each item on the CDI has three sentences representing absence of symptom, mild symptom, and severe symptom, respectively. The CDI is then graded on a 0-2 scale for each question, with about half of the questions having increasing and half decreasing order of severity. The total CDI score can range from 0-54, with a score ≥13 considered positive for risk of depression clinically, and is considered positive in most research protocols that use the CDI *(43)*. An example question is as follows:

FIGURE 1. Example of question as administered in CDI.

1.

☐ I AM SAD ONCE IN A WHILE

☐ I AM SAD MANY TIMES

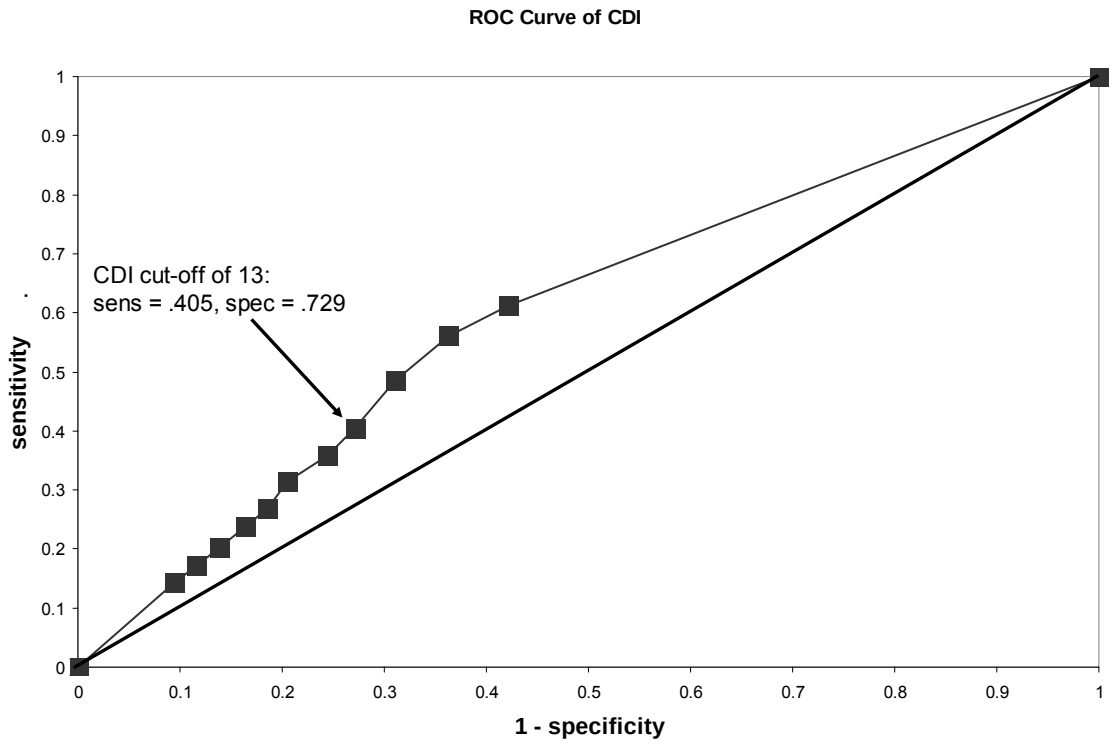
☐ I AM SAD ALL THE TIME

Note: In this case, "I am sad once in a while" would be scored as 0, "I am sad many times" as 1, and "I am sad all the time" as 2. About half of the questions have ascending severity of symptoms, such as this. The other half of the questions has descending severity of symptoms, scored 2, 1, and 0, respectively. If the total of the 27 questions' scores is ≥13, the screen is considered to be positive for risk of depression.

In the original publication of the CDI *(43)*, the cutoff which keeps the false negative rate well controlled while still having good reliability was suggested to be 13. At this cutoff, the sensitivity is 40.5%, and the specificity is 73% when compared to the gold

standard of clinical interview by a mental health professional. This gives us a positive likelihood ratio equal to 1.50 and a negative likelihood ratio of 0.81. The receiver operator characteristic (ROC) is shown in figure 2.

FIGURE 2. ROC Curve of CDI.



Note: We based our cutoff of CDI ≥13 on these normative data, trying to balance including true positives with excluding false positives. ROC = .60. With this cutoff, the positive likelihood ratio was 1.50 and the negative likelihood ratio was 0.82.

The ROC for the CDI as a whole based on these data is equal to .60. However, the original normative data are inconsistent with multiple studies performed using the CDI, as will be discussed in detail later.

Even with the original normative data, the CDI is less than optimally accurate for screening for depression, but has the advantages of being able to be administered by someone with minimal training and being much faster than clinical interview. Thus, with

the time constraints in the clinical environment, this should be a good tool to use to screen patients quickly and with some level of precision for depression. In the Yale Pediatric Diabetes Clinic, any patient with more obvious psychosocial difficulties is referred to the clinic's social worker, and so the CDI functioned as an additional diagnostic tool rather than supplanting the basic clinical screening that was already taking place.

ADMINISTERED INTRODUCTION TO CDI

Because depression screening was new to the clinic and due to some resistance in our initial 20 patient pre-trial cohort to the CDI, we chose to give the CDI improved context by explaining its use and procedure to parents and children before administering it, inviting any questions afterward. Our introduction included the following aspects:

1. *Diabetes can be difficult; in the same way we test for other associated diseases by taking blood, we want to know as early as possible if our patients are having emotional difficulty.*
2. *The screening test contains some difficult questions, but it is very important for us to know the answers to these so that we can best care for our patients.*
3. *It is important for the patient to give as accurate and unbiased answers as possible; the parent should not guide him/her towards any answer.*
4. *Anyone, including both the parent and the administrator of the test, will leave the room if the patient feels more comfortable.*
5. *We will score the test immediately and, if we are concerned based on the results, we will have the patient speak with the clinic's social worker.*

Our results include only the main cohort who were screened after this introduction was added to the process.

PROTOCOL FOR POSITIVE TEST RESULTS

Because this screening was performed in a clinic environment, it was primarily used to identify patients at risk for depression in order to better assess and treat them. As such, patients who either scored ≥13 total on the CDI or answered positively to the item pertaining to suicidal ideation and intent were immediately referred to the clinic's social worker (SL). In these cases, she would formally assess the patient's immediate risk to him/herself and others, and arrange for follow-up with her and/or other mental health professionals if necessary. In this way, we were able to ensure to the best of our ability the health and safety of our patients.

OTHER SCREENING TESTS PERFORMED IN CLINIC

HbA1C was measured using Bayer Corporation's DCA 2000+ during patients' appointment in the clinic at the beginning of each appointment. Laboratory tests including cholesterol, thyroid function tests, urine albumin and creatinine, and anti-tissue transglutaminase level were performed by Quest Diagnostics. Ophthalmologic examination was performed by the patients' individual ophthalmologists and reports were sent to the Yale Pediatric Diabetes Center.

Because these tests were also screening tests, positive results lead to more definitive testing for a disease. Also, definitive testing took place if clinical signs of disease were reported. In this way, the process of screening for medical diseases was very similar to the algorithm for depression screening, including both clinical acumen for cases in which there was concern and a formal screening test.

However, it is impossible to compare the depression screening in this study with the other screenings directly. This is because these other screening tools have been in place for some time, and therefore multiple tests increase the overall accuracy of screening. In addition, patients who have been screened positively have had the time to undergo more definitive testing in order to make a diagnosis and treat in the cases of hypercholesterolemia, thyroid disease and celiac sprue. Therefore, we will only get a general idea of the relative positive screening rates among these diseases.

STATISTICAL ANALYSIS

Statistical analysis was performed using R for Windows 2.6.0 (www.r-cran.org).

In the case of comparing two populations for the sake of cohort analysis, testing was performed comparing the contained sample and the excluded sample using 2-sided Students t-test for continuous variables and Chi-square test for categorical variables. All of these hypothesis tests were performed with $\alpha=0.05$, using Bonferroni correction for multiple tests on the same factors.

Comparison of rate of CDI ≥ 13 to prior studies was performed using 1-sided analysis of binomial distribution using a $p = .12$ and $n = 215$. The lowest published point prevalence in prior studies that used CDI was 12%. This value was used in order to be more conservative in finding differences between prior studies and the current one.

Investigation into the association of demographic factors and depression was performed both to determine the association of CDI score itself and of depression as defined by CDI ≥ 13. Covariance analysis was performed to determine whether demographic variables were significantly associated with each other. In cases of

categorical variables, the former was performed by t-test between the groups comparing logarithm of CDI in order to gain approximately normal distribution and the latter by Chi-square testing. In the case of continuous variables, analysis of association with CDI score was performed by linear regression with logarithm of CDI as the response variable, and analysis of association with CDI ≥13 was performed by logistic regression. The logarithm of CDI (offset by .5 to include 0 scores) was used in order to better fit the CDI data to a normal distribution.

RESULTS

IMPLEMENTATION OF CDI

In the initial pilot cohort, the CDI was given without verbal introduction. Five parents censored or guided the results in some way by either refusing to have their child answer particular questions or having their child change initial answers in some way. Once the verbal introduction was implemented, no patients or parents refused any part of the CDI or censor the responses.

The CDI took approximately 10 minutes on average initially and when the verbal introduction was added. The added time due to the verbal introduction was offset by the subjects' willingness to proceed without further discussion.

COHORT ANALYSIS

Overall, 215 clinic patients were administered the CDI. Of these, full demographic information was available for 184 and full information including laboratory and clinical test values were available for 162. The rate of depression was not significantly different between those whose information was fully available and those who had missing data ($p=.41$). The demographic information did not differ between those that had full laboratory and clinical information and those that did not in terms of depression ($p=.46$), gender ($p=.65$), age ($p=.51$), or HbA1C ($p=.18$).

However, having full laboratory and clinical values was positively associated with duration of diabetes ($p=.02$), likely because newly diagnosed patients were less likely to have had laboratory testing. This explanation is strengthened by the fact that 5 out of 22

patients who were missing at least one laboratory or clinical value had duration of diabetes <1 year, whereas 11 out of 162 patients with full laboratory values did (p=.01). Among those who have had diabetes for at least one year, the duration of diabetes was not significantly associated with whether or not a patient had full laboratory and clinical values available (p=.17).

DEMOGRAPHIC CHRACTERISTICS

The 184 patients with full demographic information had age of 13.6±2.8 (mean ± standard deviation) years. Duration of diabetes was 4.7±3.5 years. HbA1C was 7.3±1.3 %. Ninety-two patients were male and 92 were female. Demographic characteristics of depressed and non-depressed patients are summarized in Table 1.

TABLE 1. Demographic characteristics of the cohort.

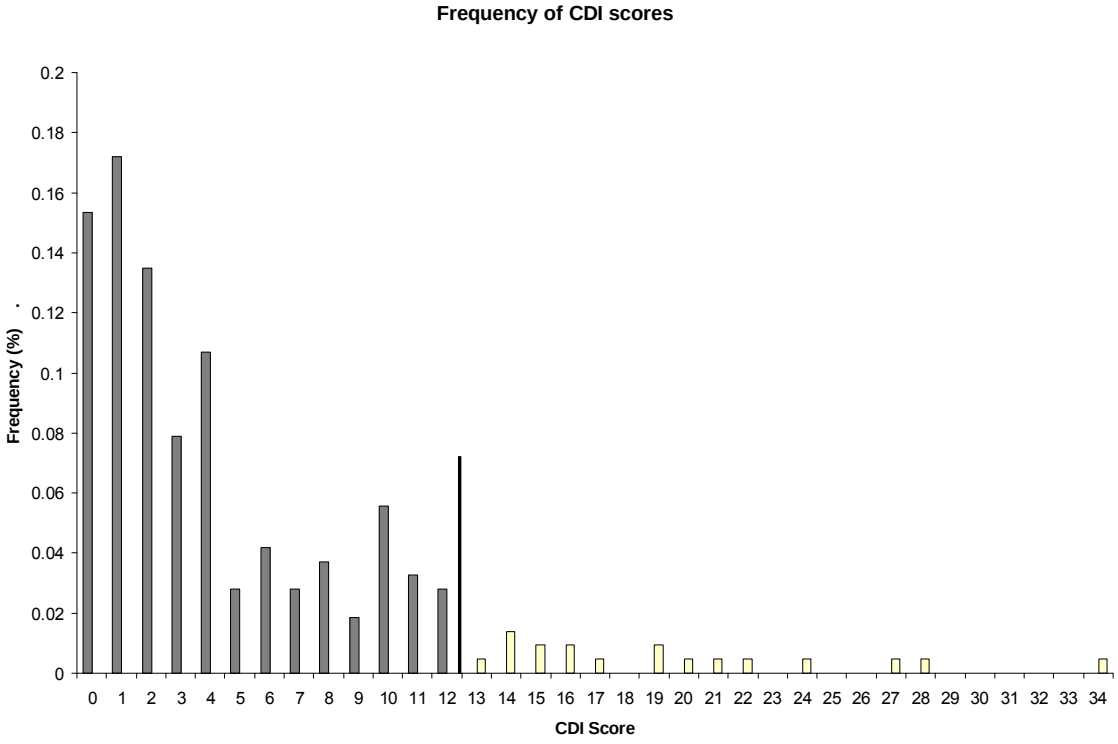
	Overall	CDI <12	CDI ≥13	
n	184	168	16	
Age	13.6 (13.2, 14.0)	13.7 (13.3, 14.1)	12.6 (11.1,14.1)	p=.12
Gender	92:92 (50:50)	83:85(49:51)	9:7 (56:44)	P=.66
T1DM Duration	4.6 (4.2,5.2)	4.6 (4.1, 5.1)	5.3 (3.7, 6.8)	p=.03
HbA1C	7.3 (7.1, 7.5)	7.3 (7., 7.5)	7.8 (7.3, 8.3)	p=.11

Note: Age, gender, duration of diabetes, and HbA1C summaries of the cohort overall, and by CDI level (negative vs. positive screen). P-values compare negative screening and positive screening groups. P-values are adjusted for multiple tests, using Bonferroni's method.

SCREENING RESULTS

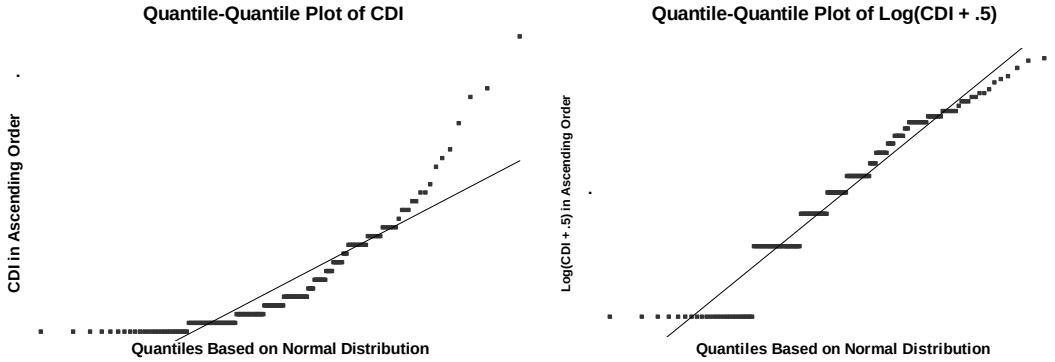
Of the 215 patients administered the CDI, 18 (8.4%) had scores ≥13, with an overall range of 0-34. Figure 3 is a histogram of CDI results.

FIGURE 3. Histogram of CDI scores.



Note: Summary histogram of CDI screens. 8.4% of the cohort had scores ≥13. This result was not significantly lower than previous screens performed within research protocols, 12% (p-.06). As expected, the results had a significant right tail.

FIGURE 4. Quantile-Quantile Plots for CDI and log(CDI + .5).



Note: Plots of the raw CDI scores and transformed scores. We see that because of the right tail in the raw scores, the logarithm is a better fit to the normal curve. Therefore, we will use the logarithm for hypothesis testing that requires a normal distribution.

These results are not significantly lower than the smallest published prevalence within a research protocol, 12%, despite using a one-sided test (p=.06), but it does trend towards significance. Assuming a minimum practically significant reduction equal to 25% of depression in our study, the power of this test was 34%, so it is still very feasible that there is a significant difference that we could not show using our study.

Of the 184 patients with demographic information, 16 (8.7%) had scores ≥13, and of the 162 with full laboratory and clinical data, 15 (9.3%) had scores ≥13. These values were not significantly different within each exclusive layer of the cohort.

In addition, the total CDI score can be divided as described above into scales for negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem. The average scale score for negative mood was 1.30±2.592, for interpersonal problems 0.50±0.92, for ineffectiveness 1.01±1.39, for anhedonia 1.81±2.06, and for negative self-esteem 0.65±1.09. These sub-scales do not have clinical or research cutoffs, and so cannot be compared epidemiologically for prevalence of these symptoms.

Moreover, the only published normative values are based on Kovac's original data, in which over 28% of patients scored ≥13 on the CDI*(43)*, which is drastically different from studies of T1DM that have used the CDI, and so comparison is without merit.

DEMOGRAPHIC ASSOCIATIONS WITH DEPRESSION

Using multivariate analysis, we found that the only factors significantly correlated with each other were age and duration of diabetes. However, the model including both was not significantly better (p=.26) than that using either individually based on ANOVA analysis. Therefore, we will analyze each factor individually so as not to dilute any associations.

Gender was not significantly associated with rate of depression. Nine (9.8%) females had CDI scores ≥13, as did seven (7.6%) males (p=.60). Age was not significantly associated with CDI scores by linear regression using the logarithm of CDI scores to fit to normal distribution (p=.38). Rate of depression based on CDI ≥13 was not associated with age by logistic regression analysis (p=.24). These p-values in addition to the ones that followed are adjusted for multiple tests per Bonferroni correction.

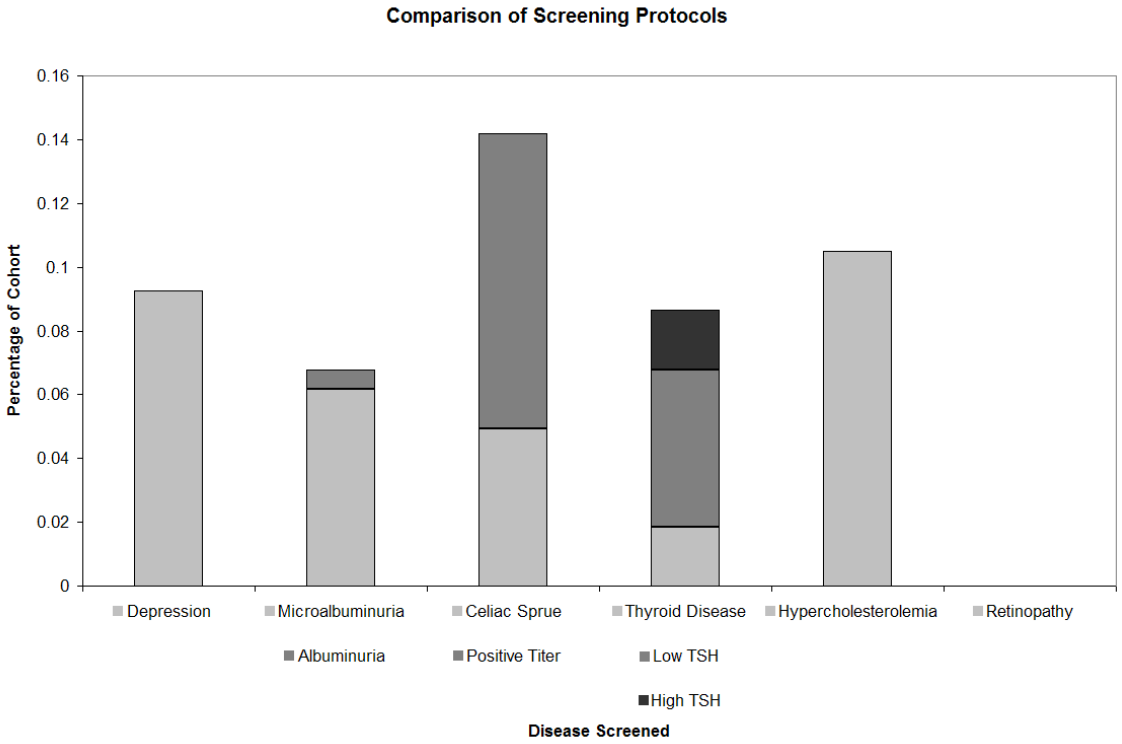
Duration of diabetes was the only demographic variable with p<.05 based on linear regression of level of depression against the logarithm of CDI (p=.068), with CDI scores decreasing as duration increases. However, the rate of CDI ≥ 13 was not associated to duration of diabetes based on logistic regression (p=.94).

HbA1C was not associated with CDI by linear regression using the logarithm of CDI as response variable (p=.34). In addition, there was not association between HbA1C and probability of CDI ≥13 by logistic regression (p=.22).

LABORATORY AND CLINICAL TESTING

In the cohort of 162 patients with full clinical and laboratory values, 10 patients (6.2%) were found to have microalbuminuria (>30 μg/mg creatinine) and one patient (0.6%) to have albuminuria (>300 μg/mg creatinine). Eight patients (4.9%) had previously diagnosed celiac sprue, and of those who did not, 15 (9.7%) had laboratory values above the screening cutoff (≥ 8 U). Three patients (1.9%) had previously diagnosed thyroid disease, and of those who did not, eight patients (5.0%) had low TSH levels (<0.7 mIU/L) and three patients (1.9%) had high TSH values (>6.4 mIU/L). Seventeen patients (10.5%) had hypercholesterolemia (>200 mg/dl). No patients (0%) were found to have consistent early retinopathy based on ophthalmology screening.

FIGURE 5. Comparison of results of screening protocols.



NOTE; In this table, the total screening prevalence is shown for each disease. Overall prevalence is divided by method. For example, thyroid disease is divided into those who had previous diagnosis, those who had low TSH on laboratory testing, and those with high TSH on laboratory testing.

DISCUSSION

ADMINISTRATION OF CDI

Including the introduction to the CDI, screening took approximately 10 minutes to complete. In a busy clinical environment, this extra time is not insubstantial, especially in cases where a patient is screened prior to seeing a clinician and the clinician is waiting to see the patient while the CDI is completed. Without knowing the results of our trial screening program, it was a leap of faith to delay an appointment in an already busy clinic for depression screening.

However, in trying initially to decrease the amount that the CDI delayed other clinical care, we found that many problems arose. In an effort to save time for both patients and clinicians, the CDI was administered with an extremely abbreviated introduction, simply stating that this was a new screening protocol we were instituting. At this point, many parents insisted on reading the questions first, and often then censored their children's responses. This censorship either took place by the parent convincing a patient to answer questions that they had originally answered in the affirmative or by removing certain questions entirely, such as the one pertaining to suicidality. This obviously invalidated the results of our screening, biasing the test towards negative results and lowering our sensitivity. In addition, parental interference led to the CDI taking approximately the same amount of time as with an extended verbal introduction, and so there was not even the advantage of shorter time that we initially sought to offset this unacceptable limitation.

Five out of the first 20 patients administered the CDI were censored in some way by their parents. Even when a written introduction was given to the parents while the

children were administered the test, a significant proportion of parents insisted on censoring either the test or the children's answers, as described above.

On the other hand, in the cohort of 215 who were given the verbal introduction that explained to parents that the information we were gathering, especially those difficult questions, was essential to the proper and safe care of their children, zero parents censored the test.

The censorship that initially took place most often was that parents refused to have their children read the question that asks about suicidal ideation.

This question is understandably disturbing to parents who do not fully understand the importance of knowing the true answer to this question. When asked about their reservations in having their child answer this question, the unanimous response was that they did not want such a thought in their child's head and were afraid that discussing such would do so. By preemptively discussing the topic of "difficult questions" and the importance of knowing the answers to them for the sake of the children's health and safety, however, none of the 215 subjects objected to any part of the CDI.

WORLD HEALTH ORGANIZATION PRINCIPLES' APPLICATION TO SCREENING FOR DEPRESSION IN T1DM

As discussed in the introduction, in order to recommend using the CDI for secondary screening of depression in the pediatric T1DM population, such screening should adhere to general screening principles such as those put forth by the World Health Organization. A discussion of each of these principles follows:

1. The condition should be an important health problem.

   Clearly, depression in an important health problem, especially in patients with T1DM. This is illustrated by estimates of 2-3 times more depression in the T1DM population than in age-matched non-diabetic cohorts, the effect that depression has on worsening metabolic control, and the 10X increased rate of suicidality in the diabetes population.

2. There should be a treatment for the condition.

   As discussed in the introduction, there exist both pharmacologic and psychotherapeutic treatments for depression in the pediatric T1DM population. Randomized controlled trials of these treatments are still rare in this population, but there is increasing evidence of their efficacy.

3. Facilities for diagnosis and treatment should be available.

   While leading to some increased time for the patients and clinicians, if effective, depression screening for children and adolescents with T1DM can take place in an organized and consistent manner at their pediatric endocrinology appointments. Especially in academic centers with a dedicated pediatric diabetes center, such as Yale, this can be well-coordinated. With the advent of increasing multidiscipliary treatment for chronic diseases, there is often a mental health professional available within the clinic environment already, but referral to one outside of the clinic itself can occur when there is not. This is the standard of care based on the American Diabetes Association's guidelines *(22).*

4. There should be a latent stage of the disease.

   While depression can be frank, it also exists on a continuum from euthymia to significant major depressive disorder. Identifying those patients who are suffering from symptoms of depression early, before the self-amplifying effects of depression on quality of life and diabetes care can occur, should benefit the patients immensely.

5. There should be a test or examination for the condition.

   The clinical interview is the gold standard for diagnosis of depression and it would be employed on referral for formal psychological evaluation in patients who had positive CDI screens.

6. The test should be acceptable to the population.

   As discussed above, with a brief introduction to the CDI, none of the patients or parents had any objection to the CDI. However, we found from our early use of the test that without such introduction, many parents object to asking their children about suicidal ideation and suicidality and to having their children answer questions to the affirmative in general.

7. The natural history of the disease should be adequately understood.

   Studies discussing the onset, associated problems, and outcomes of depression in T1DM have been performed. These have shown that without intervention, long-standing depression can lead to worsening metabolic control of diabetes, decreasing diabetes self-care, and in rare but alarming cases, suicide.

8. There should be an agreed policy on who to treat.

   Within our protocol, we referred patients who scored ≥13 on the CDI to the clinical social worker who interviewed the patients and determined the proper way to proceed in caring for their possible depression. This is one of the major difficulties in recommending the CDI for screening for depression in type 1 diabetes. The only normative data on the CDI is over 30 years old and mathematically inconsistent with more recent work using it. Therefore, the efficacy of using ≥13 as the cutoff for screening is uncertain, and further work should be performed in order to develop the evidence for a particular cutoff.

9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.

   This is one of the principles that is the most difficult to illustrate as valid for depression screening in diabetes. Estimating the cost of screening is fairly simple. The cost of screening for depression using a questionnaire such as the CDI is relatively minimal as compared with other screening protocols, and so if the epidemiology of these various screening tests is similar, then depression screening should be included as part of the care of pediatric patients with T1DM based solely on cost effectiveness. However, the cost of diagnosis, including treatment, is difficult to estimate. In addition, the cost benefit of treatment for depression both in terms of quality of life and in terms of change in metabolic management of diabetes is a complicated and somewhat subjective calculation.

10. Case-finding should be a continuous process, not just a "once and for all" project.

We recommend that any implemented screening for depression would be a continuous process, for example, annually. The reason for this is that because screening is imperfect, in addition to the fact that depression is not a static disease, repeated testing would increase the likelihood of finding a large proportion of patients with depression. In addition, the effects that duration of diabetes and age have on the prevalence of depressive symptoms are yet two more reasons to repeat testing.

ESTIMATING PREVALENCE OF DEPRESSION

One first needs to mention the previous articles reporting “prevalence” of depression among children and adolescents with diabetes. These studies varied from 11-33% in their estimates of the prevalence of depression.

The first factor that affected the prevalence among these studies was the method of screening. The tests using only a screening test actually measured positive testing rate of their test, rather than the prevalence of the disease that they were testing. Therefore, without normative data as to the sensitivity and specificity of those tests, it is impossible to convert these to prevalence estimates, which would be comparable between the differing studies. There are normative data for the CDI, but they are inconsistent with both our results and those of other studies and so cannot be used to estimate prevalence.

Contrary to intuition, many of the studies that utilized clinical interviewing had higher prevalence than those which used what were considered screening tests. This implies some weakness in the screening tools used, as there must be a significant number of false negatives by the screening tests in order for the gold standard of clinical

interview to have a higher positive testing rate. This is consistent with the results of the pilot study in which parents minimized their children's symptoms reports and/or censored questions completely.

As previously mentioned, there are multiple reasons that our results could be different from previous studies. The result that 8.4% of patients screened had CDI results ≥13 was not statistically lower than the 12% we used as the positive testing rate within research protocol studies, but we did not have sufficient power to conclude that there is not a practically significant difference.

DIFFICULTY IN USING KOVAC'S DATA

Using our results, we cannot use Kovac's original normative data*(43)* to try to determine a true prevalence of depression in our population. Using a cutoff of 13, Kovacs found the CDI to have sensitivity = .4052 and specificity = .7291. With a specificity this low, the positive testing rate should be between .2709 and .4052 regardless of the true prevalence of depression. Mathematically, this sample, as well as of those other studies that have used the CDI, had a much greater specificity than this in order to have positive testing rates lower than this range.

Therefore, we are excluding a greater number of those who do not have depression, which is admirable, but also generally associated with decreased sensitivity. We cannot mathematically exclude Kovac's sensitivity measurement in the same way we can with specificity, but there needs to be more studies of the testing parameters of the CDI in children and adolescents with T1DM in order to better assess the efficacy. Because the cost of a false positive is simply referral to the clinical social worker, whereas the costs of

false negative are the aforementioned sequelae of undiagnosed depression in T1DM, it follows that we might consider decreasing the cutoff of the CDI in order to increase sensitivity, even if this decreases specificity.

ASSOCIATION WITH DEMOGRAPHIC FACTORS

Gender was not associated with rate of depression. Previous research has also not shown differences strictly in the rates of depression (or levels of depressive symptoms) between males and females with T1DM. However, there are some data showing that the psychosocial symptoms of depression differ between males and females. Females, for instance, have greater levels of anxiety than their male counterparts. In addition, females are more likely to suffer from disordered eating behavior.

Age was also not associated with depression or with CDI scores in our study. Patients identified as having CDI ≥13 ranged in age from 8 years 10 months to 16 years 11 months. It is clear that while other studies have shown different rates of depression based on age, especially preadolescent vs. adolescent, depression is a significant problem within T1DM patients across all of the ages that we screened.

Despite the relatively small number of patients in our sample with positive CDI screening values, the duration of diabetes trended towards significant association with CDI scores. Prior studies have postulated that there is a bimodal distribution of the rate of depression, the first occurring shortly after diagnosis and the second after a two-year duration of diabetes. Albeit with relatively small sample sizes in the first two groups, the rate of CDI ≥13 was similar between those patients with diabetes <1 year (6.3%), 1-2 years (6.7%) and >2 years (9.4%).

In this study, there was not a significant association between HbA1C and either depression or CDI scores. However, based on previous work, it is clear that the cyclic nature of poor diabetes care associated with depressive symptomatology and depressive symptoms leading to worsening diabetes care. If we consider poorer glycemic control as a symptom, then psychosocial distress including depression must be in the differential diagnosis. Therefore, thoroughly assessing patients with persistently poorer glycemic control for depression likely should be performed in addition to regularly scheduled screening protocols in place.

OTHER SCREENING TESTS

It is noteworthy that the yield from CDI screening for depression was similar to that of every other screening test in our patient population other than for retinopathy, ranging from 6.8% of patients with some level of albuminuria to 10.5% of patients with cholesterol levels > 200 mg/dl. Clearly each of these screening tools is effective in identifying a relatively large percentage of patients who may have diseases that are associated with diabetes. The only screening that may need to be revised is ophthalmologic examination, as reported by Hou*(39)*. In addition, a study of the comparative cost effectiveness of these screening tools may be performed, which would include not only the screening results, but also some gold standard diagnosis.

LIMITATIONS OF CURRENT STUDY

An important limitation of this study is the relatively small sample size, especially regarding the number of subjects with positive screening scores on the CDI. Thus, the failure to demonstrated statistically significant associations between positive screening scores and clinical factors, such as HbA1c values need to be interpreted cautiously. Moreover, we did not compare the results of the screening test to the gold standard clinical diagnostic interview. With more resources and time, another study could be developed that would screen for depression within the clinic using a test such as the CDI and then secondarily use clinical interview to develop data regarding false positive and false negative results. In this way, we could gain a better sense of what the testing cutoff should be in addition to the efficacy of screening for depression per se.

CONCLUSION

There are many studies which have investigated the prevalence of depression among children and adolescents with T1DM. Most of these have shown increased rate of depression. Guidelines put forth by the ADA and ISPAD now include recommendations for some formal screening for depression, either by self-response questionnaire or by clinical interview. Previous studies using the CDI have shown positive testing rates of 12-15.8% within this population. However, these studies have been in the context of research protocol using volunteers who have some level of anonymity. When screening within the clinic environment, we had a positive testing rate of 8.4%. This rate was somewhat lower than in previous studies using the CDI in pediatric T1DM populations and was inconsistent with published testing data for the CDI. Therefore, further work

should be performed to determine the sensitivity and specificity of the CDI for screening of depression within T1DM clinic and to determine the best clinical cutoff value for positive screening.

In screening for depression using the CDI, a brief verbal introduction was important in easing both parents and patients about the use of the CDI, as well as the importance of having honest and complete answers to even the most difficult questions. When this introduction was given, the CDI took approximately 10 minutes on average to complete. This led to some delay in clinical appointments, but if consistently shown to be effective, would be worth the additional time.

Screening for depression using the CDI with a cutoff of ≥13 had similar positive testing rates to screening for albuminuria, hypercholesterolemia, thyroid dysfunction, and celiac sprue. Zero of our patients had consistent retinopathy by ophthalmologic examination, however. Thus, the yield of using the CDI as a screen for depression is similar to or higher than the yield from other biochemical and clinical screening procedures that are recommended in children and adolescents with T1DM.

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