Chapter 24

Psychosocial Aspects of Diabetes in Adult Populations

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SUMMARY

A number of studies during the past decade have investigated the comorbidity of mental illness and diabetes. Studies that used structured diagnostic interviews found that the mean prevalence of current depression in diabetic subjects was 14.0% in controlled studies and 15.4% in uncontrolled studies. These rates are at least three times the 3%-4% prevalence of major depressive disorder found in the general adult population of the United States. Investigations that used depression symptom scales found that the range of clinically significant depression symptomatology in diabetic subjects was 21.8%-60.0% (mean, 31.6%) in controlled studies and 10.0%-28.0% (mean, 19.6%) in uncontrolled studies. These findings support an increased prevalence of depression in diabetes relative to the general adult population. Whether depression is more common in diabetes than in other chronic diseases, however, is far less supported by the literature.

It is a prevalent clinical belief that depression in diabetes is secondary to psychosocial hardship brought on by increasing severity of the diabetes. Studies that have examined this relationship, however, did not find statistically significant associations between depression and severity of diabetes in 25 of 32 measurements. If a positive relationship does exist between depression and diabetes severity, it is not obvious and has defied convincing documentation. The presence of diabetes complications alone may not result in depression unless severe functional limitations such as blindness, impotence, and cognitive impairment are present. The nature of depression in diabetes is complex, and adverse life events, severity of the medical illness, genetic and personality factors, and psychiatric history are all likely contributors to its occurrence.

The prevalence of psychiatric disorders other than depression in diabetes has not been extensively studied. There is evidence that anxiety disorders are significantly more common in this group, particularly generalized anxiety disorder and simple phobia. The prevalence of anorexia nervosa and bulimia nervosa in diabetes is unknown, but interest in these disorders remains high because of their potential for adverse effects on glycemic control. Prevalence studies involving these eating disorders have examined very small numbers of subjects, were uncontrolled, or varied greatly in their case definition.

The relationship between stress and glucose regulation in diabetes has been the subject of considerable study, but findings have been inconsistent. Stress has been reported to increase, decrease, or have no significant effect on diabetic glycemic control. Identifying diabetic subgroups whose disease is influenced by stress will require consideration of differences among groups from both a physiologic and psychologic perspective.

The threshold for the reporting of diabetes symptoms may be lowered by psychological factors, particularly depression and anxiety, and both psychological and physiological factors may contribute to diabetes symptoms. Depression, but not glycosylated hemoglobin level, was found to be highly correlated with reported diabetes symptoms. Similar degrees of nocturnal penile tumescence irregularities were reported in diabetic patients with and without impotence, implying that organic factors do not account for all cases of diabetic erectile failure.

The efficacy of psychotropic medication for psychiatric disorders in diabetic populations is largely unknown. In one study, tricyclic antidepressant treatment resulted in complete remission of lower extremity pain in diabetic neuropathy patients, with concomitant relief of depression. In another study, 8 weeks of treatment with nortriptyline resulted in a significant reduction in depression symptoms. These and other conventional antidepressant agents, however, have side effects that may limit their use in persons with diabetes. Thus, psychotherapy may have a prominent place in the diabetes treatment armamentarium.

PREVALENCE OF PSYCHIATRIC DISORDERS IN ADULT DIABETIC POPULATIONS

MAJOR DEPRESSIVE DISORDER

A proliferation of studies investigating the comorbidity of mental illness and diabetes has occurred during the past decade[1]. Depression may have special clinical relevancy in diabetes through its purported association with poor glycemic control and decreased adherence to treatment modalities. Ten controlled studies[2-11] (Tables 24.1 and 24.2)[1] and 11 uncontrolled studies[12-22] (Table 24.3)[1] have been performed to investigate the prevalence of depression in adult diabetic populations. These studies addressed two issues: 1) whether diabetes was associated with an increased prevalence of depression, and 2) whether diabetes could be differentiated from other somatic illnesses in the risk of depression.

The range of the prevalence of current depression obtained from structured diagnostic interviews in samples of diabetic subjects was 8.5%-27.3% (mean, 14.0%) in controlled studies (Table 24.2)[1] and 11.0%-19.9% (mean, 15.4%) in uncontrolled studies (Table 24.3)[1]. These rates are at least three times the 3%-4% prevalence of major depressive disorder found in the general adult population of the United States. Investigations using depression symptom scales corroborated these findings, as the range of clinically significant depression symptomatology in diabetic samples was 21.8%-60.0% (mean, 31.6%) in controlled studies (Table 24.2)[1] and 10.0%-28.0% (mean, 19.6%) in uncontrolled studies (Table 24.3)[1]. An increased prevalence of depression in diabetes relative to the general adult population is highly suggested by these studies[1].

Whether depression is more common in diabetes than in other chronic diseases is far less supported by the literature. A controlled community interview study in Los Angeles,CA[2] found a significantly increased prevalence of lifetime depression for diabetes (14.4%), as well as for arthritis (14.3%), heart disease (18.6%), hypertension (16.4%), and chronic lung disease (17.9%) relative to healthy control subjects (6.9%). This study, however, suffered from numerous biases and methodological problems (Table 24.4)[1]. The controlled community interview study in Germany[3], which was the strongest investigation from a bias adjustment and methodological standpoint (Table 24.4)[1], found an increased, although nonsignificant, prevalence of current depression in diabetic individuals (27.3%) compared with individuals with another somatic illness (20.3%; Table 24.2)[1]. An increased prevalence of depression in diabetes relative to other somatic illnesses remains unproven until further research is performed[1].

Table 24.1
Controlled Studies of Depression in Adult Diabetic Populations: Methods Employed

Ref.	Type	Diabetic sample No.	Diabetic sample Source	Control sample No.	Control sample Source	Methods
Structured diagnostic interviews						
2	IDDM and NIDDM	154	Community sample, Los Angeles, CA	1,353	Medically well	DIS/DSM-III
3	NIDDM	55	Community sample, Germany	325 122	Medically ill Medically well	CIS
4	IDDM	75	Pancreatic transplantation candidates	34 9,543	First-degree relatives General population	DIS/DSM-III
5	IDDM and NIDDM	130	Outpatients	130	Medically well	PSE, ID ≥5
Depression symptom scales						
6	NIDDM	71	Outpatients	46	Medically well	BDI ≥16
7	NIDDM	32	Subjects attending weight loss clinic	32	Spouses attending weight-loss clinic	BDI ≥16
8	NIDDM	119	Outpatients	25	Medically ill	Zung SD ≥50
9	IDDM and NIDDM	56	Outpatients	56	Medically ill	CES-D ≥16
10	IDDM and NIDDM	179	Community sample, Kentucky	2,338	Community sample	CES-D ≥20
11	NIDDM	634	Community sample, U.S.	8,429	Community sample	CES-D ≥16

DIS, Diagnostic Interview Schedule for diagnosis of major depressive disorder by lay interviewers, based on criteria specified in the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-III). CIS, Clinical Interview Schedule for diagnosis of major depressive disorder by psychiatrists and psychologists. PSE, Present State Examination, which assesses the present mental state; an Index of Definition (ID) Score ≥5 designates a psychiatric case; a diagnosis of depression is subsequently based on equivalent ICD-9 criteria. BDI, Beck Depression Inventory Scale. Zung SD, Zung Self-Rating Depression Scale. CES-D, Center for Epidemiologic Studies — Depression Scale.

Source: Reference 1

Table 24.2
Controlled Studies of Depression in Adult Diabetic Populations: Prevalence Findings

Ref.	Subjects	Both sexes Current (%)	Both sexes Lifetime (%)	Males Current (%)	Males Lifetime (%)	Females Current (%)	Females Lifetime (%)	Mean depression scale scores
Structured diagnostic interviews: Prevalence of major depressive disorder								
2	Diabetes[a]	9.6	14.4					
	Controls[a]	4.4‡	6.9*					
3	Diabetes	27.3						10.6
	Other somatic disease	20.3‡						9.8‡
	No somatic disease	10.6**						6.6†
4	Diabetes	10.7	24.0	3.7	25.9	14.6	22.9	
	Relatives	2.9‡	5.9*	0.0‡	6.7‡	5.3‡	5.3‡	
	General population	3.1†	5.5†	1.7‡	3.1†	4.0†	7.1†	
5	Diabetes	8.5	17.7					
	Controls	8.5‡						
Depression symptom scales: Prevalence of clinically significant depression symptomatology								
6	Diabetes	28.2						12.2
	Controls	4.4**						5.9†
7	Diabetes	21.8						10.6
	Spouses	12.5‡						7.5*
8	Diabetes[b]							39.3
	Controls[b]							34.0**
9	Diabetes	60.0						20.4
	Controls	50.0‡						14.2*
10	Diabetes	21.8		15.5		25.4		
	Controls	16.0*		13.4‡		17.6*		
11	Diabetes	26.1						
	Controls	16.7†						

Data in this table reflect prevalences of major depressive disorder (for structured diagnostic interviews) and clinically significant depression symptomatology (for depression symptom scales). [a] Data reflects prevalences of any affective disorder, which includes major depression, dysthymia, and mania. Mania represented only 2.9% of all affective disorders in this study sample. [b] The prevalence of clinically significant depression symptomatology among the diabetic and control groups in this study was unknown. *p<0.05, **p<0.01, †p<0.001, ‡ not statistically significant. Each control group was compared with its respective overall or sex-specific diabetic group in assessing significant differences in the prevalence of depression.

Source: Reference 1

Spurious depression prevalence estimates could have resulted if diabetic and control nondiabetic individuals differed significantly on variables known to be associated with an increased risk of depression[1]. Such factors include age 30-44 years, female, low socioeconomic status, obesity, assortative mating, concomitant medical illness in the diabetic or control nondiabetic sample, and disease severity (Table 24.4)[1]. Methodological issues, such as a lack of physician verification of self-reported diabetes, variability in the time frame of depression being assessed, small sample sizes, and low participation rates could have also hindered the validity of findings[1]. Although all 10 controlled studies accounted for some factors through either sample selection or analyses, many potential biases were not addressed (Table 24.4)[1].

Despite the potential biases and methodological difficulties, the increased prevalence of depression in diabetes relative to the general adult population likely signifies a true association[1]. The relationship was found for three of four interview studies and all six corroborating depression symptom scale studies, despite the variety of diabetic and nondiabetic samples used and the different depression assessment methods employed. Future studies are needed that will address the potential biases and methodological issues outlined above to identify the absolute strength of this association. Studies are also needed that investigate depression according to sex, emphasize lifetime depression, and further discriminate between nonspecific effects of chronic illness and depression specifically related to diabetes[1].

EATING DISORDERS

Eating disorders such as anorexia nervosa and bulimia have been poorly studied in persons with diabetes. The former is characterized by extreme aversion to food, resulting in radical weight loss. Self-induced vomiting, vigorous exercise, and diuretic abuse may also help to accomplish that end. The latter is identified by frequent binge eating with accompanying

Table 24.3

Uncontrolled Studies of Depression in Adult Diabetic Populations

Ref.	Diabetes type	Sample size	Sample source	Method	Prevalence of depression (%) Current	Lifetime
Structured diagnostic interviews: Prevalence of major depressive disorder						
12	NIDDM	66	Subjects attending weight loss clinic	IDD-L		31.8
13	IDDM	109	Clinic outpatients	PSE, ID ≥5	11.0	
14	IDDM	194	Clinic outpatients	GHQ ≥12, CIS	16.5	
15	IDDM and NIDDM	114	Clinic outpatients	DIS/DSM-III	14.0	32.5
16	NIDDM	89	Community volunteers and physician referrals	BDI ≥16, SADS/RDC	17.6-22.2	
Depression symptom scales: Prevalence of clinically significant depression symptomatology						
17	IDDM	175	Hospital-based registry, duration of diabetes ≥25 years	BDI ≥16	12.7	
18	IDDM	158	Diabetes education and renal dialysis patients	BDI ≥16	10.0	
19	NIDDM	64	Female clinic outpatients	Zung SD ≥50	18.8	
20	IDDM and NIDDM	112	Clinic outpatients, duration of diabetes ≥25 years	MMPI-D ≥70	21.0	
21	IDDM and NIDDM	25	Inpatients and outpatients	MMPI-D ≥70	28.0	
22	IDDM	92	Clinic outpatients	CES-D ≥16	27.2	

Data in this table reflect prevalences of major depressive disorder (for structured diagnostic interviews) and clinically significant depression symptomatology (for depression symptom scales). IDD-L, Inventory to Diagnose Depression-Lifetime Scale; this self-report instrument assesses lifetime prevalence of major depressive disorder based on criteria specified in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) of the American Psychiatric Association. PSE, Present State Examination, which assesses the present mental state; an Index of Definition (ID) Score ≥5 designates a psychiatric case; a diagnosis of depression is subsequently based on equivalent ICD-9 criteria. GHQ, General Health Questionnaire. CIS, Clinical Interview Schedule for diagnosis of major depressive disorder by psychiatrists and psychologists. DIS, Diagnostic Interview Schedule for diagnosis of major depressive disorder by lay interviewers, based on criteria specified in DSM-III. BDI, Beck Depression Inventory Scale. SADS/RDC, Schedule of Affective Disorders and Schizophrenia/Research Diagnostic Criteria. Zung SD, Zung Self-Rating Depression Scale. MMPI-D, Minnesota Multiphasic Personality Inventory — Depression Scale. CES-D, Center for Epidemiologic Studies — Depression Scale.

Source: Reference 1

Table 24.4

Adjustment for Potential Biases and Summary of Methodologic Problems: Controlled Studies

Ref.	Age	Sex	SES	Obesity	Concomitant medical illness: Assortative mating	Concomitant medical illness: in diabetic sample	Concomitant medical illness: in control sample	Severity[a]	Verification of diabetes	Time frame of current depression	Participation rate (%)
Structured diagnostic interviews											
2	+	+	-	-	n/a	-	+	-	-	Last 6 months	68
3	+	+	+	-	n/a	+	+	+	+	Last 7 days	93
4	-[b]	+	-	-	n/a	+	-	+	+	Last 6 months	100 (D, R)
5	-[c]	+	-[d]	-	n/a	-	-	+	+	Last month	85 (D), nr (C)
Depression symptom scales											
6	+	+	-[e]	-	n/a	+	+	-	+	Last 7 days	73 (D), 100 (C)
7	+	+	+	+	-	-	-	-	+	Last 7 days	nr
8	+	+	+	-	n/a	+	-	-	+	Mood at evaluation	nr
9	+	+	-[f]	-	n/a	-	-	-	+	Last 7 days	nr
10	+	+	-	-	-	-	-	-	-	Last 7 days	80
11	+	+	-	-	n/a	-	-	-	-	Last 7 days	73

+, potential bias was adjusted for in either sample selection or analyses, or no significant differences were found between diabetic and control groups; -, potential bias was not adjusted for in either sample selection or analyses; n/a, bias is not applicable to study. SES, socioeconomic status; D, diabetes; R, relatives; C, controls; nr, not reported. [a] Severity was defined according to the focus of the study. The diabetes and other somatic illness comparison groups did not differ significantly in severity of medical illness (Reference 3); diabetes severity was unrelated to depression which minimizes an ascertainment bias from the use of treatment samples (References 4 and 5); diabetes severity was significantly associated with clinically significant depression symptomatology (Reference 6). [b] The 25-44 year age category contained 76% of the IDDM pancreatic recipients, 62% of the family donors, and 39% of the general population ($p<0.001$). [c] The mean age was 51±6.6 years in the diabetic sample and 44±10.4 years in the control sample ($p<0.01$). [d] The proportion of low SES occupations represented in the diabetic and control samples was 63% and 45%, respectively ($p<0.01$). [e] The proportion unemployed was 72% in the diabetic sample and 50% in the control sample ($p<0.01$). [f] The proportion unemployed was 75% in the diabetic sample and 37% in the control sample ($p<0.01$).

Source: Reference 1

purging, usually by self-induced vomiting. Fasting between binges and laxatives also may be used to maintain weight at normal or below normal levels. Anorexia nervosa and bulimia in diabetes predominantly occur in young women, and the onset of diabetes generally precedes the onset of the eating disorder[23,24]. Both eating disorders are aided through specific use of the diabetic condition, with accompanying harmful sequelae[25]. For example, diabetic individuals with anorexia nervosa may fail to eat after taking insulin, resulting in hypoglycemia. Diabetic patients with bulimia may intentionally lower their insulin dosage during binging to avoid weight gain, resulting in acute hyperglycemia, glycosuria, and ketoacidosis. Such binging and purging frequently results in wildly varying blood glucose levels and poor glycemic control. An increased risk of diabetic complications may result[26,27].

The prevalence of anorexia nervosa and bulimia in diabetes is currently unknown. Diabetic women with eating disorders may be reluctant to talk about them and physicians may not ask about aberrant eating patterns unless severe emaciation is present or glycemic control is poor with no apparent cause. The few prevalence studies that have been performed have varied greatly in their estimates, due mainly to differences in case definition. Controlled studies that used psychiatric diagnostic interviews with Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-III-R) criteria found no difference in the prevalence of bulimia between diabetic and nondiabetic groups (5.6% versus 3.0%[28] and 1.8% versus 0.0%[29]). These differences were based on very small case numbers of 3 versus 2[28] and 1 versus 0[29]. Another controlled study examined anorexia nervosa and bulimia symptomatology on a single continuum[30]. Diabetic women were found to have a greater prevalence of clinically significant anorexic-bulimic symptomatology than nondiabetic women (4.9% versus 0.0%, $p<0.05$). This finding was based on case numbers of 2 versus 0 and was not diagnostic for an eating disorder.

Uncontrolled studies using DSM-III diagnostic criteria in self-report questionnaires found much higher prevalences of bulimia in diabetic women. The estimates ranged from 11.9%-35.0%[31-33]. One explanation is that the more stringent DSM-III-R criteria required quantification of binging episodes (at least two per week for at least 3 months) as well as some method of purging (self-induced vomiting, laxatives or diuretics, fasting, or vigorous exercise), whereas DSM-III criteria did not[33]. The prevalence of eating disorders in diabetes may thus vary widely depending on which diagnostic criteria are employed. Greater reporting of bulimia may have also occurred due to the anonymity of a questionnaire. Response rates, however, were as low as 30%[32]. An increased prevalence of eating disorders in diabetes relative to the general population remains unproven.

OTHER PSYCHIATRIC DISORDERS

Three controlled diagnostic interview studies have examined the prevalence of psychiatric disorders other than depression in adult diabetic populations[2-4]

Table 24.5
Controlled Studies of Psychiatric Disorders Other than Depression Based on Structured Diagnostic Interviews in Adult Diabetic Populations: Prevalence Findings

Ref.	Disorder	Subjects	Both sexes		Males, lifetime (%)	Females, lifetime (%)
			Current (%)	Lifetime (%)		
2	Anxiety	Diabetes	15.7	26.2		
		Controls	5.3**	10.5**		
2	Substance use	Diabetes	5.7	21.6		
		Controls	6.0†	17.3†		
3	Any (excluding depression)	Diabetes	15.8			
		Other somatic disease	30.4*			
		No somatic disease	15.6†			
4	Simple phobia	Diabetes	18.7	21.3	3.7	31.3
		Relatives	0.0*	0.0**	0.0†	0.0*
		General population	9.0**	14.9†	9.5†	18.4*
4	Antisocial personality	Diabetes		6.7	14.8	2.1
		Relatives		11.8†	26.7†	0.0†
		General population		2.3*	4.6*	0.8†

*p<0.05; **p<0.01; †, not statistically significant. Each control group was compared with its respective overall or sex-specific diabetic group in assessing significant differences in the prevalence of each psychiatric disorder.

Source: References are listed within the table

(Table 24.5). In a study in Germany[3], the prevalence of any psychiatric disorder of any severity other than depression was virtually identical between diabetic individuals (15.8%) and healthy control subjects (15.6%) but was twice as high in those with other somatic diseases (30.4%; $p<0.05$). The diabetic group, other somatic illness group, and healthy control group had prevalences of mild psychiatric disorders (including depression) of 23.6%, 24.7%, and 10.7%, respectively, and of moderate to severe psychiatric disorders of 19.5%, 26.0%, and 15.5%, respectively ($p<0.05$). One difference between diabetic individuals and healthy control subjects thus appeared to be more mild psychiatric disorders in the diabetes group. These findings, as well as the very high prevalence of depression in the diabetic group (27.3%; Table 24.2), indicate that diabetes may have a special propensity for depression and not for other psychiatric illnesses, and that persons with diabetes may be especially at risk for mild cases of depression[1].

Differences between diabetic and control subjects in psychiatric disorders other than depression were found in other studies. Diabetic patients who were candidates for pancreatic transplantation had a significantly greater prevalence of current simple phobia than the general population (18.7% versus 9.0%; $p<0.01$)[4]. Significant differences were found for females for lifetime simple phobia (31.3% versus 18.4%; $p<0.05$). Male transplantation candidates were at higher risk for lifetime antisocial personality than males in the general population (14.8% versus 4.6%; $p<0.05$). Diabetic subjects in a Los Angeles, CA study had almost three times the rate of current anxiety (15.7% versus 5.3%; $p<0.05$) and lifetime anxiety (26.2% versus 10.5%; $p<0.01$) than the general population[2]. Corroboration was provided by an uncontrolled study that found a prevalence of lifetime anxiety disorder of 40.9% in diabetic patients[34].

RELATIONSHIP OF PSYCHOLOGICAL FACTORS TO THE CLINICAL PRESENTATION OF DIABETES

STRESS AND GLUCOSE REGULATION

The effect of stress on glucose regulation has been the subject of considerable study. Acute stress in the general population typically results in an increase in heart rate, high-amplitude galvanic skin response, vasoconstriction in the peripheral vascular system, and elevated levels of skeletal muscle activity. Stress also causes increased production of pituitary hormones, catecholamines, corticosteroids, and suppression of insulin release. These actions serve to increase glucose levels in the blood. Stress in diabetic individuals has also been traditionally viewed as a hyperglycemic stimulus.

The hyperglycemic effect of stress in diabetes, however, has eluded consistent documentation. Stress has been reported to increase[35-37], decrease[38-40], or have no significant effect[41-45] on diabetic glucose regulation. The response to stress may not be uniform across all persons with diabetes. Controlled laboratory studies do suggest that the stress-blood glucose response is reliable within diabetic individuals[44].

Recent studies have focused on the role of coping styles in moderating the relationship of stress and glucose regulation. Stress has been associated with poor glycemic control in diabetic persons whose keynote response to stress was one of anger or lacking in stoicism[46]. Coping styles marked by avoidance, detachment, or denial may also adversely affect glycemic control in diabetes, as well as compliance with diabetic treatment regimens[47,48].

The study of stress in diabetes has arguably drawn more attention than any other psychosocial area of investigation in the disease. The inconsistent nature of the findings has served to document that the role of stress in diabetic persons may be far more complex than in nondiabetic individuals. The effects of stress in insulin-dependent diabetes mellitus (IDDM) are influenced by aberrant regulation of stress hormones, the relative presence of insulin at the time of stress, and autonomic nervous system abnormalities associated with diabetic neuropathy, as well as individual psychological differences[49]. Identifying diabetic subgroups whose disease is responsive to stress will require researchers to consider host differences from both a physiologic and psychologic perspective.

PSYCHOLOGICAL FACTORS AND THE REPORTING OF DIABETES SYMPTOMS

Diabetes is a progressive metabolic disorder with cumulative symptoms across multiple organ systems. Physical symptoms are frequently reflexively attributed to diabetes with little consideration given to the potential role of psychological factors in their production and/or maintenance. Evidence is beginning to emerge suggesting that psychological as well as diabetic factors may contribute to the reporting of gastrointestinal[50], metabolic[51], and neuropathic[52,53] symptoms in diabetes.

A study was made of the relationship of depression to

the reporting of symptoms typically presumed to result from diabetes[51]. Scores for individual symptoms were correlated with glucose regulation (HbA1 and fasting plasma glucose) and depression (Beck Depression Inventory Scale). The findings are summarized in Table 24.6[51]. HbA1 was poorly correlated with nine of 11 symptoms and made a significant independent contribution only to the reporting of polyuria. Findings were similar when fasting plasma glucose was used as the measure of glucose regulation. Depression was correlated with nine symptoms and had a significant independent effect on the reporting of two of three hyperglycemic symptoms, five of six hypoglycemic symptoms, and both nonspecific symptoms. Diabetes symptom reporting may be more related to depressive mood than to conventional markers of glucose control. Diabetes symptoms may also be unreliable indicators of poor control when features suggestive of depression are present.

Another study further illustrates how psychological factors may influence the clinical presentation of diabetes[50]. Symptoms suggesting gastrointestinal motor dysfunction were examined for their relationship with diabetic neuropathy and psychiatric illness. Log-linear analysis revealed that each group of symptoms (upper gastrointestinal symptoms, altered bowel habits, and abdominal discomforts) was significantly associated with psychiatric illness ($p<0.01$) but not with peripheral neuropathy. Individual gastrointestinal symptoms were also found to be more related to psychiatric illness than to peripheral neuropathy (Table 24.7)[50].

Table 24.6
Correlations of Diabetes Symptoms with Beck Depression Inventory Scores and Glycosylated Hemoglobin

Symptom	BDI	HbA1
Hyperglycemic symptoms		
Thirst	.41*	.18
Frequent urination	.46*	.22
Losing weight	.18	.00
Hypoglycemic symptoms		
Hunger	.31*	.14
Sweating	.37*	.04
Trembling	.47*	.12
Fainting or dizziness	.25*	.11
Confused thoughts	.48*[a]	.12
Loss of consciousness	.08	.26*
Nonspecific symptoms of poor control		
Fatigue	.65*[a]	.11
Fever, feelings of illness	.48*	.13

BDI, Beck Depression Inventory. [a]A component of this association results from the overlap of the symptom with an item on the BDI. *$p<0.05$; all statistically significant associations remained significant in multiple logistic regression analysis when the effects of depression and glucose control were examined simultaneously, except for the association of loss of consciousness with HbA1.

Source: Reference 51

Table 24.7
Positive Predictive Value of Gastrointestinal Symptoms for Psychiatric Illness and Neuropathy

Symptom	Psychiatric illness	Peripheral neuropathy	Autonomic neuropathy[a]
Nausea	0.83	0.58	0.20
Vomiting	0.72	0.50	
Diarrhea	0.75	0.71	0.50
Constipation	0.71	0.64	
Abdominal pain	0.65	0.57	0.67
Bloating	0.78	0.78	

[a] Only symptom groups were examined since the number of subjects undergoing autonomic nerve testing was small.

Source: Reference 50

Psychological factors, particularly depression and anxiety, may lower the threshold for the reporting of diabetes symptoms. This may be especially prevalent in the area of sexual dysfunction. Impotence in diabetic men may result from neuropathic or vascular complications associated with their diabetes. Psychiatric illness, however, is also associated with sexual dysfunction in that at least 25% of depressed nondiabetic males complain of impotence. Sexual dysfunction in diabetes may thus at times be falsely ascribed to neurovascular disease. Abnormal nocturnal penile tumescence, frequently thought to be confirmatory of an organic pathogenesis, has been observed in nondiabetic depressed individuals[54,55]. These anomalous physiological findings normalized upon resolution of the depressive episode. A similar degree of nocturnal penile tumescence irregularities was reported in diabetic patients with and without impotence[56], implying that organic factors do not account for all cases of diabetic erectile failure. Psychological as well as physiological factors may contribute to diabetes symptom reporting and should be considered in causal speculations.

RELATIONSHIP OF DEPRESSION TO DIABETES SEVERITY

It is a prevalent clinical belief that depression in diabetes is secondary to psychosocial hardship brought on by increasing severity of the medical condition. Despite its intuitive appeal, such a hypothesis has been difficult to prove. Severity of diabetes has been examined in numerous ways, including duration of diabetes, presence of diabetes complications, and

functional limitations perpetuated by worsening diabetes. While one study found a significant correlation between depression symptomatology and the duration of diabetes[6], other investigations reported no association between diabetes duration and either major depressive disorder[15] or depression symptomatology[19,20]. One explanation for this inconsistent relationship between diabetes duration and depression is that diabetic patients may adapt psychologically to their medical illness over time. Another explanation is that the onset of depression usually precedes the diagnosis of non-insulin-dependent diabetes mellitus (NIDDM) and recurrent episodes of depression are common in the early stages of this form of diabetes.

Eleven studies have examined the association of depression with different measures of diabetes severity[4-6,15,17,19,20,57-60] (Table 24.8). One 10-year prospective study reported that coronary heart disease had developed at followup in 39% of diabetic patients who had been diagnosed with major depressive disorder at baseline, compared with only 15% of diabetic patients who were not depressed at initial examination ($p<0.05$)[59]. Such positive findings, however, have been the exception. Statistically significant associations between depression and severity of diabetes were not found in 25 of 32 measurements (Table 24.8). If a positive relationship does exist between depression and diabetes severity, it is not obvious and has defied convincing documentation.

The lack of a consistent association between depression and diabetes severity is counterintuitive, and further studies are needed to ascertain the true nature of the relationship. The presence of diabetes complications alone may not result in depression unless severe functional limitations, such as blindness, impotence, and cognitive impairment, are present. Depression may be related to other indices of advancing disease, such as changes in cerebral vasculature[4]. Inconsistencies in the definition of diabetes severity itself may also explain the lack of a significant association with depression. For example, asymptomatic nerve conduction velocity, as well as debilitating neuropathic symptoms, may both be deemed positive for diabetic neuropathy. The nature of depression in diabetes is complex, and adverse life events, severity of the medical illness, genetic and personality factors, and psychiatric history are all likely contributors to its occurrence.

Table 24.8
Association of Depression with Measures of Diabetes Severity

Ref.	Duration of diabetes	Neuropathy	Nephropathy	Retinopathy	Macrovascular disease
Structured diagnostic interviews					
4	No	No	No		
5	No			No	No[a]
15	No	No	No	No	
57	No	No	No	No	No
59					Yes
Depression symptom scales					
17		No	No	No	Yes[b]
6	Yes	Yes	No	No	
19		Yes			
58				Yes	
20		No			
60[c]	No	No	No	No	No

[a] Current and borderline current depression cases combined were at higher risk for macrovascular complications than those with no current or 5-year history of depression or borderline depression ($p<0.05$); all other comparisons were nonsignificant. [b] Males only. [c] Type of complication was not specified.

Source: References are listed within the table

PSYCHOSOCIAL TREATMENTS IN ADULT DIABETIC POPULATIONS

PSYCHOPHARMACOLOGICAL THERAPIES IN DIABETES

The efficacy of psychotropic medication for criteria-defined psychiatric disorders in diabetic populations is largely unknown. While such studies have been conducted on groups of primary care patients that included patients with diabetes, the outcome in this subset was not analyzed and reported separately[61-63]. Two controlled studies have examined the effect of psychopharmacological therapies in diabetic patients. In one, tricyclic antidepressant treatment resulted in complete remission of lower extremity pain in diabetic neuropathy patients, with concomitant relief of depression[52]. In the second study, 8 weeks of treatment with nortriptyline resulted in a significant reduction in depression symptoms[64].

The conventional antidepressant agents have side-effect profiles that may limit their use in persons with diabetes (Table 24.9)[65]. Insomnia, agitation, extrapyramidal symptoms, and drug interactions that are not specifically relevant to diabetes may also be encountered[66-69]. Antidepressant agents may provoke cardiac arrhythmias and conduction delays as well as induce dangerous orthostatic hypotension[66-68]. This risk may be even greater in diabetic individuals. While the reduced chance for weight gain with fluoxetine increases the attraction of this agent in NIDDM, intolerance to the medication from nonspecific gastrointestinal distress or from overstimulation may limit its use[65].

Table 24.9
Side Effects of Antidepressant Medications with Potential Relevance in Diabetes

Side effect	Tricyclic agents[a]	MAO inhibitors	Psycho-stimulants[b]	Alprazolam[b]	Amoxapine	Fluoxetine	Trazodone	Potential relevance in diabetes
Anticholinergic effects	2[c]	0	0	0	1	0	0	Worsened bowel motility (increased gastroparesis or constipation); urinary bladder dysfunction
Sedation	2[c]	1	0	2	2	1	2	Impairment of daily activities involved with glycemia management
Cardiovascular, conduction delay/ arrhythmias	2	0	1[d]	0	1	0[e]	1	Interaction with macro-vascular diabetic complications
Orthostasis	2[c]	2	0	0	1	0	2	Worsening of neuropathy-related hypotension
Weight gain	2	2	0	0	0	0	1	Interference with glycemia management
Sexual dysfunction	2	2	1	1	1	1	0[f]	Worsening of diabetes-related erectile dysfunction and orgasm management

Relative occurrence of side effect among agents listed: 2, common; 1, less common; 0, rare or does not occur. [a] Excludes amoxapine. [b] Psychostimulants (dextroamphetamine, methylphenidate) and alprazolam are not approved by the U.S. Food and Drug Administration for treatment of depression. [c] Some stratification within category more common with tertiary amines (amitriptyline, doxepine) than secondary amines (desipramine, nortriptyline). [d] Also may exacerbate hypotension and symptoms of coronary artery disease. [e] Not fully known. [f] Rare occurrence of priapism with this agent.

Source: Reference 65

PSYCHOLOGICAL THERAPIES IN DIABETES

Important advancements in the treatment of affective and anxiety disorders have been realized over the past decade using the techniques of cognitive-behavioral psychotherapy (CBT)[70,71]. CBT evolved from observations that depression is characterized by habitual errors in thinking that are themselves amenable to systematic reprogramming. Depression is removed by systematically challenging "unrealistic" negative thinking, including negative predictions ("I'll always be alone") and overgeneralizations ("nothing ever goes right for me"). The techniques of CBT may not be fully effective for depression in diabetes because there is a certain negative realism in thinking that often attends the experience of advancing diabetes ("I'll never be the same sexually"; "I won't be able to see like other people"). Nevertheless, psychotherapy may have a uniquely prominent place in the treatment armamentarium because antidepressant medications may interfere with diabetes or be contraindicated by extant comorbid medical conditions. Despite a large literature in nondiabetic subjects, there have been no studies of the efficacy of CBT for depression or other psychiatric disorders in diabetes. Controlled outcome studies of psychotherapy for DSM-IV-defined psychiatric disorders are needed.

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