

The Prevalence of Comorbid Depression in Adults With Diabetes

A meta-analysis

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OBJECTIVE — To estimate the odds and prevalence of clinically relevant depression in adults with type 1 or type 2 diabetes. Depression is associated with hyperglycemia and an increased risk for diabetic complications; relief of depression is associated with improved glycemic control. A more accurate estimate of depression prevalence than what is currently available is needed to gauge the potential impact of depression management in diabetes.

RESEARCH DESIGN AND METHODS — MEDLINE and PsycINFO databases and published references were used to identify studies that reported the prevalence of depression in diabetes. Prevalence was calculated as an aggregate mean weighted by the combined number of subjects in the included studies. We used χ^2 statistics and odds ratios (ORs) to assess the rate and likelihood of depression as a function of type of diabetes, sex, subject source, depression assessment method, and study design.

RESULTS — A total of 42 eligible studies were identified; 20 (48%) included a nondiabetic comparison group. In the controlled studies, the odds of depression in the diabetic group were twice that of the nondiabetic comparison group (OR = 2.0, 95% CI 1.8–2.2) and did not differ by sex, type of diabetes, subject source, or assessment method. The prevalence of comorbid depression was significantly higher in diabetic women (28%) than in diabetic men (18%), in uncontrolled (30%) than in controlled studies (21%), in clinical (32%) than in community (20%) samples, and when assessed by self-report questionnaires (31%) than by standardized diagnostic interviews (11%).

CONCLUSIONS — The presence of diabetes doubles the odds of comorbid depression. Prevalence estimates are affected by several clinical and methodological variables that do not affect the stability of the ORs.

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Recent meta-analyses link depression in diabetes with hyperglycemia (1) and with an increased risk for complications of the metabolic disorder (2). There is also evidence from three controlled trials to suggest that treatment of depression improves glycemic control (3–5). An accurate estimate of depression prevalence is needed to help gauge the

potential impact of depression management in patients with comorbid diabetes. Gavard et al. (6) last reviewed studies of the prevalence of depression in diabetes in 1993. Since then, the literature on this subject has expanded considerably. In the present study, we comprehensively reviewed the scientific literature to determine the odds of clinically significant

depression in those with diabetes versus those without diabetes and to estimate the aggregate prevalence. These estimates were also studied in relation to the type of diabetes, sex, source of subjects, study design, and method of depression assessment.

RESEARCH DESIGN AND METHODS

Inclusion/exclusion criteria.

MEDLINE and PsycINFO search engines were used to identify published studies that measured the point and/or lifetime prevalence of depression in adults with diabetes. The terms *depression*, *depressive disorder*, *minor depressive disorder*, or *dysthymic disorder* were combined with the terms *diabetes* or *diabetes mellitus*. The search was limited to studies published before January 1, 2000. Studies were limited to those that 1) were published or available in English, 2) had a sample size ≥ 25 , and 3) included only adults (≥ 18 years of age) diagnosed with type 1 or type 2 diabetes. Reference lists of published studies were also examined to obtain additional reports.

The review includes all available studies that identified clinically relevant depression, (i.e., depression severe enough to warrant clinical intervention). This definition includes major depressive disorder as well as minor and subsyndromal depression. In patients with diabetes and other chronic medical illnesses, each of these presentations of depression has been shown to have adverse effects on social and physical functioning and quality of life that are independent of the effects of the medical illness (7–11). Both major and minor depressions are associated with increased medical morbidity and mortality, even after adjustment for health status and health behaviors (12–14). Similarly, there is evidence that therapy to treat these depressive conditions is effective and associated with improvements in mood, functioning, and quality of life (15–17).

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Abbreviations: BDI, Beck Depression Inventory; OR, odds ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Procedures and statistical analyses.

Studies meeting the inclusion criteria were examined, and study demographics (age, race, sex, and type of diabetes) as well as depression information (assessment method, prevalence, and mean scale scores) were recorded using a structured form based on the ones used by the Cochrane Library's Database of Systematic Reviews, produced by the Cochrane Collaboration (18). Two reviewers independently abstracted data from each study. The articles were divided into subgroups of controlled and uncontrolled studies. For the purposes of this review, the term *controlled* does not imply that the condition under study (depression) was randomly manipulated or followed longitudinally. A study was considered controlled if the prevalence of depression in diabetic patients was compared with that of a nondiabetic comparison group. A study was considered uncontrolled if it did not have a nondiabetic comparison group.

Major depressive disorder was assessed with structured or semistructured diagnostic interviews (e.g., the Diagnostic Interview Schedule [19] or the Structured Clinical Interview for DSM-III-R [20]) and diagnosed according to the criteria for major depressive disorder specified in the version of the *Diagnostic and Statistical Manual of Mental Disorders* (21,22) that was current at the time of the study. In these studies, depression prevalence was equal to the percentage of patients in the sample who met the criteria for the diagnosis.

In some studies, depression was assessed by self-report symptom scales (e.g., the Beck Depression Inventory [BDI] [23] or the Center for Epidemiologic Studies–Depression Scale [24]). In these studies, depression prevalence was equal to the percentage of subjects with scale scores above a specified threshold value. The threshold score used to identify a depression case varied somewhat across studies (e.g., BDI score ≥ 10 in some studies [25–27] and ≥ 13 [28] or ≥ 16 [29] in others). This variance is to be expected, since the threshold score used to identify depression is to some extent dependent on the importance placed on depression recognition and the resources available for this purpose within a particular clinical setting (30,31).

Odds ratios (ORs) were calculated only for controlled studies, because these calculations derive from comparing the

odds of depression in the diabetic group with the odds in the nondiabetic comparison group. Potential moderator variables were analyzed to determine whether it would be necessary to estimate the odds of depression separately by these variables. The Breslow-Day test for homogeneity was used to determine whether the likelihood of depression in diabetic versus nondiabetic patients differed depending on type of diabetes, sex, source of subjects, or depression assessment method. Cochran-Mantel-Haenszel statistics were used to test the significance of the aggregate odds of depression in diabetic versus nondiabetic patients after adjusting for these variables.

Depression prevalence was calculated as an aggregate mean, weighted by the number of subjects in the study or grouping of interest (e.g., type 1 vs. type 2 diabetes). This method factors study sample size into the calculation of the overall prevalence estimate. We used χ^2 tests to statistically compare the prevalence of depression in the diabetic and nondiabetic comparison groups. An overall estimate of depression prevalence adjusted for potential moderators (e.g., age, sex, and type and severity of diabetes) could not be calculated with precision because none of the studies fully characterized the depressed and nondepressed subsets in this regard.

RESULTS— The literature search identified 48 studies, 6 of which were excluded for having < 25 subjects or having poorly described or inadequate depression or diabetes assessment methods. The 42 included studies had a combined sample size of 21,351 subjects. Of these studies, 20 (48%) were controlled (i.e., included a nondiabetic comparison group) and 22 (52%) were uncontrolled (Tables 1 and 2). Of the 20 controlled studies, 3 (15%) were comprised exclusively of patients with type 1 diabetes; 8 (40%) included only patients with type 2 diabetes; and 9 (45%) included a mixed sample (i.e., one that contained patients having either type 1 or type 2 diabetes). None of the mixed-sample controlled studies reported depression prevalence separately by type of diabetes. Of the 22 uncontrolled studies, 6 (27%) were limited to patients with type 1 diabetes, 5 (23%) to patients with type 2 diabetes, and 11 (50%) to patients with either type 1 or type 2 diabetes. The majority (6 of 11

[64%]) of the mixed-sample uncontrolled studies did not report depression prevalence separately by type of diabetes. Of the 42 total studies, 3 (7%) did not provide enough information to be included in the OR or point prevalence calculations. Two of these three studies (32,33) reported only the statistical comparison of the mean depression scale scores of diabetic versus nondiabetic subjects, and the other (34) reported only lifetime rates of depression.

Odds of depression in diabetes

Ten of the controlled studies reported depression estimates separately by type of diabetes (type 1, $n = 3$; type 2, $n = 7$). The odds of depression were significantly increased in both type 1 (OR = 2.9, 95% CI 1.6–5.5, $\chi^2 = 12.8$, $P = 0.0003$) and type 2 diabetes (OR = 2.9, 95% CI 2.3–3.7, $\chi^2 = 84.3$, $P < 0.0001$) over nondiabetic control subjects. The increased odds of depression associated with diabetes were similar in type 1 versus type 2 diabetes (2.9 vs. 2.9, Breslow-Day $\chi^2 = 0.004$, $P = 0.95$), and the significant effect of diabetes on depression remained after controlling for type of diabetes (Cochran-Mantel-Haenszel $\chi^2 = 95.5$, $P < 0.0001$).

Seven controlled studies reported the prevalence of depression separately for men and women. The odds of depression were significantly elevated in both women (OR = 1.7, 95% CI 1.4–2.0, $\chi^2 = 34.0$, $P < 0.0001$) and men (OR = 1.7, 95% CI 1.4–2.2, $\chi^2 = 19.6$, $P < 0.0001$) with diabetes compared with control subjects. The increased odds of depression associated with diabetes were similar in women versus men with diabetes (1.7 vs. 1.7, Breslow-Day $\chi^2 = 0.08$, $P = 0.8$), and the significant effect of diabetes on depression remained after controlling for sex (Cochran-Mantel-Haenszel $\chi^2 = 53.9$, $P < 0.0001$).

The controlled studies were divided into subsets of community ($n = 11$) and clinical ($n = 7$) studies. All of the community studies identified diabetic and nondiabetic subjects from random samples of community-dwelling individuals. In the clinical studies, the diabetic and nondiabetic subjects were drawn mostly from nonrandom samples of patients recruited from health care clinics, patient support groups, or physician referrals. The odds of depression were significantly increased in people with diabetes versus those with-

Table 1—Prevalence of clinically significant depression in adults with diabetes: controlled studies (n = 20)

Study	Subjects (Diabetic: n) (Control: n)	Sex (% female)	Age (years)	Race (% white)	Depression assessment method	Prevalence of depression			Depression scale scores
						Overall (%)	Males (%)	Females (%)	
Kokkonen (62)	T1: 63 ^c	41.3	20.9 ± 1.9	—	PSE ID ≥5	14.3	—	—	Men: 9.3 ± 9.4* Women: 14.2 ± 10.2
	Medically well: 123 ^a	51.2	21.9 ± 1.4	—		11.4†	—	—	—
Songar et al. (25)	T1: 60 ^c	68.3	29.7	—	BDI ≥14	43.3	—	—	15.2
	Medically well: 30 ^c	60.0	29.2	—		3.3*	—	—	4.1*
Popkin et al. (63)	T1: 75 ^c	64.0	31	—	DIS/DSM-III	10.7	3.7	14.6	—
	1 st degree relatives: 34 ^f	55.9	36	—		2.9†	0.0†	5.3†	—
Amato et al. (64)	T2: 197 ^a	68.0	73.9 ± 5.9	—	GDS ≥21	13.6	11.4	14.7	13.2 ± 6.8
	1142 ^a	55.9	74.2 ± 6.4	—		8.7‡	6.6*	10.6§	11.1 ± 6.5*
Eaton et al. (50)	T2: 148 ^a	—	—	—	DIS/DSM	6.1	—	—	—
	1600 ^a	—	—	—		5.3†	—	—	—
Viinamäki et al. (65)	T2: 82 ^a	46.3	66.9 ± 0.7	—	Zung ≥50	11.0	11.4	10.5	39.4 ± 1.3
	115 ^a	55.7	65.6 ± 0.5	—		6.9†	—	—	36.9 ± 0.8†
Leedom et al. (26)	T2: 71 ^c	70.4	50 ± 2.0	18.3	BDI ≥10	49.3	—	—	12.2
	46 ^c	67.4	46 ± 1.7	23.9		21.7§	—	—	5.9 ± 0.7
Palinkas et al. (28)	T2: 93 ^a	39.8	72.4 ± 8.7	—	BDI ≥13	11.5	8.8	13.6	6.5
	1284 ^a	54.5	68.5 ± 9.5	—		4.6‡	2.6‡¶	6.2‡¶	5.4§
Wing et al. (29)	T2: 32 ^c	50.0	52.1 ± 7.7	—	BDI ≥16	21.8	—	—	10.6 ± 6.4
	Spouses: 32 ^c	50.0	50.8 ± 8.8	—		12.5†	—	—	7.5 ± 6.2‡
Weyerer et al. (66)	T2: 55 ^a	72.7	—	—	CIS/ICD 8	27.3	—	—	—
	Medically well: 122 ^a	54.1	—	—		10.6§	—	—	—
Tun et al. (32)#	T2: 119 ^c	48.7	63.4	—	Zung##	—	—	—	39.3
	Nondiabetic out- patients: 25 ^c	56.0	63.0	—		—	—	—	34.0§
Black (67)	T1 & 2: 636 ^a	58.2	—	0.0	CES-D ≥16	31.1	22.6	37.9	—
	2196 ^a	58.4	—	0.0		24.1*	15.9§	30.2§	—
Penninx et al. (33)#	T1 & 2: 204 ^a	52.9	73.3 ± 7.7	—	CES-D##	—	—	—	10.1 ± 9.2
	Medically well: 719 ^a	42.4	67.2 ± 8.6	—		—	—	—	5.4 ± 6.3*
Bourdrel-Marchasson et al. (68)	T1 & 2: 237 ^a	50.6	—	—	CES-D Men: ≥17 Women: ≥23	21.3	—	—	Men: 9.3 ± 9.4* Women: 14.2 ± 10.2
	2555 ^a	60.7	—	—		12.7*††	—	—	Men: 7.2 ± 7.6§§ Women: 11.8 ± 9.6
Rajala et al. (69)	T1 & 2: 62 ^a	40.3	55	—	Zung ≥45	19.3	18.9	20.0	—
	480 ^a	58.5	55	—		11.7†	10.1†	12.8†	—
Zhang et al. (70)	T1 & 2: 209 ^a	58.4	—	0.0	DIS/DSM-III + CES-D	3.8¶	1.8¶	5.1¶	8.3¶
	1289 ^a	55.6	—	0.0		3.6†¶	1.7†¶	5.1†¶	7.8†¶
Wells et al. (71)	T1 & 2: 154 ^a	—	—	—	DIS/DSM-III	9.6	—	—	—
	Medically well: 1353 ^a	—	—	48.5¶		4.4†	—	—	—

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Table 1—Continued

Study	Subjects (Diabetic: n) (Control: n)	Sex (% female)	Age (years)	Race (% white)	Depression assessment method	Prevalence of depression			
						Overall (%)	Males (%)	Females (%)	Depression scale scores
Robinson et al. (72)	T1 & 2: 60:70 ^e	45.4	51 ± 6.6	56.9	PSE/Bedford Col. criteria	8.5	—	—	—
	130 ^f	45.4	44 ± 10.4	72.3		8.5†	—	—	—
Friis et al. (73)	T1 & 2: 56 ^b	71.4	57.0	60.7	CES-D ≥16	60.7	—	—	20.4
	Medically ill: 56 ^b	73.2	53.0	63.2		48.2†	—	—	14.2‡
Murrell et al. (74)	T1 & 2: 175 ^a	65.7	—	92.9¶¶	CES-D ≥20	21.7	15.5	25.4	—
	2277 ^a	61.5	—	—		16.0‡	13.4	17.6	—

Data are means ± SD, unless otherwise indicated. T1 = type 1 diabetes, T2 = type 2 diabetes, n = sample size, PSE = Present State Examination, DIS/DSM-III = Diagnostic Interview Schedule/Diagnostic and Statistical Manual-III, GDS = Geriatric Depression Scale, Zung = Zung Self-Rating Depression Scale, CIS = Clinical Interview Schedule, CES-D = Center for Epidemiologic Studies-Depression Scale.

Sample randomly selected from a ^acommunity, ^bclinic or hospital, or ^cunspecified setting.

Sample not randomly selected from a ^dcommunity, ^eclinic or hospital, or ^funspecified setting.

*P ≤ .001 vs. the prevalence of the overall or sex-specific diabetic group; †nonsignificant vs. the prevalence of the overall or sex-specific diabetic group; ‡P ≤ .05 vs. the prevalence of the overall or sex-specific diabetic group; §P ≤ .01 vs. the prevalence of the overall or sex-specific diabetic group; ¶age- and sex-adjusted; ¶¶age-adjusted; #these studies reported only mean depression scale scores for diabetic and nondiabetic subjects, and thus were not included in the prevalence calculations; ††sex-adjusted; §§greater (P < .001) in nondiabetic females vs. male counterparts; ||||prevalences are any affective disorder including major depression, dysthymia, and mania. Mania represented just 2% of all affective disorders in this study. ¶¶¶the number is the percentage of Caucasian subjects in the entire sample.

out diabetes in both the community (OR = 1.8, 95% CI 1.6–2.1, $\chi^2 = 98.6$, $P < 0.0001$) and the clinical (OR = 2.1, 95% CI 1.5–2.8, $\chi^2 = 19.0$, $P < 0.0001$) studies. The increased odds associated with diabetes were similar in the community and clinical studies (1.8 vs. 2.1, Breslow-Day $\chi^2 = 0.37$, $P = 0.5$), and the significant effect of diabetes on depression remained after controlling for subject source (Cochran-Mantel-Haenszel $\chi^2 = 117.6$, $P < 0.0001$).

Seven of the controlled studies used clinician interviews and psychiatric diagnostic criteria to determine depression, and the other 11 controlled studies used threshold scores on self-report depression symptom scales. The pattern of ORs related to method of depression assessment was similar to that of type of diabetes, sex, and subject source (Fig. 1). The odds of depression were significantly elevated in diabetic patients over control subjects whether depression was assessed with diagnostic interviews or with self-report scales. There was no significant difference in ORs between methods (Fig. 1), and the significant effect of diabetes on depression remained after controlling for method of assessment (Cochran-Mantel-Haenszel $\chi^2 = 170.9$, $P < 0.0001$).

Because the incremental increases in the odds of depression did not differ as a function of type of diabetes, sex, subject source, or method of depression assess-

ment, the findings from all of the controlled studies (n = 18 studies, 17,399 subjects) were combined to calculate an aggregate OR. In this combined sample, the odds of depression were twice as high in those with diabetes compared with the control subjects (OR = 2.0, 95% CI 1.8–2.2, $\chi^2 = 159.8$, $P < 0.0001$).

Prevalence of depression in diabetes

Prevalence estimates were determined by aggregating data reported in the controlled and uncontrolled studies to capitalize on the combined subject pool. These rates were determined by sex, subject source, method of depression assessment, and type of diabetes. These unadjusted prevalence estimates are displayed in Table 3, and should be viewed cautiously, because they do not adjust for other factors (e.g., sex, method of depression assessment, and study design) that may affect prevalence.

The aggregate estimate of depression was lower in type 1 vs. type 2 diabetes ($\chi^2 = 11.5$, $P = 0.007$). However, the rates for type 1 vs. type 2 diabetes were statistically similar in the studies that determined depression by diagnostic interview (13.6 vs. 10.9%) or with self-report scales (29.1 vs. 32.9%) ($P > 0.1$ for both comparisons). As would be predicted from the similar ORs for male and female subjects, women had an increased prevalence of depression in comparison to

men, just as they do in the nondiabetic population. The combined prevalence was significantly higher in women with diabetes than in men with diabetes (28.2 vs. 18.0%, $\chi^2 = 42.1$, $P < 0.0001$; OR = 1.6, 95% CI 1.4–1.8). Self-report-based estimates were higher than interview-based estimates in both the controlled (26.1 vs. 9.0%, $\chi^2 = 100.6$, $P < 0.0001$) and uncontrolled studies (34.9 vs. 14.2%, $\chi^2 = 109.2$, $P < 0.0001$) (Fig. 2). Similarly, estimates from the uncontrolled studies were significantly higher than in controlled studies whether depression was assessed with diagnostic interviews (14.2 vs. 9.9%, $\chi^2 = 10.3$, $P = 0.001$) or with self-report scales (34.9 vs. 26.1%, $\chi^2 = 34.2$, $P < 0.0001$). Major depressive disorder (per diagnostic interviews) was present in 11.4% of patients with diabetes; elevations in depressive symptoms (per self-report scales) were significantly more common and were present in 31.0% of patients with diabetes ($\chi^2 = 159.8$, $P < 0.0001$).

Of the 42 studies identified by the search, 8 (19.0%) determined the lifetime prevalence of major depression (2 controlled and 6 uncontrolled). Lifetime prevalence is the proportion of study subjects who met criteria for the disorder at any point during their life, either before or during the time of assessment. The lifetime prevalence of depression was significantly higher in those with diabetes than

Table 2—Prevalence of clinically significant depression in adults with diabetes: uncontrolled studies (n = 22)

Study	Subjects (Diabetic: n) (Control: n)	Sex (% female)	Age (years)	Race (% white)	Depression assessment method	Prevalence of depression			
						Overall (%)	Males (%)	Females (%)	Depression scale scores
Berlin et al. (75)	T1: 102 ^e	45.1	43 ± 13	—	MINI/DSM-IV	12.7	—	—	—
Cohen et al. (76)	T1: 49 ^e	55.1	34.3 ± 9.2	—	SCID/DSM-III-R	14.3*	—	—	—
Mayou et al. (77)	T1: 109 ^e	53.2	21.9 ± 2.8	—	PSE ID ≥ 5	11.0	7.8	13.8	—
Winocour et al. (78)	T1: 130 ^e	36.2	40.3 ± 1.1	100.0	Zung Men: >25.7 Women: >29.8	14.6†	12.0	19.1	13.4 ± 0.6
Stone et al. (27)	T1: 57 ^e	56.1	43.5 ± 15.7	—	BDI ≥ 10	33.3	—	—	8.5 ± 6.1
SurrIDGE et al. (79)	T1: 50 ^e	46.0	38.1 ± 14.5	—	BDI† + Hamilton† + psychiatric interview	0	0	0	5.9 ± 6.3
Marcus et al. (34)§	T2: 66 ^e	66.6	52.9 ± 9.5	—	IDDD-L	—	—	—	—
Connell et al. (80)	T2: 191 ^d	57.6	70.3 ± 6.7	86.0	Zung†	47.0	—	—	49.7 ± 8.6
Naliboff and Rosen- thall (81)	T2: 102 ^e	0.0	66.6	—	BDI ≥ 17 + MMPI ≥ 80	23.5	23.5	—	—
Geringer et al. (82)	T2: 64 ^e	100.0	63 ± 5.3	—	Zung ≥ 50	18.8	—	18.8	41.5
Biglan et al. (83)	T2: 36 ^e	—	—	—	SADS/RDC	22.2	—	—	—
Kohen et al. (84)	T1: 36 ^e T2: 64 ^e	42.0	T1: 37.7 ± 13.3 T2: 62.5 ± 12.7	—	HADS†	T1: 16.7 T2: 35.9 x̄: 29.0	—	—	T1: 4.6 ± 4.3 T2: 6.3 ± 4.3 x̄: 5.7
Peyrot et al. (85)	T1: 203 ^e T2: 431 ^e	59.0	—	60.3	CES-D ≥ 16	T1: 42.4 T2: 40.8 x̄: 41.3	31.1	48.4	—
Bailey (86)	T1 & 2: 180 ^e	60.0	46	71.1	CES-D ≥ 16	33.9	—	—	13.5 ± 1.1
Haire-Joshu et al. (87)	T1: 163 ^e T2: 23 ^e	54.8	42.7 ± 14.7	72.6	BDI ≥ 10	27.4	—	—	7.8
Jalenques et al. (88)	T1: 34 ^e T2: 27 ^e	41.0	T1: 49.8 T2: 59.0 x̄: 53.9	—	Psychiatric interview/ DSM-III-R criteria	T1: 20.6 T2: 22.2 x̄: 21.39	13.9	32.0	—
Padgett et al. (89)	T1: 33 ^b T2: 147 ^b	51.1	—	—	Zung ≥ 50	60.5	—	—	52.5
Lee et al. (90)	T1 & 2: 93 ^e	58.1	27 ± 6.7	—	DSM-III symptom checklist	5.4#	—	—	—
Von Dras and Lichty (91)	T1: 66 ^a T2: 50 ^a	52.6	T1: 33.7 ± 10.9 T2: 55.4 ± 9.0 x̄: 43.1 ± 14.8	—	Zung†	40.0	—	—	48.4 ± 11.4
Lustman et al. (92)	T1: 57 ^b T2: 57 ^b	66.7	T1: 30.8 ± 9.7 T2: 49.1 ± 13.0 x̄: 40.0 ± 15.1	62.3	DIS/DSM-III	14.0	—	—	—

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Table 2—Continued

Study	Subjects		Age (years)	Race (% white)	Depression assessment method	Prevalence of depression			Depression scale scores
	(Diabetic: n) (Control: n)	Sex (% female)				Overall (%)	Males (%)	Females (%)	
Slawson et al. (93)	T1 & 2: 25 ^c	20.0	46.6	—	MMPI-D ≥70	36.0	35.0	40.0	63.0
Samson et al. (94)	T1: 111 ^c T2: 129 ^c	50.8	52.1 ± 15.7	—	SCID/DSM-III-R	T1: 16.2 T2: 10.9 \bar{x} : 13.3**	11.9**	13.9**	—

Data are means ± SD, unless otherwise indicated. T1 = type 1 diabetes, T2 = type 2 diabetes, MINI/DSM-IV = Mini International Neuropsychiatric Interview/Diagnostic and Statistical Manual-IV, SCID = Structured Clinical Interview for DSM-III-R, PSE = Present State Examination, Zung = Zung Self-Rating Depression Scale, HADS = Hospital Anxiety and Depression Scale, CES-D = Center for Epidemiologic Studies-Depression Scale, MMPI-D = Minnesota Multiphasic Personality Inventory-Depression Scale, IDD-L = Inventory to Diagnose Depression-Lifetime, SADS = Schedule for Affective Disorders and Schizophrenia. Sample randomly selected from a ^acommunity, ^bclinic or hospital, or ^cunspecified setting. Sample not randomly selected from a ^dcommunity, ^eclinic or hospital, or ^funspecified setting. *Includes diagnoses of dysthymia, major depression, and depression NOS; †sex adjusted in the threshold scores for clinically significant depression; ‡cutoff score for the symptom scale not specified; §reported only the lifetime prevalence of depression for diabetic subjects, and was not included in the point prevalence calculations; ||depression scale of the Faschingbauer abbreviated version; ¶diagnosis of depressive neurosis + depression NOS; #dysthymia; **diagnoses of major depression, depression NOS, and dysthymia.

in control subjects (17.5 vs. 6.8%, respectively, $\chi^2 = 34.2$, $P < 0.0001$). The aggregate estimate of the lifetime prevalence of major depression based on all eight studies was 28.5%.

CONCLUSIONS — We estimated the odds and prevalence of depression in diabetes from 39 studies having a combined total of 20,218 subjects. The principal conclusion of the review is that diabetes doubles the odds of depression. The OR of depression is more consistent across studies than is the prevalence, which varies by sex, study design, subject source, and method of depression assessment. The overall OR estimate generalizes across community and clinical settings despite differences in prevalence rates between these settings. Both clinicians and epidemiologists can expect individuals with diabetes to be twice as likely to be depressed than otherwise similar nondiabetic individuals in similar settings (i.e., individuals selected by similar procedures, of the same sex, and assessed with comparable depression assessment methods). In contrast, the prevalence estimate must be adjusted for moderators such as sex.

Aggregate estimates based on all of the eligible studies indicate that major depression and elevated depression symptoms were present, respectively, in 11 and 31% of individuals with diabetes. The odds of depression were significantly higher in women than in men with diabetes (OR = 1.8), a pattern that mirrors the female preponderance of depression ob-

served in epidemiological surveys of the general population (35–37). The findings are similar to the unadjusted rates reported in other medical illnesses (38–40) and in an earlier review of the diabetes literature by Gavard et al. (6) that included 18 studies. These investigators found that major depression was present in 14.7% and elevated depression symptoms in 26% of diabetic patients. Thus, as many as one in every three individuals with diabetes (at least in those participating in clinical studies) has depression at a

level that impairs functioning and quality of life (7–11), adherence to medical treatment (41–43), and glycemic control (1), and increases the risk of diabetes complications (2).

The prevalence of depression varied systematically as a function of the method used to identify depression cases and the study design. Furthermore, in both controlled and uncontrolled studies, the depression rates were approximately two to three times higher in studies that used self-report measures versus diagnostic

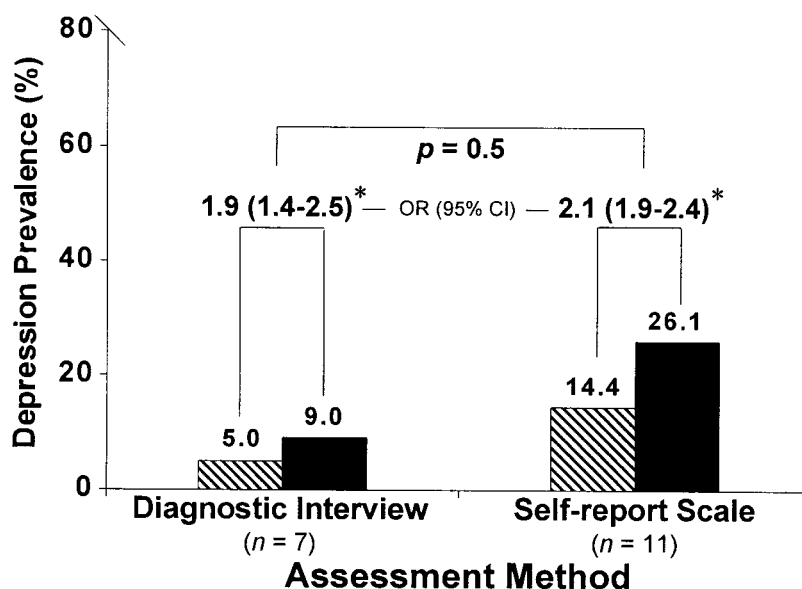


Figure 1—Likelihood of depression by assessment method. The ORs were significantly higher in diabetic patients than in control subjects (*), but they did not differ as a function of method (1.9 vs. 2.1, $P = 0.5$). n = Number of controlled studies used in the calculations. ▨, Control subjects; ■, diabetic patients.

Table 3—Unadjusted prevalence of depression in controlled and uncontrolled studies and subsets thereof

Grouping of studies	Controlled studies		Diabetic subjects: uncontrolled studies	Diabetic subjects: controlled + uncontrolled studies
	Nondiabetic subjects	Diabetic subjects		
All studies	11.4 (18)	20.5 (18)*	29.7 (21)†	25.3 (39)
Type 1	8.6 (3)	21.7 (3)*	21.2 (10)	21.3 (13)
Type 2	6.4 (7)	16.5 (7)*	33.8 (8)†	27.0 (15)
Male	9.3 (7)	15.0 (7)*	20.7 (8)†	18.0 (15)
Female	16.3 (7)	24.3 (7)*	33.0 (8)†	28.2 (15)
Community	12.7 (11)	19.0 (11)*	39.7 (1)†	20.1 (12)
Clinic	15.1 (7)	26.7 (7)*	32.7 (19)†	31.7 (26)
Diagnostic interview	5.0 (7)	9.0 (7)*	14.2 (7)†	11.4 (14)
Self-report	14.4 (11)	26.1 (11)*	34.9 (14)†	31.0 (25)

Data are % (n); n indicates number of studies used in the calculation. *The prevalence of depression was greater in diabetic subjects compared with nondiabetic control subjects ($P < .001$); †the prevalence of depression in diabetic individuals was greater in uncontrolled studies compared with controlled studies ($P < 0.05$).

interviews. It is likely that the two approaches identify somewhat different but overlapping samples of depressed individuals. Diagnostic interviews identify major depressive disorder but exclude other clinically relevant presentations. Self-report measures also identify most cases of major depressive disorder. In patients with diabetes, BDI cutoff scores of ≥ 10 and ≥ 16 have sensitivities of 0.98 and 0.73, respectively, for major depressive disorder (31). Self-report measures may identify a broader spectrum of depression disorders (e.g., dysthymic disorder, or minor or subsyndromal depression) or symptoms that reflect comorbid psychiatric illness (e.g., anxiety or substance-abuse disorders) or general distress.

The reason that depression was more prevalent in the uncontrolled than in the controlled studies is unclear. One possibility is that the uncontrolled studies included a higher proportion of individuals recruited from settings with higher prevalences of depression (e.g., physician referrals or university-based clinics). Although similar ORs describing the likelihood of depression were found between the clinical and community studies, the uncontrolled studies were comprised almost exclusively of clinic-based samples. Of the 11 community studies in the controlled subset, 8 restricted their samples to older individuals; this further contributes to lower rates of depression in the controlled studies, since depression is less common in older than younger adults (44). There may also be other unmea-

sured differences in clinical or functional characteristics that might account for the differences in the controlled and uncontrolled studies. For example, the associations of depression with hyperglycemia and with increased risk of complications described in recent meta-analytic reviews (1,2) support the hypothesis that the severity of diabetes and/or functional impairment may increase the risk for depression.

A difference in the prevalence of depression in type 1 vs. type 2 diabetes

could not be established. The ORs from the controlled studies were nearly identical between types, and aggregate estimates of prevalence using controlled and uncontrolled studies, segregated by depression assessment method, also yielded equivalent depression rates. Many of the studies, including some with the largest numbers of patients, did not report the fraction of depressed individuals by type of diabetes. This omission exemplified a more general failure of many studies to fully characterize the depressed and non-depressed samples. Such information is needed to assess the effects of other factors (e.g., age, socioeconomic status, and severity of diabetes) on the prevalence of depression. In particular, failure to report race or ethnicity is common in the psychosocial literature on diabetes (45).

The findings of this review echo the observation, first made by Willis (46) in 1684, that depression is associated with diabetes. The complex interactions of physical, psychological, and genetic factors that contribute to this association remain uncertain. Depression may occur secondary to the hardships of advancing diabetes or to diabetes-related abnormalities in neurohormonal or neurotransmitter function (47–49). On the other hand, evidence from prospective studies in the U.S. and Japan indicates that depression doubles the risk of incident type 2 diabe-

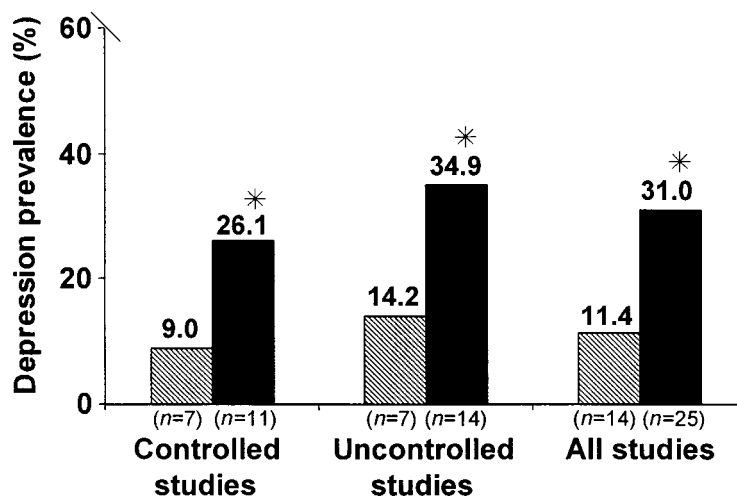


Figure 2—Aggregate prevalence of depression determined from self-report scales or diagnostic interviews in controlled and uncontrolled studies, and in all studies combined. Estimates based on self-report scales were significantly higher than those based on diagnostic interviews in all three comparisons. Depression was also higher in uncontrolled studies than in controlled studies that used the same depression assessment method (diagnostic interviews: 14.2 vs. 9.0%; self-report scales: 34.9 vs. 26.1%; $P < 0.001$ for both). ▨, Diagnostic interview; ■, self-report scale. * $P < 0.001$ between methods.

tes independent of its association with other risk factors (50,51). In patients with preexisting diabetes, depression is an independent risk factor for coronary heart disease, and appears to accelerate the presentation of coronary heart disease (52–54). Additional studies are needed to identify the behavioral and physiological mechanisms that account for these findings.

This review has several limitations. First, publication bias (i.e., nonpublication of studies that fail to find the phenomenon of interest) may limit the generalizability of the findings. However, this possibility is diminished by the fact that depression was not the principal focus of many of the included studies and was instead only one of a number of measured psychosocial variables. Second, the depression prevalence estimates may be unstable due to the small sample sizes of some studies, the small number of studies, and the fact that many of the samples were not population based. Third, the methods used to calculate the overall prevalence of depression in diabetic subjects were certainly suboptimal in that we were unable to perform a multivariate analysis controlling for all potential moderators. The fact that the ORs were uniformly similar in the bivariate tests was encouraging, and suggests that the two-fold increased likelihood of depression associated with diabetes is the most robust and generalizable finding of this review. Additional studies would be required to determine more precisely the prevalence of major depression and elevated depression symptoms in the general population of individuals with diabetes. These studies should carefully measure and report potential moderators so that both adjusted and unadjusted depression prevalence can be calculated and included in the findings.

The third U.S. National Health and Nutrition Education Examination Survey found that 49% of insulin-treated diabetic patients and 56% of those on oral hypoglycemic agents had HbA_{1c} values <8.0%, and very few patients sustained HbA_{1c} levels <7.0%, the goal set by the American Diabetes Association (55,56). Depression may oppose efforts to achieve normoglycemia via behavioral (41–43) and physiological (57–60) pathways, and, as shown in this review, is clinically relevant in nearly one of every three patients with diabetes. Successful treatment of depression is associated with improve-

ments in glycemic control (3–5). Nevertheless, two of every three cases of depression are left untreated by primary care physicians (61). Better recognition and better treatment of depression are important in themselves, but they could also improve medical outcome in a substantial portion of patients with diabetes. This meta-analysis helps to define the prevalence of depression in diabetes using data from available studies and firmly establishes the increased risk of comorbidity.

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