

# On the Association Between Diabetes and Mental Disorders in a Community Sample

## Results from the German National Health Interview and Examination Survey

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**OBJECTIVE** — To determine the relationship between mental disorders and diabetes in a representative community sample.

**RESEARCH DESIGN AND METHODS** — This was a cross-sectional study. Data on diabetes and HbA<sub>1c</sub> values were obtained by structured questionnaires and by laboratory assessments. Current psychiatric disorders were diagnosed by a modified version of the Composite International Diagnostic Interview (CIDI).

**RESULTS** — People with diabetes (PWD) were not more likely to meet Diagnostic and Statistical Manual of Psychiatric Disorders, 4th edition (DSM-IV) criteria for at least one mental disorder than were individuals without diabetes. However, a different diagnostic pattern occurred compared with the general population: odds ratios (ORs) for anxiety disorders in PWD were higher (OR 1.93, 95% CI 1.19–3.14). Although PWD had higher prevalence rates of affective disorders, the relationship between diabetes and affective disorders was not statistically significant after controlling for age, sex, marital status, and socioeconomic status. In contrast, the relationship between diabetes and anxiety disorders remained significant after controlling for these variables. In contrast to individuals without mental disorders, PWD with affective or anxiety disorders more frequently had adequate glycemic control.

**CONCLUSIONS** — Diabetes was associated with an increased likelihood of anxiety disorders. The association between mental disorders, diabetes, and glycemic control should be evaluated carefully in terms of potentially confounding sociodemographic variables, sample characteristics, and definitions of the disorders.

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**D**uring the last years, the comorbidity of mental disorders with chronic health conditions has emerged as a topic of considerable clinical and policy interest. Diabetes is considered one of the

most psychologically demanding of the chronic medical illnesses because it requires strict daily management of the treatment by the patients themselves (1). Lack of active involvement can lead to

poorer outcomes and increased risk of complications. The presence of psychiatric comorbidity can result in difficult clinical courses, because it may affect adherence to medication and self-care regimens (2). On the other hand, poor diabetes control might cause or exacerbate depression via direct effects on brain functions or indirectly through complications, functional impairment, or decreased quality of life (3).

There has been a growing interest in the study of psychological distress and mental disorders in diabetes. Some epidemiological studies have found higher prevalence rates of depression and anxiety disorders in people with diabetes (PWD) compared with the general population (4–8). Studies evaluating the relationship between depression and diabetes have yielded mixed results. For example, the prevalence of depression in PWD ranges from 3.8% (9) to as high as 49.5% (10).

Similarly, studies evaluating the relationship between depression and hyperglycemia in PWD have yielded controversial results. Some studies suggested that depression is associated with hyperglycemia in people with both type 1 and type 2 diabetes (11), whereas other studies did not find any correlation at all (12). Concerning treatment of prevalent depression in PWD, the results of Lustman and colleagues (13,14) suggest that glycemic control can be improved by appropriate treatment of the comorbid mental disorders.

Although a number of studies have evaluated the association between mental disorders and diabetes, several problems remain. The heterogeneous results may reflect differences in the method of assessment (self-report questionnaire versus standardized clinical interview), sample differences (community versus clinical samples), type of diabetes (type 1 versus

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**Abbreviations:** CIDI, Composite International Diagnostic Interview; DSM-IV, Diagnostic and Statistical Manual of Psychiatric Disorders, 4th edition; GNHIES, German National Health Interview and Examination Survey; OR, odds ratio; PWD, people with diabetes.

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

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type 2), and definition of the mental disorders. The prevalence of depression varies systematically as a function of the assessment method. The prevalence rates are two to three times higher in studies that use self-report measures versus diagnostic interviews (4). Substantially higher prevalence rates are obtained in clinical samples than in community samples.

Because early studies in this area have been based on small sample sizes or unrepresentative samples (e.g., volunteers, specific age cohorts), some results may have been influenced by selection bias. In many studies, the impact of modifying or confounding variables like sex, age, socioeconomic status, and marital status has not been considered.

Additionally, most of these studies focus on depression rather than anxiety and other mental disorders. However, we believe it is essential to include these other mental disorders into the investigation because of their frequent comorbidity with diabetes and their exceptional clinical importance.

Another difficulty with early and current studies pertains to the issue of case identification. Studies with standardized diagnostic interviews are often restricted to the assessment of major depressive disorder, whereas investigations with screening questionnaires frequently determine psychological distress or symptoms that reflect comorbid psychiatric illness (e.g., anxiety or substance abuse disorders).

The present study aims at further elucidating the relationship between mental disorders and diabetes using a large epidemiological sample and modern diagnostic technology. We analyzed a broad spectrum of psychiatric disorders to present information on the general association between diabetes, glycemic control, and mental disorders in a representative community sample.

## RESEARCH DESIGN AND METHODS

The German National Health Interview and Examination Survey (GNHIES) is based on a stratified, multistage, cross-sectional, national representative sample of individuals aged 18–79 years from the noninstitutionalized population of Germany (15–18). Subjects were recruited from October 1997 to March 1999 and were eligible if they were familiar with the German language and were able to complete the questionnaires.

The GNHIES surveyed 7,124 persons. Foreign subjects (4% of the participants) were underrepresented in this survey. Nearly the same number of foreign subjects could not be included in the survey due to language problems.

Among others, questions regarding sociodemographic variables and chronic illness were asked in the survey. Participants underwent a thorough physical examination and blood samples were collected. Information on diabetes was obtained for all participants by a standardized questionnaire, which was checked by a physician during an interview. Diabetes was considered present if survey participants had ever been diagnosed with the condition (19). The following information was obtained from each subject: age at diagnosis of diabetes, duration of diabetes, BMI, current treatment, and nature of any complications. A blood sample was collected for measurement of clinical parameters. HbA<sub>1c</sub> was evaluated using a Bio-Rad Diamat fully automated HbA<sub>1c</sub> analyzer system (REC-IPE-ClinRep; Bio-Rad, Richmond, CA).

For the purpose of this study, we classified PWD as having type 1 diabetes if they were 35 years of age or younger at diagnosis and were treated with insulin and as having type 2 diabetes if they were treated with diet alone or oral hypoglycemic agents or were older than 35 years at diagnosis, irrespective of treatment.

All participants completed the Composite International Diagnostic Screener (CID-S) (17) for mental disorders. Subjects aged 65 years and younger who screened positive and a 50% random sample of subjects who screened negative were selected for stage 2 of the survey, in which participants were administered the full Composite International Diagnostic Interview (CIDI) (20) for Diagnostic and Statistical Manual of Psychiatric Disorders, 4th edition (DSM-IV) disorders by clinical interviewers ( $n = 4,181$ ). Diagnoses included affective disorders (major depression, dysthymia, mania, bipolar disorder), anxiety disorders (panic disorder, agoraphobia, social phobia, simple phobia, generalized anxiety disorder, obsessive-compulsive disorders), somatoform disorders, and substance abuse/dependence disorders (alcohol and drug abuse and dependence). Because of low prevalence rates in some mental disorders (e.g., eating disorders), we focused on these four diagnostic groups. Axis II diag-

noses were generally not included in the study because the diagnostic instrument was unreliable for these diagnoses. For logistical and financial reasons, the CIDI module for trauma-related disorders was not used in the present survey. Therefore, we have no information about post-traumatic stress disorders.

Current diagnoses (30-day prevalence) for all disorders were used for evaluating the relationship between diabetes and mental disorders. Subjects who suffered from a combination of affective, anxiety, somatoform, or abuse/dependence disorders were categorized as exhibiting a comorbid psychiatric disorder. Details of the psychometric properties of the CIDI are reported by Wittchen (21). Test-retest reliability was good for almost all specific disorders, with  $\kappa$ -values ranging from 0.62 (somatoform disorders) to 0.81 (any anxiety disorder) (22). The main survey was performed at the sampling units' examination centers ( $n = 120$ ), whereas the CIDI interviews were conducted in the homes of the respondents (mean interview time 34 min). Most interviews took place within 4 weeks of the initial appointment.

The data regarding the mental disorders were released for public use in 2000 (23). The overall response rate in the main survey was 61.5%, whereas the response rate in the second stage (psychiatric interview) was 87.6%. Nonresponse was mainly due to refusal to participate and inability to reach the selected respondent. Rates of nonresponse did not differ significantly between screen-negative and screen-positive respondents from the main survey [ $\chi^2(1) = 1.56, P = 0.211$ ] (17).

Data were weighted by demographic characteristics and selection probabilities. In the following analyses, only weighted data are used. Subjects with unknown diabetes status due to missing data ( $n = 12$ ) were excluded from all analyses. Differences in group characteristics were examined by using either independent-groups Student's  $t$  tests or  $\chi^2$  analyses. We undertook both unadjusted and adjusted logistic regression to assess the association between diabetes and mental disorders. The fit of the logistic model was assessed with the Hosmer and Lemeshow (24) goodness-of-fit test;  $P < 0.05$  was considered evidence of a statistically significant difference between observed and pre-

**Table 1—Sociodemographic and clinical characteristics of the sample**

Variable	PWD (n = 141)	Subjects without diabetes (n = 4,028)
Female sex	43.0 (4.7)	49.9 (0.9)
Age (years)	53.9 ± 11.1	41.1 ± 13.1
Socioeconomic status		
Low	32.3 (4.5)	18.7 (0.7)
Medium	60.7 (4.7)	57.7 (0.9)
High	7.0 (2.0)	23.8 (0.8)
Marital status		
Married	80.3 (3.7)	63.5 (0.9)
Divorced/widowed/separated	10.9 (2.9)	11.0 (0.5)
Single	8.8 (2.5)	24.7 (0.8)
HbA <sub>1c</sub> (%)	7.74 ± 1.75	5.40 ± 0.56
BMI (kg/m <sup>2</sup> )	29.7 ± 5.8	26.2 ± 4.5
Duration of diabetes (years)	8.4 ± 7.5	
Diabetes treatment		
Insulin	26.2 (4.6)	
Oral agents	14.9 (3.5)	
Diet	14.2 (3.1)	
Oral agents and diet	24.2 (3.9)	
No treatment	20.6 (3.7)	

Data are % (SE) or mean ± SD. Weighted data are presented.

dicted survival. Odds ratios (ORs) and corresponding 95% CIs are reported. Collinearity was assessed by calculating tolerance levels and variance inflation factors for each predictor variable (25).

Analyses were performed using Stata software (College Station, TX), which included commands for analysis of complex survey data (26).

**RESULTS**— Demographic and clinical characteristics for the participants of stage 2 are shown in Table 1. A total of 141 PWD were identified (57% men), indicating a prevalence of 3.4%. More than one fourth (26.2%) of the PWD received insulin treatment and 7.2% of the PWD had type 1 diabetes. There were only small differences in mean HbA<sub>1c</sub> levels between patients with type 1 diabetes and those with type 2 diabetes (means ± SE 8.23 ± 0.21 and 7.57 ± 0.31, respectively; *t* = 1.75, *df* = 139, *P* = 0.082). In keeping with previous findings, PWD were older, more often married, and had lower socioeconomic status than subjects without diabetes.

A total of 26.6% (SE 3.9) of the PWD had a DSM-IV–defined mental disorder (Table 2). PWD were not significantly more likely to meet DSM-IV criteria for at

least one disorder than subjects without diabetes [ $\chi^2(1) = 0.026, P = 0.870$ ]. However, we found a significantly higher prevalence of affective and anxiety disorders among PWD than among individuals without diabetes [ $\chi^2(1) = 4.03, P = 0.044; \chi^2(1) = 7.33, P = 0.007$ ]. Comorbidity of depression and anxiety in PWD

was substantial: 64% of the affective disorders coincided with an anxiety disorder, and 41% of individuals with an anxiety disorder also had depression. A high comorbidity rate was also observed for the somatoform disorders. With one exception, all people with a somatoform disorder had a comorbid anxiety disorder.

The crude and adjusted ORs obtained from logistic regression models are shown in Table 3. The results show that the presence of diabetes increased the odds of affective disorders (OR = 1.73, *P* = 0.047) and anxiety disorders (OR = 1.93, *P* = 0.008). Cases of somatoform disorders and substance abuse, however, did not occur in large numbers.

It is known that sociodemographic variables such as sex, age, socioeconomic factors, and marital status have an impact on the prevalence of mental disorders. Including sociodemographic confounders in the multivariate analyses only slightly changed the ORs (Table 3). Interestingly, this analysis showed different associations for the diagnostic category of affective disorders. The ORs for these diagnoses decreased when sociodemographic confounders were adjusted for simultaneously.

There was an inverse relationship between depression/anxiety and HbA<sub>1c</sub>. PWD who did not fulfill the criteria for a current mental disorder showed poorer metabolic control, with a mean HbA<sub>1c</sub> value of 7.88% (95% CI 7.55–8.22), than those with affective disorders (*M* =

**Table 2—Prevalence rates of mental disorders (30 days)**

DSM-IV disorder	PWD (n = 141)	Subjects without diabetes (n = 4,028)
Any mental disorder	26.6 (3.9)	26.0 (0.8)
Any affective disorder	10.2 (2.4)	6.2 (0.4)
Any noncomorbid affective disorder	2.8 (1.2)	2.3 (0.3)
Comorbid affective disorder	7.4 (2.1)	3.9 (0.3)
Any anxiety disorder	15.6 (3.2)	8.8 (0.5)
Any noncomorbid anxiety disorder	4.5 (1.6)	4.0 (0.3)
Comorbid anxiety disorder	11.1 (2.8)	4.8 (0.3)
Any somatoform disorder	7.9 (2.5)	7.4 (0.4)
Any noncomorbid somatoform disorder	0.3 (0.3)	4.1 (0.4)
Comorbid somatoform disorder	7.6 (2.5)	3.4 (0.3)
Any substance abuse/dependence	9.0 (2.5)	12.6 (0.6)
Any noncomorbid substance abuse/dependence	7.0 (2.3)	8.9 (0.5)
Comorbid substance abuse/dependence	2.1 (1.0)	3.7 (0.3)

\*Data are % (SE). Note: among the anxiety disorders, the most prevalent diagnoses were simple phobia (8.4%) and agoraphobia (6.0%). Dysthymia was more prevalent (8.0%) than major depressive disorder (4.5%) among the class of affective disorders.

**Table 3—Association between diabetes and mental disorders (30 days)**

DSM-IV disorder	OR (95% CI)	Adjusted* OR (95% CI)
Any mental disorder	1.03 (0.69–1.54)	1.11 (0.73–1.69)
Affective disorder	1.73 (1.01–2.96)	1.41 (0.78–2.55)
Anxiety disorder	1.93 (1.19–3.14)	2.05 (1.22–3.43)
Somatoform disorder	1.07 (0.54–2.14)	1.02 (0.51–2.04)
Substance abuse/dependence	0.69 (0.37–1.28)	0.97 (0.52–1.83)

\*Adjusted for age, sex, socioeconomic status, and family status.

6.25%, 95% CI 5.66–6.84) and anxiety disorder (M = 6.79%, 95% CI 6.01–7.56). Results for both disorders were statistically significant ( $P < 0.001$  and  $P = 0.010$ , respectively). However, we did not find an inverse relationship between somatoform and substance abuse disorders and HbA<sub>1c</sub>. Table 4 shows the results of the logistic regression with HbA<sub>1c</sub> (dichotomized:  $\leq 7$  vs.  $> 7$ %) as an additional covariate.

**CONCLUSIONS**— The main objective of this study was to identify the association between mental disorders and diabetes in a large representative community sample. Owing to the large sample size and the incorporation of sociodemographic variables, the design of the study was suited to perform this task. Particular attention was given to affective and anxiety disorders.

In the present analysis, PWD were not more likely to meet DSM-IV criteria for at least one mental disorder than subjects without diabetes. However, a different diagnostic pattern was observed: PWD had an increased prevalence of current anxiety disorders but not of somatoform and substance abuse disorders. Overall levels of psychiatric comorbidity were higher in these patients than in the general population sample, which did not comprise PWD.

Our results are consistent with other studies regarding depression and anxiety symptoms (6). In a recent meta-analysis, Anderson et al. (4) found similar unadjusted prevalence rates and ORs for depression in PWD. In our analyses, the relationship between diabetes and affective disorders was not statistically significant after controlling for age, sex, marital status, and socioeconomic status. In contrast, the relationship between diabetes and anxiety disorders remained significant after controlling for sociodemo-

graphic variables. The prevalence of mental disorders in clinical samples has been reported to be even higher. However, our results are not directly comparable to these studies because we used a representative community sample. Mental disorders do have an influence on the consultation of medical institutions (5,27). Medical comorbid conditions such as heart disease and hypertension were significantly more common among PWD. These comorbid conditions were also associated with mental disorders. Therefore, the association between mental disorders and diabetes should be evaluated carefully in terms of potentially confounding sociodemographic variables, sample characteristics (clinical versus community samples), and medical comorbid conditions. It should be kept in mind that identification and effective

treatment of comorbid diabetes and mental disorders is considered an essential component of high-quality clinical care in the specialty medical setting (28).

The relationship between mental disorder and glycemic control remains unclear. In contrast to the meta-analysis conducted by Lustman et al. (11), we could not find a positive association between depression and HbA<sub>1c</sub> in a logistic regression model. We found that PWD with an HbA<sub>1c</sub> level  $\leq 7$ % ( $n = 50$ ) suffered more often from affective and anxiety disorders than those with poor glycemic control (HbA<sub>1c</sub>  $> 7$ %,  $n = 86$ ). These associations were independent of insulin treatment. A similar pattern of association was observed for type 2 diabetics with and without insulin treatment. To replicate this pattern, we analyzed the relationship between HbA<sub>1c</sub> and self-reported mental health. Additional data collected during the main survey included self-reported service utilization and health-related quality of life from the Medical Outcomes Study 36-item short form (SF-36) (29), which examines, in addition to physical health, general mental health. However, a poor but positive correlation (0.12) between self-reported mental health and HbA<sub>1c</sub> was observed ( $n = 347$  PWD in the main survey).

There may be several reasons for these findings. PWD with comorbid men-

**Table 4—Association between affective and anxiety disorders (30 days), HbA<sub>1c</sub>, and sociodemographic variables**

	Affective disorder OR (95% CI)	Anxiety disorder OR (95% CI)
Diabetes status		
No diabetes	1.0 (reference)	1.0 (reference)
Diabetes and HbA <sub>1c</sub> $< 7$ %	3.17 (1.48–6.79)	3.47 (1.75–6.87)
Diabetes and HbA <sub>1c</sub> $> 7$ %	0.65 (0.26–1.62)	1.26 (0.57–2.81)
Sex		
Male	1.0 (reference)	1.0 (reference)
Female	1.54 (1.14–2.08)	2.67 (2.08–3.43)
Age	1.02 (1.01–1.03)	0.99 (0.98–1.01)
Socioeconomic status		
Low	1.0 (reference)	1.0 (reference)
Medium	0.66 (0.48–0.91)	0.70 (0.54–0.92)
High	0.38 (0.24–0.60)	0.47 (0.33–0.68)
Marital status		
Married	1.0 (reference)	1.0 (reference)
Divorced/widowed/separated	2.32 (1.62–3.31)	1.23 (0.87–1.73)
Single	1.53 (1.04–2.27)	1.01 (0.74–1.39)

Data are ORs (95% CIs). Note: tolerance levels ranged from 0.58 to 0.98 and variance inflation factors ranged from 1.01 to 1.74, which were deemed acceptable. According to Fox (25), variance inflation factors should be  $< 4$  and tolerance levels should be  $> 0.30$  to avoid potential multicollinearity problems.

tal disorders showed higher medical service utilization than PWD without comorbid mental disorders (5). It is possible that the health care utilization was associated with good glycemic control. This interpretation is consistent with our finding that the mean (average) number of physician visits per year is considerably higher among PWD with comorbid mental disorder and a HbA<sub>1c</sub> level  $\leq 7\%$  than among PWD with poor glycemic control (HbA<sub>1c</sub>  $> 7\%$ ).

It should be considered that previous studies analyzing the association between major depression and glycemic control using standardized interviews focused exclusively on major depressive disorder. In our study, the most prevalent affective disorder was dysthymia, a chronic low-grade depression that results in little impairment of daily life.

Other possible explanations for these results include clinical, sociodemographic (30), and personality characteristics. For example, there is some evidence that personality characteristics may help explain variations in glycemic control achieved by patients under conditions of standard diabetes management (31). On the other hand, it should be kept in mind that we have small subsamples and that differences may be caused by sampling and measurement errors. It seems that the association between mental disorders and glycemic control is modulated by several variables. Therefore, further research is needed to evaluate the relationship between diabetes, glycemic control, and mental disorders, including functional impairment, medical conditions, service utilization, and sociodemographic and personality characteristics.

Several limitations of our data are noteworthy. First, the data are cross-sectional and although the German National Health Interview and Examination Survey was population based, we were unable to determine the relationship between diabetes and mental disorders longitudinally. Because we were interested in the influence of diabetic status and glycemic control on mental disorders, we focused only on current mental disorders (30-day prevalence). Prospective longitudinal studies are required to clarify these interactions and to identify the temporal relationship between onset of diabetes and of mental disorders.

Second, the prevalence of diabetes in our sample was low (3.4%) because sub-

jects aged 66 years and older were excluded from stage 2 of the survey due to psychometric shortcomings of the CIDI in older populations. The prevalence of diabetes in the main survey (age range 18–79 years) was 5.3%. Therefore, a number of older subjects with diabetes were excluded, which may affect the relationship between psychiatric disorders and diabetes. Moreover, the data regarding diabetic status were gathered by self-report questionnaire and physician interview. Some of the subjects in the reference group may have had undetected diabetes. The portion of subjects with undetected diabetes in the present survey (19) was estimated to be  $\sim 1\%$ , considering the values of blood and urine parameters (glucose in serum and urine, fructosamine, and HbA<sub>1c</sub>). This might affect the associations. For example, Mooy et al. (32) reported a significant association between psychological stress and prevalence of undetected type 2 diabetes in a population-based study. On the other hand, we cannot exclude the possibility of false positives (subjects who do not truly have diabetes) in the diabetes group. However, it is likely to have only a few false positives, because all subjects with diabetes were interviewed regarding their diabetes-specific medications, symptoms, and clinical parameters.

Due to the small prevalence rates of diabetes, we did not distinguish between type 1 and type 2 diabetes. It is possible that the association between mental disorders and diabetes is different for type 1 and type 2 diabetes. However, we obtained similar results when we replicated our analysis for people with type 2 diabetes. Several studies suggest that the relationship between depression and diabetes is independent of type of diabetes (4).

Finally, the omission of race as a (possible) correlate in the present analyses deserves mention, given that other surveys often include race as a demographic characteristic. In Germany, citizenship instead of race is usually measured. This was the case in the present study. Foreign subjects were underrepresented in this survey. Therefore, citizenship was biased and we did not use it in our analyses.

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