Depression and Diabetes

A large population-based study of sociodemographic, lifestyle, and clinical factors associated with depression in type 1 and type 2 diabetes

Anne Engum, MD1,2
Arnstein Myklethun, MA3
Kristian Midtöll, MD, PhD4

OBJECTIVE — The purpose of this study was to investigate factors associated with depression in type 1 and type 2 diabetes and test whether these differ from factors associated with depression in the nondiabetic population.

RESEARCH DESIGN AND METHODS — In an unselected population study comprising 60,869 individuals, potential sociodemographic, lifestyle, and clinical factors were investigated in participants with and without diabetes. The associations between hyperglycemia and depression in types 1 and 2 diabetes were also studied. The levels of depression were self-rated by using the Hospital Anxiety and Depression Scale.

RESULTS — Several factors were correlated with depression in types 1 and 2 diabetes. However, these factors were not different from those of the nondiabetic population. Comorbid chronic somatic diseases were associated with depression in type 2 but not type 1 diabetes. In type 2 diabetes, those without comorbidity had the same odds of depression as the nondiabetic population with no chronic somatic diseases. No significant associations were found for hyperglycemia in relation to depression in type 1 and type 2 diabetes.

CONCLUSIONS — Type 2 diabetes without other chronic somatic diseases did not increase the risk of depression. Factors associated with depression in type 1 and type 2 diabetes were shared with the nondiabetic population.

Diabetes Care 28:1904–1909, 2005

Past research has shown that a relationship exists between depression and diabetes (1). Depression has been associated with hyperglycemia (2), diabetes-related complications (3), and perceived functional limitations of diabetes (4). Moreover, depression among individuals with diabetes has also been associated with potential sociodemographic, lifestyle, and clinical factors shared with the general population. The contributions of socioeconomic status (5), marital status (6), obesity (7), smoking habits (8), and physical limitations and inactivity (9) have been extensively tested.

When the relationship between diabetes and depression is examined, the role of comorbid chronic somatic diseases has to be taken into account (10). In general, previous research has indicated a higher prevalence of depression in samples of patients with various chronic somatic diseases. The coexistence of chronic somatic diseases is common (11,12), and there is a strong connection between symptoms of depression and the number of different chronic diseases (13,14).

Nevertheless, the question remains: Are the factors associated with depression in types 1 and 2 diabetes different from those in the nondiabetic population? We have not been able to find any studies that include interaction tests to investigate whether factors associated with depression actually interact with having diabetes. Multiple health problems, as well as personal, social, and community factors, may combine to bring about depression in individuals with diabetes. Several of the factors claimed to be linked to depression are not limited to those with diabetes and may be related to the general psychological distress of having a chronic disease (4).

In a large study of the general population, the relationship between diabetes and reported symptoms of depression were studied. This study investigated the role of some sociodemographic, lifestyle, and clinical factors associated with depression in types 1 and 2 diabetes and examined whether these factors were different from those of the nondiabetic population.

RESEARCH DESIGN AND METHODS — The population study was part of the second Nord-Trøndelag Health Study, Norway (HUNT 2). The data were collected from 1995 to 1997. All inhabitants of Nord-Trøndelag County aged ≥20 years received written invitations together with questionnaires and appointed dates for physical tests and blood samples. In the questionnaires, the participants were asked about demographic characteristics, health status, lifestyle, health habits, and their living conditions. Of 92,100 individuals invited, 65,648 (71.3%) responded. The
youngest and oldest age-groups had the lowest rates of attendance, whereas the highest rates were found among women and middle-aged persons.

Our sample comprised individuals aged 20–89 years with valid ratings of depression, self-report of diabetes, data about marital status, level of education, smoking habits, BMI, and physical activity. Included were also self-reports about somatic diseases and physical impairments. The non-diabetic population comprised 59,329 individuals. A total of 223 had type 1 diabetes, 958 had type 2 diabetes, and 359 individuals had other subtypes of diabetes or did not take the verifying blood tests and were left unclassified. In this study, the main topic was to compare individuals with types 1 and 2 diabetes with nondiabetic responders. Accordingly, individuals with unclassified diabetes were excluded from the analyses.

Psychological features
Symptoms of depression were screened using the Hospital Anxiety and Depression Scale (HADS) (15,16). The scale consists of seven items for depression (HADS-D) and seven for anxiety. Only HADS-D scores were utilized in this study. A main characteristic of HADS-D is that items covering somatic symptoms of depression have been eliminated to avoid false-positive results when used in somatic settings. In this study, we used the recommended cutoff of eight for caseness of depression. However, this should not imply a level of clinical depression, which cannot be inferred from the screening instrument used in the present study. HADS has been extensively tested and has well-established psychometric properties (17). Several studies have demonstrated good sensitivity, specificity, and receiver operating characteristics of HADS. High correlation between HADS scores has been obtained in relation to other questionnaires and structured interviews detecting depression (18,19).

Somatic health
The initial selection of individuals with diabetes was based on self-reports. Metabolic control was determined by HbA1c (A1C) in all individuals who had diabetes. A1C values reflect the average level of blood glucose in the past 3 months. The test is widely accepted as a reliable and valid index of metabolic control. In addition, all participants indicating a history of diabetes (n = 1,638) received a specific questionnaire about the disease and 1,540 responded. Of those, 1,181 participated in additional fasting blood test for glucose, C-peptide, and anti-GAD antibodies. According to autoantibodies to GAD, C-peptide tests, and information on start of insulin treatment, the respondents were further divided into types 1 and 2 diabetes. C-peptide was tapped by the radioimmunoassay method (Diagnostic System Laboratories, Webster, TX), and anti-GAD antibodies were measured via immunoprecipitation by using [3H] leucine translation-labeled GAD65 as the indicator.

A total of 19,979 individuals reported a history of one or more of the following health problems: cardiovascular diseases (including angina pectoris, myocardial infarction, stroke, and hypertension), musculoskeletal diseases (including ankylosing spondylitis, osteoarthritis, rheumatoid arthritis, and osteoporosis), thyroid diseases (including hypothyroidism, goiter, and hyperthyroidism), cancer, and asthma. A dichotomous variable for “somatic diseases” was defined as one or more of the above-mentioned health problems, as opposed to none.

The participants were asked to assess how much their function was impaired or restricted with regard to vision, hearing, and movement. Two dichotomous variables were made from the self-reported data about the presence (moderately or severely impaired vision and/or impaired hearing and/or restricted movement) or absence of physical impairment.

The variable “somatic complaints” including symptoms such as pain, stiffness, or gastrointestinal symptoms (diabetes, nausea, or diarrhea) were divided into one or more complaints versus none.

Demographic and lifestyle variables
Education was classified into low and high: low levels of education covered compulsory education (≤9 years), whereas high education was defined as >9 years of school. Two dichotomous categories were developed for marital status: single (unmarried, widowed, divorced, or separated) versus married or cohabiting.

Lifestyle variables covered information about smoking, BMI, and physical activity. Smokers were defined dichotomously into current smokers or not. BMI was treated as a continuous variable. The participants were asked to give information about how many hours they spent on physical activity in their spare time during the last year (hours per week). In a dichotomous variable, physical inactivity was scored as positive whenever the person spent <1 h per week on physical activities.

Statistics
The t test or χ² test were used to investigate differences on demographic characteristics, somatic health, and depression as measured by HADS-D between type 1 or type 2 diabetes and the nondiabetic population. Then bivariate analyses between depression and demographic, lifestyle, and somatic variables were computed in type 1 and type 2 diabetes and in the nondiabetic population.

To determine whether the factors identified in type 1 or type 2 diabetes as correlating with depression were specific or shared with the nondiabetic population, logistic regression models were used with depression as a dependent variable. The factors, type 1 (or type 2) diabetes, and the interaction term between the factors and type 1 (or type 2) diabetes were used as independent variables in 20 separate runs. The models were adjusted for demographic, lifestyle, and clinical variables that were related to the exposure and that in a stepwise logistic regression were related to the outcome (depression) with P < 0.20. All the variables in the full models contributed to the models and were retained. No factors were strongly correlated in a collinearity analyses. The Hosmer-Lemeshow goodness-of-fit test was used to assess model fit. If the interaction term was positive, the factor was more associated with depression in type 1 or type 2 diabetes than in the nondiabetic population and accordingly less associated if the interaction term was negative. We examined the potential for effect modification by including interaction terms between age and sex with each factor in the analyses.

The relationship between A1C and HADS-D was investigated by linear regression analyses adjusted for age and sex in type 1 and type 2 diabetes. The dependent variable, HADS-D, was fairly normally distributed both in type 1 (skewness = 1.092, kurtosis = 1.458) and in type 2 diabetes (skewness = 0.813, kurtosis = 0.353).

We undertook both unadjusted and
adjusted logistic regression analyses to assess the associations between groups with and without chronic somatic diseases as independent variables and depression (HADS-D ≥8) as the dependent variable with the “no chronic disease” group serving as the reference category. In a stepwise logistic regression, all covariates were significantly related to the outcome and were retained in the model. All the factors were correlated, but a collinearity analysis revealed no factors were strongly correlated with one another.

The level of significance was set at \( P < 0.05 \). All tests were two way and SPSS-PC 12.0 was used as the statistical package.

The National Data Inspectorate and the Board of Medical Research Ethics in Health Region IV of Norway approved the HUNT 2 study.

**RESULTS**— In Table 1, the characteristics of participants with type 1, type 2, and no diabetes were compared with regard to demographics, lifestyle variables, somatic health, and depression as measured by HADS-D. Compared with the nondiabetic population (\( n = 59,329 \)) individuals with type 1 (\( n = 223 \)) and type 2 diabetes (\( n = 958 \)) were more likely to be depressed (15.2 and 19.0%, respectively, vs. 10.7% in the nondiabetic population). In both type 1 and type 2 diabetes, participants were older, were more often male, had low levels of education, were considerably more obese, and smoked less. In addition, they reported more somatic diseases and more physical impairment. Furthermore, individuals with type 2 diabetes were more physically inactive and also reported more somatic complaints.

In the nondiabetic population, 31.8% (\( n = 18,896 \)) reported one or more chronic somatic diseases: cardiovascular diseases, 13.6%; musculoskeletal diseases, 13.2%; thyroid diseases, 5.2%; cancer, 3.4%; and asthma, 8.4%. In type 1 diabetic subjects, 60.5% (\( n = 135 \)) reported comorbidity: cardiovascular diseases, 43.0%; musculoskeletal diseases, 19.7%; thyroid diseases, 13.0%; cancer, 4.0%; and asthma, 7.2%. In type 2 diabetic subjects, 74.0% (\( n = 709 \)) reported comorbidity: cardiovascular diseases, 55.4%; musculoskeletal diseases, 28.9%; thyroid diseases, 9.3%; cancer, 8.5%; and asthma, 13.4%.

**Factors correlated with depression**

Bivariate analyses between depression (HADS-D ≥8) and demographic, lifestyle, and somatic covariates (Table 2) revealed several significant correlations with depression in type 2 diabetes. Those having depression compared with subjects without depression had significantly lower levels of education (72.5 vs. 64.7%) and were less physically active (77.2 vs. 62.8%). The subjects with depression also had a higher proportion of comorbid somatic diseases (83.5 vs. 71.8%), subjective somatic complaints (75.3 vs. 55.2%), and physical impairment (45.6% vs. 32.0%). In type 1 diabetes, low levels of education (62.5 vs. 40.0%) and physical impairment (50.0 vs. 27.0%) were significantly correlated with depression. Logistic regression analyses (both crude and adjusted) demonstrated that the factors correlated with depression in type 1 and type 2 diabetes were not different from those of the nondiabetic population; the interaction terms (type 1 and type 2 diabetes by factors) were not significantly different from the odds ratio (OR) of 1. The interaction with age and sex did not modify the results.

**Association between hyperglycemia and depression**

The associations between hyperglycemia and depression were tested by using linear regression analyses with HADS-D and A1C as continuous variables and adjustments for age and sex. The analyses demonstrated nonsignificant associations for both type 1 diabetes (\( b = -0.094, P = 0.164 \)) and type 2 diabetes (\( b = -0.030, P = 0.357 \)).

**Association between comorbidity and depression**

Dividing the participants into subgroups with and without diabetes and with and without other chronic somatic diseases, the odds of depression were compared with the reference category without any reported chronic somatic diseases (Table 3). The associations were adjusted for age, sex, marital status, level of education, smoking, physical inactivity, BMI, somatic complaints, and physical impairment. In the nondiabetic population,
those with chronic somatic diseases had significantly higher odds of depression in both crude (OR = 1.93) and adjusted (OR = 1.16) analyses. In type 1 diabetes, the odds of depression were also higher in those with comorbid chronic somatic diseases, but the difference did not reach significance when adjusted. Individuals with type 2 diabetes without comorbidity were not at higher risks of depression than those in the reference category when adjusted. However, comorbidity between diabetes and chronic somatic diseases carried the highest adjusted odds of depression (OR = 1.38). In analyses of the subtypes of comorbid chronic somatic diseases, only the comorbidity between cardiovascular diseases and type 2 diabetes was significantly associated with depression (data not shown).

**CONCLUSIONS**  — There were three major findings in this study. First, comorbid chronic somatic diseases were associated with depression in type 2 diabetes but not in type 1 diabetes. Individuals with type 2 diabetes without comorbidity had the same odds of depression as the nondiabetic population without any reported chronic somatic diseases. Second, hyperglycemia was not associated with depression in type 1 or type 2 diabetes. Finally, the factors correlated with depression in type 1 and type 2 diabetes were shared with the nondiabetic population.

The prevalence of depression was significantly higher in subjects with types 1 and 2 diabetes compared with the nondiabetic population. Several factors were correlated with depression in type 2 diabetes, such as low levels of education, physical inactivity, subjective somatic complaints, and physical impairment. In type 1 diabetes, low levels of education and physical impairment were correlated with depression. In types 1 and 2 diabetes, a large proportion of subjects had one or more comorbid chronic somatic diseases with cardiovascular diseases being the most prevalent condition. Comorbid-

---

### Table 2—Factors correlated with depression in type 1 and type 2 diabetes compared with the nondiabetic population

<table>
<thead>
<tr>
<th></th>
<th>Type 1 diabetes</th>
<th></th>
<th>Type 2 diabetes</th>
<th></th>
<th>Nondiabetic population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HADS-D ≥8</td>
<td>HADS-D &lt;8</td>
<td>P value*</td>
<td>HADS-D ≥8</td>
<td>HADS-D &lt;8</td>
</tr>
<tr>
<td>n</td>
<td>223</td>
<td>958</td>
<td></td>
<td>59,329</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.7 ± 12.7</td>
<td>56.8 ± 17.5</td>
<td>0.356</td>
<td>67.9 ± 11.3</td>
<td>67.0 ± 11.4</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>50.0</td>
<td>38.1</td>
<td>0.192</td>
<td>52.2</td>
<td>47.4</td>
</tr>
<tr>
<td>Low education (%)</td>
<td>62.5</td>
<td>40.0</td>
<td>0.018</td>
<td>72.5</td>
<td>64.7</td>
</tr>
<tr>
<td>Marital status (single) (%)</td>
<td>35.3</td>
<td>41.0</td>
<td>0.535</td>
<td>37.9</td>
<td>36.0</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>19.4</td>
<td>18.4</td>
<td>0.897</td>
<td>17.1</td>
<td>16.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.5 ± 4.6</td>
<td>27.3 ± 4.3</td>
<td>0.349</td>
<td>30.0 ± 5.3</td>
<td>29.5 ± 4.7</td>
</tr>
<tr>
<td>Physical inactivity (%)</td>
<td>56.3</td>
<td>63.7</td>
<td>0.426</td>
<td>77.2</td>
<td>62.8</td>
</tr>
<tr>
<td>Somatic diseases (≥1) (%)</td>
<td>67.6</td>
<td>59.3</td>
<td>0.357</td>
<td>83.5</td>
<td>71.8</td>
</tr>
<tr>
<td>Somatic complaints (≥1) (%)</td>
<td>58.8</td>
<td>50.8</td>
<td>0.388</td>
<td>75.3</td>
<td>55.2</td>
</tr>
<tr>
<td>Physical impairment (%)</td>
<td>50.0</td>
<td>27.0</td>
<td>0.007</td>
<td>45.6</td>
<td>32.0</td>
</tr>
</tbody>
</table>

Data are means ± SD unless otherwise indicated. To determine whether the factors correlated with depression identified in type 1 diabetes were specific or shared with the nondiabetic population, logistic analyses with interaction terms between type 1 diabetes and the factors were carried out. Positive interaction occurred when the interaction term (type 1 diabetes by factor) is significantly different from OR = 1. The same analyses were conducted for type 2 diabetes. All interactions were nonsignificant. *χ² significance in type 1 diabetes, type 2 diabetes, and in the nondiabetic population, respectively.

---

### Table 3—Odds ratios of depression as function of chronic somatic diseases in groups with and without diabetes

<table>
<thead>
<tr>
<th></th>
<th>OR crude (95% CI)</th>
<th>P value</th>
<th>OR adjusted* (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nondiabetic population</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without any known chronic somatic diseases</td>
<td>40,433 (68.2)</td>
<td>1.00</td>
<td>1.93 (1.83–2.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>With one or more chronic somatic diseases</td>
<td>18,896 (31.8)</td>
<td>2.23</td>
<td>1.53 (0.82–2.89)</td>
<td>0.185</td>
</tr>
<tr>
<td>Type 1 diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without comorbid chronic somatic diseases</td>
<td>88 (39.5)</td>
<td>1.53</td>
<td>1.53 (0.82–2.89)</td>
<td>0.185</td>
</tr>
<tr>
<td>With one or more comorbid chronic somatic diseases</td>
<td>135 (60.5)</td>
<td>2.21</td>
<td>1.41 (1.41–3.46)</td>
<td>0.001</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without comorbid chronic somatic diseases</td>
<td>249 (26.0)</td>
<td>1.47</td>
<td>1.47 (1.00–2.16)</td>
<td>0.048</td>
</tr>
<tr>
<td>With one or more comorbid chronic somatic diseases</td>
<td>709 (74.0)</td>
<td>2.93</td>
<td>2.93 (2.44–3.52)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*OR obtained from logistic regression analysis with HADS-D as a dependent variable adjusted for age, sex, marital status, level of education, smoking, physical inactivity, BMI, somatic complaints, and physical impairment.
Depression and diabetes

Dysphoric emotions may lower the motivation for maintaining the self-care regimen, which was suggested as the explanation for the decreased metabolic control.

Factors correlated with depression in type 1 and type 2 diabetes were not different from those in the non-diabetic population. In general, sociodemographic, lifestyle, and clinical variables are often reported to correlate with depression in diabetic populations, leaving the impression that these are of particular relevance to individuals with diabetes. Our findings indicate that this is far from the case. There are no obvious reasons for why factors correlated with depression would have a particular impact on persons with diabetes. Nevertheless, contributors to depression have been examined within rather diverse clinical and epidemiological diabetic populations. By reviewing prior research, we have been unable to find any reports demonstrating that factors correlated with depression interact with diabetes.

Findings of this study indicate that factors correlated with depression in diabetes have the same relevance as those in the general population and that the presence of comorbid chronic somatic diseases might explain the association between type 2 diabetes and depressive symptoms. This supports the notion that the general burden of having chronic diseases is linked to depression. Comorbidity between diabetes and other chronic somatic diseases may increase the risks of depression as a result of the psychosocial consequences of the diseases due to an additive effect of the perception of having the diseases as disabling or an awareness of having a chronic disease. As illustrated in a population-based study (13), individuals in whom diabetes has already been diagnosed had significantly higher rates of depressive symptoms than those with newly diagnosed diabetes. In addition, having a number of coexisting chronic conditions was a significant and independent predictor of depressive symptoms. Furthermore, a community-based study showed that general aspects such as physical limitations might be more important determinants of depression than specific diagnoses (24).

However, this conclusion does not exclude other hypotheses addressing the connections between depression and diabetes. The analyses of this study indicated increased risks of depression in type 2 diabetes only when comorbid cardiovascular diseases were present; this is a frequently occurring macrovascular complication in type 2 diabetes. The result may support theories suggesting that depression increases the risks of developing type 2 diabetes and diabetes-related vascular complications (25). Hypotheses have advanced that underlying factors may include increased insulin resistance and reduced glucose uptake (26). Another hypothesis is that stress-induced disturbances of the hypothalamo-pituitary-adrenal axis and the development of visceral obesity as a pathway to type 2 diabetes in individuals with genetic susceptibility (27).

The study was carried out on an unselected population, thus reducing selection bias. The population was large enough to allow for statistical adjustments of potential moderators. Some limitations of the present study have to be addressed. First, HADS is a self-report symptom scale that measures depressive symptoms only. Studies of HADS (18,19,28) have shown that the cutoff point chosen has sensitivity and specificity of ~0.80 for depression as defined in the Diagnostic and Statistical Manual of Mental Disorders III/III-R. Second, our study focused on current, not lifetime, psychiatric disorders. Third, the sample was predominantly of white origin and race as a possible correlate may not be studied. Fourth, the diagnosis of diabetes and other chronic somatic diseases was based on self-reported data. This approach may lead to underreporting of diagnoses. It seems unlikely, however, that this is a major bias as earlier research has reported relatively good agreement between self-report and in-person interview with regard to chronic somatic diseases such as diabetes (29,30). Finally, it is also worth considering that a proportion of the non-diabetic population might have undiagnosed diabetes. In this study, only 218 (0.003%) individuals in the non-diabetic population had increased nonfasting blood glucose levels ≥11 mmol/l, indicating the diagnosis of diabetes.

Acknowledgments—The HUNT Study is a collaboration between the HUNT Research Centre, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), Verdal, Norway, The National Institute of

DIABETES CARE, VOLUME 28, NUMBER 8, AUGUST 2005

1908

References