Published in final edited form as:

Ophthalmic Epidemiol. 2012 August ; 19(4): 196–203. doi:10.3109/09286586.2012.692006.

Relationship between Retinopathy Severity, Visual Impairment and Depression in Persons with Long-term Type 1 Diabetes

Flavio E. Hirai^{1,2}, James M. Tielsch³, Barbara E. K. Klein⁴, and Ronald Klein⁴

¹Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

²Department of Ophthalmology, Federal University of Sao Paulo, Sao Paulo, Brazil

³Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

⁴Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison, Wisconsin, USA

Abstract

Purpose—Our aim was to investigate the proportion of individuals with depression and its association with diabetic retinopathy and visual impairment in a cohort with 25 or more years of type 1 diabetes.

Methods—This was a cross-sectional analysis at the 25-year follow-up of the population-based cohort of the Wisconsin Epidemiologic Study of Diabetic Retinopathy. Examinations followed standardized protocols and included clinical and ophthalmic evaluations and questionnaires to assess current and past medical history, use of medications, and cigarette smoking. The Center for Epidemiologic Studies Depression Scale (CES-D) was administered to all participants. Depression was defined as use of antidepressant or CES-D score ≥ 16 .

Results—A total of 484 individuals were included in the analysis. The proportion of depression was 37.8% (95% confidence interval 33.4–42.3%). A higher proportion of individuals with depression was observed among those with more severe diabetic retinopathy and visual impairment. However these associations were not statistically significant while controlling for other factors in the multivariable analyses.

Conclusions—Diabetic retinopathy severity and visual acuity in persons with long duration of type 1 diabetes were not cross-sectionally associated with depression in this cohort.

Keywords

Diabetic retinopathy; Visual impairment; Depression; Type 1 diabetes; Epidemiology

Correspondence: Flavio E. Hirai, MD, PhD, Federal University of Sao Paulo, Department of Ophthalmology, Rua Botucatu 820, Sao Paulo, SP, Brazil, CEP 04023-062. Tel: +55 11 9117 8076. Fax: +55 11 3831 4488. fhirai@jhsph.edu.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

INTRODUCTION

Diabetes mellitus, a common chronic disorder that affects millions of people worldwide, is a leading cause of blindness.¹ Depression has also been shown to be present in up to 30% of people with type 1 diabetes.² Poor glycemic control and the presence of functional impairment due to the development of chronic complications such as visual impairment due to retinopathy, renal failure due to nephropathy, and pain and limitation of movement due to neuropathy found in persons with long-term type 1 diabetes, have been associated with depression.^{2–4}

We hypothesize that those with more severe retinopathy and visual impairment would have higher chances of having depression. The purpose of this study is to examine this relationship and report the proportion of depression in persons with 25 or more years of type 1 diabetes who participated in the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR).

METHODS

Study Population

The WESDR is a prospective cohort study initiated in 1979–80 of individuals with types 1 and 2 diabetes living in 11 counties of southern Wisconsin. Details of the methodology have been described previously.^{5–7} The Institutional Review Board of the University of Wisconsin, Madison, approved the study, and all participants provided consent. This research followed the tenets of the Declaration of Helsinki.

Individuals who had their diabetes diagnosed before 30 years of age were categorized as “younger-onset” and were shown to have type 1 diabetes using C-peptide testing. Examinations were performed at baseline (1980–82) and every 4–6 years thereafter. The current study is a cross-sectional analysis including those with type 1 diabetes who participated in the 2005–07 follow-up examination.

Procedures

All information used in the current analysis was collected during the 2005–07 follow-up examination. Examinations followed standardized protocols and were performed in a mobile van in or near locations where the participants resided. Examinations consisted of a clinical examination which included measurements of blood pressure, height, and weight using standardized protocols.^{5,6} An ophthalmic evaluation included measurement of best-corrected visual acuity using a modified Early Treatment Diabetic Retinopathy Study (ETDRS) chart after refraction, anterior segment biomicroscopy, tonometry, and funduscopy after pupil dilation.^{5,6} All procedures and measurements were done according to codified protocols. Stereoscopic color 30° fundus photographs of seven standard fields were taken to assess diabetic retinopathy status and other fundus abnormalities.⁵ While pupils were dilated, participants were asked questions by trained interviewers regarding their current and past medical conditions, use of medications, and history of cigarette smoking and alcohol consumption.

Assessment of Depression

Depression was assessed using a self-administered Center for Epidemiologic Studies Depression (CES-D) questionnaire. The CES-D scale is an index of affective and behavioral depressive features. It is an instrument for screening assessment of depressive symptoms that has been developed and validated for use in epidemiological surveys in the general population.^{8,9} CES-D scores of 16 or more are indicative of depression, and sensitivity and specificity varies across studies from 86–100%, and 70–90%, respectively.^{10–12} The CES-D consists of a 20-item questionnaire and scores range from 0–60. Forms were completed at home and brought in at the time of examination. Forms were printed with black ink on a white sheet, using large font (Arial, 14 point). For those with known visual impairment, a relative was asked to read the questions carefully. The forms were checked for missing items, which were ascertained by the examiner asking the question and filling in the response prior to the start of the examination.

Definitions

Age was defined as age at the time of the follow-up exam. Duration of diabetes was the period between the age of onset and age at the 2005–07 examination. Employment was categorized as “full- or part-time job”, “retired”, or “not working” for those who were unemployed, had lost jobs, or were homemakers. Participants were asked to rate the level of physical activity in one of three categories: “sedentary”, “moderate”, or “strenuous”. A person was classified as “never smoker” if he/she had smoked less than 100 cigarettes in his/her lifetime, as “former smoker” if he/she smoked more than 100 cigarettes and stopped, and as “current smoker” if he/she had not stopped. Pack years smoked was calculated by the number of packs per day multiplied by the number of years smoked.

Nephropathy was defined as history of kidney transplant, being on renal dialysis, or having gross proteinuria (defined as urine concentration of $\geq 0.30\text{g/L}$ measured by reagent strip). Neuropathy was defined as history of numbness or tingling in hands or feet, loss of sensation in hands or feet, and/or decreased ability to feel the hotness or coldness of things touched. Limb amputation was assessed by questionnaire or direct observation. Cardiovascular disease was defined as history of angina, myocardial infarction, coronary bypass surgery, and/or stroke.

The ETDRS protocol was used to determine best-corrected visual acuity and the total number of letters read by a person was recorded.¹³ Visual acuity measurements were converted to a logarithm of the minimum angle of resolution (LogMAR) scale¹⁴ for the purpose of statistical analyses. Individuals were classified as visually impaired if they presented with best-corrected visual acuity worse than 20/40 (≥ 35 letters) in the better eye. Severe visual impairment was defined as best-corrected visual acuity worse than 20/200. Diabetic retinopathy was graded according to a modified Airlie House classification scheme.¹⁵ For each eye, the maximum grade in any of the seven standard photographic fields was determined for each of the lesions used in defining retinopathy levels. The retinopathy level for a participant was derived by concatenating the levels for both eyes, giving the eye with the higher level greater weight. This scheme provided a 15-step scale (10/10, 21/<21, 21/21, 31/<31, 31/31, 37/<37, 37/37, 43/<43, 43/43, 47/<47, 47/47, 53/<53,

53/53, 60+/ $<60+$, and 60+/60+) when all levels of proliferative retinopathy were grouped as one level. For purposes of classification, if retinopathy severity could not be graded in an eye, it was considered to have a score equivalent to that in the other eye. Diabetic retinopathy was grouped according to the worse eye into none to mild non-proliferative diabetic retinopathy (NPDR; level 10 to 37), moderate-severe NPDR (level >37 to <60), and proliferative diabetic retinopathy (level 60).

Depression was defined as those using antidepressants or having a CES-D score ≥ 16 , and treated as a binary variable in the analyses.^{8,9} Some studies have shown that higher cutoff levels (eg, 21 or more) could improve the diagnosis of individuals with major depression.^{16,17} Therefore, we also analyzed our data with a CES-D score cutoff level of 21 or more.

Statistical Analysis

The proportion of individuals with depression at the 2005–07 follow-up visits was calculated. Continuous and categorical variables were compared with the t-test and Fisher exact test, respectively. Multivariable analyses were performed with logistic regression to control for potential confounders and test interactions. Because of possible correlations among microvascular long-term complications of diabetes (nephropathy, neuropathy, and diabetic retinopathy), these variables were included in separate multivariable models. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated and P -values < 0.05 were considered statistically significant. Analyses were performed with Stata v.10 (College Station, Texas, USA).

RESULTS

A total of 484 individuals provided complete data regarding their depressive symptom status and covariates. Their data were included in the current analysis. Those with no information about depressive symptoms were excluded ($n = 63$) from the analyses. These individuals did not differ from those included in terms of age, sex, level of glycosylated hemoglobin, frequency of insulin use, number of hypoglycemic events, and use of antidepressants (data not shown). They had poorer visual acuity, higher prevalence of proliferative diabetic retinopathy, tended to be unemployed, unmarried, and drink less alcohol than those who had information regarding depression.

A total of 996 individuals participated in the baseline examination. Characteristics at the baseline examination of those who participated in the 25-year follow-up, those who did not participate because they could not be located or refused ($n = 56$), and those who had died ($n = 120$) show, with the exception of less education, there were no significant differences in characteristics of those who participated compared with those who survived but did not participate. Persons with younger-onset type 1 diabetes who had died were older and had longer duration of diabetes, higher glycosylated hemoglobin, worse proteinuria, higher systolic blood pressure, greater BMI, more pack years smoked, more severe retinopathy, and poorer visual acuity than those who participated.

The mean age of the study population was 49.1 ± 9.25 years, mean duration of diabetes was 34.9 ± 7.03 years, 99.6% were Caucasian, and 51.5% were female. Mean glycosylated hemoglobin was $7.5 \pm 1.32\%$, and 37.6% used an insulin pump. Most of the participants were employed full- or part-time (70.3%), 10.1% were retired, and 19.6% were unemployed. Only 8.1% classified their level of physical activity as strenuous, 58.4% classified it as moderate, and 33.5% as sedentary. The majority of participants (59.1%) had never smoked, 28.5% were former smokers, and 12.4% were current smokers. Proliferative diabetic retinopathy was present in 47.3%, visual impairment in 5.5%, nephropathy in 48.5%, neuropathy in 58.1%, cardiovascular disease in 24.9%, and limb amputation in 5.8% of the population.

The proportion of individuals with depression was 37.8% (95% CI 33.4–42.3%, $n = 183$). Univariable relationships of depression status with various factors are shown in Table 1. Those with proliferative diabetic retinopathy had more depressive symptoms than those with none-to-moderate diabetic retinopathy. Individuals with visual impairment had a higher chance of being depressed compared to those with normal visual acuity. The proportion of people with depression was also higher among females, smokers, those who were unmarried, not working, with lower family income, and those with other long-term complications. Levels of glycosylated hemoglobin and diabetes duration were not different between those with and those without depressive symptoms. The proportion of individuals with depressive symptoms did not differ in regard to use of an insulin pump and number of hypoglycemic reactions.

The associations of more severe retinopathy and a decrease in 3-line visual acuity with depression were not statistically significant after controlling for confounders (Table 2). Over the 10-year period preceding the 25-year follow-up examination, 4.2% of subjects had a doubling of the visual angle, 4.2% became visually impaired, 10.6% developed proliferative diabetic retinopathy and 16.6% had panretinal or focal/grid photocoagulation. In those who developed at least one of these changes, the likelihood of being depressed at the 25-year examination was 40% higher than in those who did not develop any (OR 1.40, 95% CI 0.77–2.54).

Associations with depression were observed with employment status and the presence of neuropathy (Table 2). Participants who were not working had 3–4 times the odds of having depression compared to those who were employed full- or part-time as shown in all models. We further explored the role of unemployment in this population. Among those who stopped working ($n = 101$), 32.6% reported that they stopped working because of complications of diabetes (data not shown). Individuals who stopped working due to diabetes had 2–3 times higher odds of having depression than those who did not report diabetes as the main cause for stopping working (OR 3.03, 95% CI 1.33–6.92, OR 2.24, 95% CI 1.01–4.96, OR 2.47, 95% CI 1.15–5.31, for models including nephropathy, neuropathy, and retinopathy, respectively, and controlling for other confounders). Current smokers had approximately 3 times higher odds than never smokers of having depression. The presence of comorbidities increased the odds of depression compared to those without these conditions. The strongest association was seen with the presence of neuropathy.

There were no significant interactions between visual impairment or proliferative diabetic retinopathy and glycosylated hemoglobin, visual impairment or proliferative diabetic retinopathy and working status, or visual impairment or proliferative diabetic retinopathy and smoking (data not shown).

Using a higher cutoff level of CES-D scores, the proportion of individuals with scores 21 or above was 31.8% (95% CI 27.6–35.9%; $n = 154$). We observed that those who were not working had approximately 1.5 times higher odds of having depression. Among longterm complications, neuropathy still had the strongest association with depression (OR 2.83, 95% CI 1.61–4.97). Diabetic retinopathy and visual acuity were not predictors of depression when using a cutoff value of 21.

In addition, antidepressants can be used to treat other conditions such as neuropathy. Therefore, we also analyzed the data defining depression based only on the CES-D scores excluding those using antidepressants. The associations between characteristics and depression using only the CES-D scores were consistent with the findings for the outcome chosen in the current analysis (data not shown).

DISCUSSION

The WESDR provides the opportunity to investigate the association between visual impairment and retinopathy severity and the presence of depression in a cohort with long duration of type 1 diabetes. Although we observed a higher proportion of individuals with depression among those with visual impairment and proliferative diabetic retinopathy, these associations were not statistically significant.

Jacobson showed that patients with type 1 diabetes and proliferative diabetic retinopathy were more likely to be depressed and to report more negative life events than those with none or mild diabetic retinopathy.¹⁸ Their finding was significant among those who had developed proliferative diabetic retinopathy in less than 2 years. It is possible that these patients are more likely to have had fluctuations in their visual acuity compared to those with longstanding diabetic retinopathy and, therefore, were more susceptible to depression.

In a group of individuals with diabetes and low vision, Bernbaum¹⁹ showed that those with fluctuating visual acuity associated with laser photocoagulation sessions or surgery were more likely to present with depressive symptoms than individuals with stable vision. We have observed that only 4.15% of our cohort seen over the 10-year period developed any visual impairment, suggesting that retinopathy and vision in the cohort was relatively stable. In addition, the mean visual acuity ($20/20^{+1}$) in our population could be considered excellent at this last follow-up visit considering a mean duration of diabetes of approximately 35 years. This might explain, in part, the non-significant association between visual acuity and symptoms of depression in this population.

The CES-D questionnaire was developed for large surveys as a screening test to identify individuals with depressive symptoms. It has been shown that those scoring 16 points or more are more likely to have depression. The application of the CES-D questionnaire alone

should not be used as a diagnostic tool for depression.⁸ Those with higher scores would probably need a more comprehensive psychiatric evaluation for a final diagnosis.²⁰

The proportion of individuals with depression was 37.8%. One meta-analysis combining 13 studies of adults with type 1 diabetes found an overall prevalence of depression of 21.3%.² Prevalence of depression among people with type 1 diabetes has varied from approximately 10–30% in previous studies.^{21,22} Possible explanations for this wide range include differences in methods of assessment and definition of depression, diabetes duration, and whether the study was clinic- or community-based.² Studies that applied the CES-D questionnaire only in the assessment of depression showed a prevalence variation from 21–30%.^{23,24} However, all had individuals with type 1 and 2 together in the study sample.^{23,24}

Depression has been associated with severity of other diabetes complications.^{4,25,27} The presence of neuropathy showed a statistically significant association with depression in our study. In a clinic-based group with type 1 diabetes, Stone²⁸ showed that neuropathy was the complication with strongest correlation with scales measuring depression. In a Japanese population with diabetes, those with neuropathy had 3 times the chance of having depression than those without.²⁹ This may be related to the painful nature of this condition.²⁸

WESDR also offered an opportunity to investigate the relation of behavioral factors such as smoking, alcohol consumption, and physical activity to depression. Although neither physical activity nor alcohol consumption was related to depression, smoking was positively associated with depression in our multivariable models. In a study of a nationally representative sample of non-institutionalized adults in the United States, Egede and Zheng found that among individuals with diabetes, smokers had approximately 2 times higher odds of developing depression than non-smokers after controlling for confounders.³⁰ Collins also showed that smoking was independently associated with higher anxiety and depression scores in a cross-sectional study of 2049 individuals with type 1 or 2 diabetes in Ireland.²⁵ Besides the increased risk of developing macro- and some microvascular complications,³¹ smokers with type 1 diabetes are more likely to have episodes of severe-hypoglycemia³² and tend to engage in less health-related behaviors than former or never smokers,^{33,34} increasing the chances of negative health effects of diabetes on their lives. In addition, pulmonary symptoms and signs may be related to depression.³⁵

Depression has also been associated with low income,³⁰ less education,³⁰ unemployment,^{22,27} and not being married³⁰ in people with diabetes. In our analysis, we observed that those who stopped working because of complications of diabetes had 2 times the odds of having depression compared to those who stopped due to other reasons. Friis and Nanjundappa²² showed that those who had type 2 diabetes had higher rates of unemployment than those without diabetes and that unemployment had the strongest association with depression in this population. The authors emphasized the importance of counseling programs for diabetic persons to include coping strategies to deal with the stresses of unemployment.²²

While there are many strengths of our study such as the use of standardized protocols, long follow-up, and representativeness to similar groups with long-term type 1 diabetes, there are

also limitations and results should be interpreted with caution. Most of the participants were Caucasian and results might not be generalizable to other populations (eg, African-Americans or Latinos). The direction of the relationship between depression and diabetes has been the subject of intense debate.³ In our case, however, we believe that it would be more likely that depression occurred after the development of diabetes because of the relatively young age at onset of diabetes. Nevertheless, the cross-sectional design of the analysis limits our ability to determine antecedent-consequent associations especially with complications. Although the CES-D scale has been used in many studies to assess depression,^{8,9} it tends to overestimate the prevalence of depression.³⁶ Low power for some risk factors (eg, severe visual impairment) may have limited our ability to find some associations. Attrition bias is an important issue in prospective cohort studies, especially due to long follow-up periods. Because the individuals who did not participate in the current analysis seemed to have poorer health conditions and if these conditions were associated with depression, we could have underestimated the strength of the associations due to selection bias. However, WESDR provides a unique opportunity to evaluate associations between depressive symptoms and many clinical and behavioral factors in a group of participants with such a long follow-up period.

In conclusion, our study did not show an association between depression and severity of diabetic retinopathy or visual impairment in a cohort of persons with long-term type 1 diabetes. Further follow-up is needed to understand the antecedent-consequent associations of severe ocular complications with depression in persons with long duration of diabetes.

Acknowledgments

Financial Support: Supported by the National Institutes of Health (Bethesda, MD) Grant No. EY016379, (R Klein, BEK Klein) and, in part, by Research to Prevent Blindness (R. Klein and BEK Klein, Senior Scientific Investigator Awards), New York, NY. The National Eye Institute provided funding for the entire study including collection and analyses of data; RPB provided further additional support for data analyses. This research was also supported by the Mentor-based Postdoctoral Fellowship Award from the American Diabetes Association, Alexandria, VA (to RK).

References

1. DIAMOND Project Group. Incidence and trends of childhood type 1 diabetes worldwide 1990–1999. *Diabet Med*. 2006; 23:857–866. [PubMed: 16911623]
2. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care*. 2001; 24:1069–1078. [PubMed: 11375373]
3. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a meta-analytic review of the literature. *Diabetes Care*. 2000; 23:934–942. [PubMed: 10895843]
4. De Groot M, Anderson R, Freedland KE, et al. Association of depression and diabetes complications: a meta-analysis. *Psychosom Med*. 2001; 63:619–630. [PubMed: 11485116]
5. Klein R, Klein BE, Moss SE, et al. The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol*. 1984; 102:520–526. [PubMed: 6367724]
6. Klein R, Klein BE, Moss SE, et al. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol*. 1984; 102:527–232. [PubMed: 6367725]
7. Klein R, Klein BE, Moss SE, et al. Prevalence of diabetes mellitus in southern Wisconsin. *Am J Epidemiol*. 1984; 119:54–61. [PubMed: 6691336]

8. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *App Psychol Meas.* 1977; 1:385–401.
9. Roberts RE, Vernon SW. The Center for Epidemiologic Studies Depression Scale: its use in a community sample. *Am J Psychiatry.* 1983; 140:41–46. [PubMed: 6847983]
10. Beekman AT, Deeg DJ, Van Limbeek J, et al. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in The Netherlands. *Psychol Med.* 1997; 27:231–235. [PubMed: 9122304]
11. Thomas JL, Jones GN, Scarinci IC, et al. The utility of the CES-D as a depression screening measure among low-income women attending primary care clinics. The Center for Epidemiologic Studies-Depression. *Int J Psychiatry Med.* 2001; 31:25–40. [PubMed: 11529389]
12. Parikh RM, Eden DT, Price TR, et al. The sensitivity and specificity of the Center for Epidemiologic Studies Depression Scale in screening for post-stroke depression. *Int J Psychiatry Med.* 1988; 18:169–181. [PubMed: 3170080]
13. Early Treatment Diabetic Retinopathy Study Research Group. Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics. ETDRS report number 7. *Ophthalmology.* 1991; 98:741–756. [PubMed: 2062510]
14. Holladay JT. Proper method for calculating average visual acuity. *J Refract Surg.* 1997; 13:388–391. [PubMed: 9268940]
15. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs – an extension of the modified Airlie House classification. ETDRS report number 10. *Ophthalmology.* 1991; 98:786–806. [PubMed: 2062513]
16. Cheng ST, Chan AC. The Center for Epidemiologic Studies Depression Scale in older Chinese: thresholds for long and short forms. *Int J Geriatr Psychiatry.* 2005; 20:465–470. [PubMed: 15852439]
17. Zich JM, Attkisson CC, Greenfield TK. Screening for depression in primary care clinics: the CES-D and the BDI. *Int J Psychiatry Med.* 1990; 20:259–277. [PubMed: 2265888]
18. Jacobson AM, Rand LI, Hauser ST. Psychologic stress and glycemic control: a comparison of patients with and without proliferative diabetic retinopathy. *Psychosom Med.* 1985; 47:372–381. [PubMed: 4023165]
19. Bernbaum M, Albert SG, Duckro PN. Psychosocial profiles in patients with visual impairment due to diabetic retinopathy. *Diabetes Care.* 1988; 11:551–557. [PubMed: 3203572]
20. de Groot M, Jacobson AM, Samson JA, et al. Glycemic control and major depression in patients with type 1 and type 2 diabetes mellitus. *J Psychosom Res.* 1999; 46:425–435. [PubMed: 10404477]
21. Popkin MK, Callies AL, Lentz RD, et al. Prevalence of major depression, simple phobia, and other psychiatric disorders in patients with long-standing type I diabetes mellitus. *Arch Gen Psychiatry.* 1988; 45:64–68. [PubMed: 3257379]
22. Friis R, Nanjundappa G. Diabetes, depression and employment status. *Soc Sci Med.* 1986; 23:471–475. [PubMed: 3764497]
23. Penninx BW, van Tilburg T, Boeke AJ, et al. Effects of social support and personal coping resources on depressive symptoms: different for various chronic diseases? *Health Psychol.* 1998; 17:551–558. [PubMed: 9848806]
24. Rajala U, Keinanen-Kiukaanniemi S, Kivela SL. Non-insulin-dependent diabetes mellitus and depression in a middle-aged Finnish population. *Soc Psychiatry Psychiatr Epidemiol.* 1997; 32:363–267. [PubMed: 9299931]
25. Collins MM, Corcoran P, Perry IJ. Anxiety and depression symptoms in patients with diabetes. *Diabet Med.* 2009; 26:153–161. [PubMed: 19236618]
26. Lustman PJ, Griffith LS, Freedland KE, et al. The course of major depression in diabetes. *Gen Hosp Psychiatry.* 1997; 19:138–143. [PubMed: 9097068]
27. Winocour PH, Main CJ, Medlicott G, et al. A psychometric evaluation of adult patients with type 1 (insulin-dependent) diabetes mellitus: prevalence of psychological dysfunction and relationship to demographic variables, metabolic control and complications. *Diabetes Res.* 1990; 14:171–176. [PubMed: 2132190]

28. Stone JB, Bluhm HP, White MI. Correlates of depression among long-term insulin-dependent diabetics. *Rehabil Psychol*. 1984; 29:85–93.
29. Yoshida S, Hirai M, Suzuki S, et al. Neuropathy is associated with depression independently of health-related quality of life in Japanese patients with diabetes. *Psychiatry Clin Neurosci*. 2009; 63:65–72. [PubMed: 19067994]
30. Egede LE, Zheng D. Independent factors associated with major depressive disorder in a national sample of individuals with diabetes. *Diabetes Care*. 2003; 26:104–111. [PubMed: 12502665]
31. Haire-Joshu D, Glasgow RE, Tibbs TL. Smoking and diabetes. *Diabetes Care*. 1999; 22:1887–1898. [PubMed: 10546025]
32. Hirai FE, Moss SE, Klein BE, et al. Severe hypoglycemia and smoking in a long-term type 1 diabetic population: Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Diabetes Care*. 2007; 30:1437–1441. [PubMed: 17372156]
33. Boyle RG, O'Connor P, Pronk N, et al. Health behaviors of smokers, ex-smokers, and never smokers in an HMO. *Prev Med*. 2000; 31:177–182. [PubMed: 10938219]
34. Solberg LI, Desai JR, O'Connor PJ, et al. Diabetic patients who smoke: are they different? *Ann Fam Med*. 2004; 2:26–32. [PubMed: 15053280]
35. Maurer J, Rebbapragada V, Borson S, et al. Anxiety and depression in COPD: current understanding, unanswered questions, and research needs. *Chest*. 2008; 134:43S–56S.
36. Fisher L, Skaff MM, Mullan JT, et al. Clinical depression versus distress among patients with type 2 diabetes: not just a question of semantics. *Diabetes Care*. 2007; 30:542–548. [PubMed: 17327318]

TABLE 1

Characteristics of the study population according to depression status, 2005–07.

	Depression		<i>p</i> value
	No (<i>n</i> = 301)	Yes (<i>n</i> = 183)	
Age, mean (SD), years	48.5 (9.4)	50.2 (8.9)	0.06
Sex, %			0.03
Female	47.6	57.8	
Male	52.4	42.2	
Diabetes duration, mean (SD), years	34.8 (7.2)	35.3 (6.8)	0.45
Glycosylated hemoglobin, mean (SD), %	7.5 (1.3)	7.6 (1.3)	0.42
Insulin use, mean (SD), times per day	3.3 (1.0)	3.3 (1.1)	0.76
Use of insulin pump, %			0.60
No	63.2	60.8	
Yes	36.8	39.2	
Hypoglycemic reaction, %			0.67
1/day	3.6	4.9	
1–5/week	39.8	42.6	
1–3/month	36.1	36.4	
Less	20.5	16.1	
Married, %			0.02
No	31.6	42.1	
Yes	68.4	57.9	
Live alone, %			0.12
No	85.7	80.3	
Yes	14.3	19.7	
Education, mean (SD), years in school	14.6 (2.6)	13.9 (2.5)	<0.01
Employment, %			<0.01
Full/Part-time job	78.7	56.3	
Retired	9.3	11.5	
Not working	12.0	32.2	
Family income, %			<0.01
Less than \$30,000	38.3	55.7	
\$30,000–\$45,000	24.1	22.2	
More than \$45,000	37.6	22.1	
Health insurance, %			0.35
No	3.3	4.4	
Yes	96.7	95.6	
Physical activity, %			0.48
Sedentary	31.6	36.8	
Moderate	59.8	56.0	
Strenuous	8.6	7.2	
Alcohol consumption, %			0.59

	Depression		<i>p</i> value
	No (<i>n</i> = 301)	Yes (<i>n</i> = 183)	
Never or previous	20.6	18.6	
Current	79.4	81.4	
Smoking, mean (SD), pack years	5.5 (14.9)	10.0 (17.9)	<0.01
Smoker, %			<0.01
Never	66.1	47.4	
Former	27.0	30.8	
Current	6.8	21.8	
Cardiovascular disease, %			<0.01
No	82.4	63.0	
Yes	17.6	37.0	
Nephropathy, %			0.01
No	55.9	44.2	
Yes	44.1	55.8	
Neuropathy, %			<0.01
No	54.5	21.3	
Yes	45.5	78.7	
Limb amputation, %			0.33
No	95.0	92.9	
Yes	5.0	7.1	
Diabetic retinopathy, %			0.17
None-mild NPDR	40.5	33.3	
Moderate-severe NPDR	16.6	12.0	
Proliferative diabetic retinopathy	42.9	54.7	
Visual acuity, mean (SD), LogMAR	-0.01 (0.15)	0.06 (0.25)	<0.01
Visual acuity, %			0.02
Normal	96.4	91.2	
Visual impairment	3.6	8.8	

NPDR, non-proliferative diabetic retinopathy; SD, standard deviation; LogMAR, logarithm of the minimum angle of resolution.

TABLE 2

Multivariable analyses of factors related to depression in individuals with type 1 diabetes, 2005–07 (odds ratio (95% confidence interval)).

	Diabetic retinopathy	Neuropathy	Nephropathy
Sex, male vs. female	0.71 (0.44–1.16)	0.63 (0.39–1.04)	0.72 (0.44–1.18)
Glycosylated hemoglobin, per 1 unit %	0.99 (0.83–1.17)	0.96 (0.80–1.15)	1.02 (0.85–1.21)
Married, vs. not	0.93 (0.56–1.54)	0.92 (0.55–1.55)	0.99 (0.59–1.66)
Employment, vs. full- or part-time job			
Retired	0.94 (0.43–2.09)	0.86 (0.38–1.93)	1.05 (0.47–2.35)
Not working	2.62 (1.40–4.89) ^a	2.26 (1.19–4.28) ^a	2.55 (1.34–4.83) ^b
Smoker vs. never			
Former	1.27 (0.74–2.18)	1.23 (0.72–2.13)	1.24 (0.72–2.12)
Current	3.76 (1.84–7.67) ^a	3.12 (1.51–6.45) ^a	4.13 (1.99–8.52) ^a
Cardiovascular disease, vs. no	1.85 (1.08–3.20) ^b	1.64 (0.42–2.85)	1.79 (1.04–3.10) ^b
Visual acuity, per 3-line decrease	1.25 (0.72–2.17)	1.14 (0.68–1.89)	1.22 (0.73–2.05)
Diabetic retinopathy, vs. none-mild NPDR			
Moderate-severe NPDR	0.91 (0.42–1.95)		
Proliferative diabetic retinopathy	1.22 (0.68–2.17)		
Neuropathy, vs. no		3.12 (1.82–5.35) ^a	
Nephropathy, vs. no			1.26 (0.77–2.08)

All variables listed were included in the multivariable models.

NPDR, non-proliferative diabetic retinopathy.

^a $P < 0.01$;

^b $P < 0.05$.