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ARTICLE

The course of depressive symptoms in primary care patients with type 2 diabetes: results from the Diabetes, Depression, Type D Personality Zuidoost-Brabant (DiaDDZoB) Study

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Abstract
Aims/hypothesis The aim of the study was to examine the course (incidence, recurrence/persistence) of depressive symptoms in primary care patients with type 2 diabetes and to identify significant predictors of these different course patterns.
Methods A cohort of 2,460 primary care patients with type 2 diabetes was assessed for demographic, clinical and psychological factors in 2005 and followed-up in 2007 and 2008. Depression was defined as a score of ≥12 on the Edinburgh Depression Scale. Multivariate logistic regression analyses were used to determine whether several depression-course patterns could be predicted by means of demographics, medical co-morbidities and psychological factors.
Results A total of 630 patients (26%) met the criterion for depression at one or more assessments. In the subgroup with no baseline depression, incident depression at follow-up was present in 14% (n=310), while recurrence/persistence in those with baseline depression was found in 66% (n=212). The presence of any depression was associated with being female, low education, non-cardiovascular chronic diseases, stressful life events and a self-reported history of depression. Incident depression was predicted by female sex, low education and depression history, while patients with a history of depression had a 2.5-fold increased odds of recurrent/persistent depression.
Conclusions/interpretation Depression is common in primary care patients with type 2 diabetes, with one in seven patients reporting incident depression during a 2.5 year period. Once present, depression often becomes a chronic/recurrent condition in this group. In order to identify patients who are vulnerable to depression, clinicians can use questionnaire data and/or information about the history of depression.

Keywords Course · Depression · Incidence · Persistence · Prevalence · Recurrence · Type 2 diabetes

Abbreviations

COPD	Chronic obstructive pulmonary disease
DiaDDZoB	Diabetes, Depression, Type D Personality Zuidoost-Brabant
EDS	Edinburgh Depression Scale
M_0	Baseline assessment in 2005
M_1	Follow-up assessment in 2007
M_2	Follow-up assessment in 2008

Introduction

Compared with controls without diabetes, the risk of depression is nearly doubled in individuals with type 2 diabetes, affecting approximately one in every five patients [1]. A recent meta-analysis has shown that individuals with previously diagnosed diabetes have an increased risk of depression relative to those with impaired glucose metabolism or undiagnosed diabetes [2]. Co-morbid depression not only has a profound negative impact on patients' quality of life [3], but is also related to worse glycaemic control [4], the

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development of macro- and microvascular complications [5, 6] and a higher mortality risk [7]. Despite the growing body of literature demonstrating the harmful effects of depression in this patient group, the course of depression in type 2 diabetes has received relatively little research attention.

Previous cross-sectional research has mainly focused on prevalence estimates of depression, finding particularly high rates in women, patients treated in specialist settings and those with co-morbid medical conditions [1, 8–11]. Furthermore, the longitudinal studies that have been conducted have mainly focused on incident depression in type 2 diabetes. A recent meta-analysis of 11 studies concluded that people with type 2 diabetes have a 24% increased odds of incident depression compared with people without diabetes [12]. However, as only one of the studies excluded people with a history of depression in the years before study onset, the results of this study are likely to overestimate the risk for incident depression in the strictest sense (i.e. first occurrence) [12]. Although a few studies have examined the course of depression once symptoms were present (recurrence/persistence, remission), most had considerable limitations: for example, a small sample size (n<175) [13–15], recruitment from specialist settings [15] or only two assessments of depression [15, 16]. Two studies did not provide strictly observational findings as they assessed depression in the framework of an intervention study [13, 14]. One observational study of 506 patients with type 2 diabetes assessed depression three times over a period of 18 months (with 9 month intervals) [17]. However, the authors combined persistence estimates into the categories 'condition at only a single wave', 'condition at any two waves' and 'condition at all three waves', thereby impeding an evaluation of specific course patterns.

To our knowledge, a large study simultaneously addressing different aspects of the course of depression in primary care patients with type 2 diabetes is currently lacking. Therefore, the main aim of the present study was to examine several course trajectories of depressive symptoms (incidence, recurrence/persistence) using data from three separate assessments during a 2.5 year period and to gain insight in the demographic, medical and psychological risk factors predicting these different course patterns.

Methods

Methods and response rates of the Diabetes, Depression, Type D *['distressed']* Personality Zuidoost-Brabant (DiaDDZoB) Study have been described in detail elsewhere [18]. In short, 2,460 patients with type 2 diabetes (82% of those considered for study inclusion) treated within 77 primary care practices in South-East Brabant, the Netherlands, were recruited at the baseline assessment in the second half of 2005 (M_0). Of these patients, nearly all (2,448) attended a baseline nurse-led interview, while 75% (1,850) returned the self-report questionnaire that had to be completed at home. This cohort was re-contacted for follow-up assessments in 2007 (M_1) and 2008 (M_2), and included 2,225 and 2,032 participants, respectively. The study protocol of the DiaDDZoB Study was approved by the medical research ethics committee of a local hospital, the Máxima Medical Centre in Veldhoven (NL27239.015.09). Written informed consent was obtained from all participants.

Assessment of depression Symptoms of depression during the last 7 days were assessed using a validated Dutch version of the Edinburgh Depression Scale (EDS) [19]. The EDS was originally designed to assess postpartum depression [20], but has now been validated in non-postnatal women [21], women around menopausal age [22], men [23], community samples [24] and primary care patients with type 2 diabetes [25]. The EDS is a ten-item self-report questionnaire, in which each item is scored on a four-point scale. Total EDS scores are determined by summing the scores of all ten individual items (total score range 0–30), with higher scores indicating higher levels of depressive symptoms. A total score of 12 or more is commonly used to identify patients with depression [24]. Using this cut-off, we calculated dichotomised depression scores (no depression/depression) for all three measurements. Patients were considered to suffer from 'any depression' if they obtained an EDS score ≥12 during at least one of the three measurement occasions. To specify the course trajectory of these depressive symptoms, we split the total sample into two groups based on the baseline (M_0) EDS score. 'Incident depression' was determined in the subgroup with an EDS score <12 at M_0 (no baseline depression). Patients in this group who obtained an EDS score ≥12 at M_1 and/or M_2 were considered incident cases. Rates of 'recurrence/persistence' were examined in the remaining group of participants who had an EDS score ≥12 at M_0 (baseline depression). Depression was labelled 'recurrent/persistent' if patients had at least one other high EDS score at M_1 or M_2.

Baseline demographic, medical and psychological predictors Baseline demographic data included sex, age, marital status (having a partner vs being single) and educational level (middle/high vs low), and were acquired during a patient interview led by the primary care practice nurse and also by means of a self-report questionnaire. The primary care practice nurse took a medical history, after which all self-reported medical diagnoses were verified through inspection of the medical record. Indicators of microvascular disease were derived from standard-care laboratory tests and physical examinations carried out by the Diagnostic Centre Eindhoven, a primary care diagnostic institute. The results from patients' yearly digital fundus photography

were available to ascertain retinopathy (yes/no), while albumin level in a random urine sample was used as a proxy of nephropathy [26]. Macro- and microalbuminuria were defined as urine albumin concentrations >200 and 20–200 mg/l, respectively. All medical co-morbidities were combined into three composite disease measures, i.e. cardiovascular diseases (myocardial infarction, bypass/angioplasty, stroke and/or arterial disease), microvascular complications (retinopathy and/or micro-/macroalbuminuria) and other chronic conditions (kidney disease, asthma/chronic obstructive pulmonary disease [COPD], cancer, arthrosis and/or rheumatoid arthritis). In addition, patients were asked if they had ever suffered from depression. Non-diabetes-related stressful life events in the previous 12 months (e.g. loss of a loved one, burglary, relationship problems) were assessed by means of a single questionnaire item.

Other patient characteristics The interview included one question regarding ethnicity (white vs non-white). Baseline treatment for diabetes and diabetes duration were documented by the primary care practice nurse. Standard-care determinations of HbA_{1c} concentrations and BMI were provided by the Diagnostic Centre Eindhoven.

Statistical analyses Baseline sample characteristics and descriptive statistics for the EDS data at all three measurement occasions were calculated. To compare differences between men and women, χ^2 tests were used for categorical data and independent samples *t* tests for continuous data. Of all demographic, clinical and psychological data needed for the analyses, 27% was missing. As complete case analysis would restrict the sample to 511 patients (21%), multivariate imputation by chained equations was applied to impute missing values (Electronic supplementary material [ESM] Table 1), using the package MICE V2.0 [27] and the software program R [28]. Adequate results can generally be obtained by creating five to ten imputed datasets, retaining final imputations per dataset after ten iterations [27, 29]. For the present study, 20 imputed datasets were generated, allowing ten iterations per set.

Following imputation, depression prevalence rates and estimates for any, incident and recurrent/persistent depression were calculated, pooling the results over the 20 individual datasets. Multivariate logistic regression analyses were used to determine whether these different depression course trajectories could be predicted by means of: (1) demographics (female sex, age, low education, being single); (2) medical co-morbidities (prior cardiovascular disease, the presence of microvascular complications, other co-morbid conditions); (3) stressful life events; and (4) self-reported history of depression. As missing EDS baseline data were also imputed, the number of individuals classified in either the 'incident depression' or 'recurrent/persistent depression' subgroup varied slightly per individual imputed dataset. Therefore, in addition to reporting the pooled results of the regression analyses for incident and recurrent/persistent depression, the range of *n* across all 20 individual imputed datasets was provided. With the exception of the multiple imputation procedure, all analyses were performed using PASW Statistics version 17.0 (IBM SPSS Statistics, Somers, NY, USA). A p value <0.05 was considered to be statistically significant.

Results

Baseline sample characteristics Table 1 presents the characteristics of the total DiaDDZoB sample before multiple imputation (n=2,460, 49% men, mean age 67 years) and the number of missing values per variable. Overall, participants were in relatively good glycaemic control (mean HbA_{1c} 6.7% [50 mmol/mol]), and the majority were being treated with a combination of diet and oral glucose-lowering agents. Co-morbid diseases were common, with vascular disease and other major (chronic) medical conditions being present in one-third and one-half of all patients, respectively. Advanced microvascular complications, including retinopathy and macroalbuminuria, were relatively rare. However, almost one in four patients had microalbuminuria. When examining results separately for men and women, women were shown to be significantly older, more commonly had a low educational level and were more likely to be single. Myocardial infarction, bypass/angioplasty procedures and albuminuria were more prevalent in men, while the medical history of women included more diagnoses of cancer, arthrosis and rheumatoid arthritis. Furthermore, women were more likely to report a history of depression and at least one stressful life event in the past year.

Prevalence of depression Figure 1 shows the number of patients with depression (EDS score ≥12) at the baseline assessment in 2005 (M_0) and the two follow-up occasions (M_1 and M_2), after multiple imputation. Depression slowly increased from 13% (M_0) to 14% (M_1) to 16% (M_2). This pattern was evident for both men and women after splitting by sex. Compared with men, the prevalence of depression was twice as high for women at each assessment.

Any depression, incidence and recurrence/persistence After multiple imputation, 26% of the total sample (n=630) reported an EDS score ≥12 at M_0, M_1 and/or M_2 ('any depression'). The presence of any depression was significantly more likely in women compared with men (32%, n=412 vs 18%, n=218; p<0.001). In the subgroup of patients with an M_0 EDS score <12 (no depression; n=2,140), incident depression at M_1 or M_2 was present in 310 individuals (14%), with a higher rate for women (18%, n=193

Table 1 Baseline characteristics before multiple imputation

Characteristic	All (n=2,460)	n missing	Men (n=1,192)	Women (n=1,268)	p value
Demographics					
Age (years)	67±11	5	66±11	68±11	<0.001
Non-white	3 (78/2,424)	36	3 (36/1,174)	3 (42/1,250)	0.68
Low education level	64 (1,140/1,770)	690	53 (459/866)	75 (681/904)	<0.001
Being single	25 (455/1,831)	629	16 (144/893)	33 (311/938)	<0.001
Medical history					
Cardiovascular disease	36 (842/2,368)	92	40 (458/1,157)	32 (384/1,211)	<0.001
Myocardial infarction	12 (280/2,353)	107	16 (188/1,149)	8 (92/1,204)	<0.001
Bypass/angioplasty	13 (312/2,358)	102	18 (207/1,153)	9 (105/1,205)	<0.001
Stroke	7 (164/2,360)	100	8 (88/1,154)	6 (76/1,206)	0.21
Arterial disease	24 (559/2,349)	111	25 (287/1,142)	23 (272/1,207)	0.14
Microvascular disease	35 (612/1,769)	691	38 (334/886)	32 (278/883)	0.006
Retinopathy	5 (86/1,767)	693	4 (37/878)	6 (49/889)	0.21
Microalbuminuria[a]	23 (477/2,077)	383	26 (264/1,003)	20 (213/1,074)	
Macroalbuminuria[b]	4 (72/2,077)		5 (46/1,003)	2 (26/1,074)	<0.001
Other chronic conditions	50 (1,184/2,377)	83	44 (510/1,157)	55 (674/1,220)	<0.001
Kidney disease	4 (95/2,339)	121	4 (47/1,144)	4 (48/1,195)	0.91
Asthma/COPD	13 (315/2,360)	100	13 (153/1,147)	13 (162/1,213)	0.99
Cancer	9 (222/2,351)	109	8 (90/1,144)	11 (132/1,207)	0.01
Arthrosis	34 (793/2,365)	95	27 (309/1,152)	40 (484/1,213)	<0.001
Rheumatoid arthritis	7 (161/2,352)	108	4 (44/1,146)	10 (117/1,206)	<0.001
Clinical values					
Hyperglycaemia treatment		38			
No treatment	1 (19/2,422)		1 (9/1,179)	1 (10/1,243)	
Diet only	18 (432/2,422)		19 (219/1,179)	17 (213/1,243)	
Diet, oral agents	75 (1,821/2,422)		76 (892/1,179)	75 (929/1,243)	
Diet, oral agents, insulin	5 (114/2,422)		4 (46/1,179)	6 (68/1,243)	
Diet, insulin	1 (33/2,422)		1 (10/1,179)	2 (23/1,243)	
Other	0 (3/2,422)		0 (3/1,179)	0 (0/1,243)	0.04
Diabetes duration ≥3 years	61 (1,467/2,424)	36	59 (697/1,175)	62 (770/1,249)	0.24
HbA_{1c},% (mmol/mol)	6.7±0.9 (50±10)	61	6.7±0.8 (50±9)	6.7±0.9 (50±10)	0.28
BMI (kg/m^2)	29±5	234	28±4	30±5	<0.001
Psychosocial factors					
History of depression	11 (248/2,345)	115	9 (97/1,146)	13 (151/1,199)	0.001
Stressful life event(s)	35 (635/1,800)	660	32 (280/881)	39 (355/919)	0.002
M_0 depressive symptoms					
EDS total score	6±5	715	5±4	7±5	<0.001
EDS score ≥12	12 (216/1,745)		8 (70/861)	17 (146/884)	<0.001
M_1 depressive symptoms					
EDS total score	6±5	918	5±4	7±5	<0.001
EDS score ≥12	14 (210/1,542)		9 (66/741)	18 (144/801)	<0.001
M_2 depressive symptoms					
EDS total score	6±5	1,226	5±5	7±5	<0.001
EDS score ≥12	15 (188/1,234)		10 (60/580)	20 (128/654)	<0.001

Values are means±SD or % (n/n)

[a] Albumin concentration of 20–200 mg/l

[b] Albumin concentration of >200 mg/l

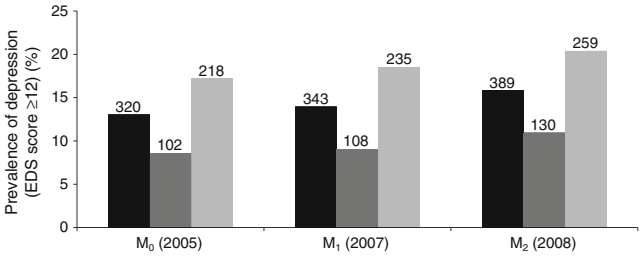

Fig. 1 Prevalence of depression (EDS score ≥12) at baseline (M_0) and the two follow-up assessments (M_1, M_2) for the total sample (n=2,460) and examined separately for men (n=1,192) and women (n=1,268). Bars represent total group (black), men (dark grey) and women (light grey); the number shown above each bar represents the number with depression in that group. $p<0.001$ for men vs women for all three assessments

vs 11%, n=116; $p<0.001$). An additional χ^2 analysis showed that participants who were not depressed at baseline but did have a self-reported history of depression were significantly more likely to experience incident depression during follow-up than those without such a history (33%, n=52 vs 13%, n=257; $p<0.001$). Of the 320 patients with an EDS score of ≥12 at M_0, 66% also met the criterion for depression at M_1 and/or M_2 and were therefore considered to be recurrently/persistently depressed. The rate of recurrence/persistence was similar for female and male patients (69%, n=151 vs 60%, n=61; p=0.09), but was significantly higher in those with a self-reported history of depression (79%, n=79 vs 60%, n=133; p=0.001). When considering specific patterns of remission and relapse, 34% (n=109) of all initially depressed patients at M_0 recovered and remained below the EDS score cut-off at M_1 and M_2, 15% (n=47) relapsed at M_2 and 38% (n=123) were still depressed at both follow-ups.

Baseline risk factors predicting any depression Table 2 shows the pooled effect estimates of a multivariate logistic regression analysis predicting the presence of any depression (EDS score ≥12 at M_0, M_1 and/or M_2) by several baseline characteristics. In the first step, female sex and low education were the only significant demographic predictors. In the second step, having co-morbid chronic medical conditions was positively associated with depression, while the presence of cardiovascular disease and microvascular complications also increased the odds of depression but did not reach statistical significance (p=0.27 and p=0.09, respectively). In the third step, having experienced stressful life events during the past year nearly doubled the odds for depression, while in the final step participants with a history of depression had an almost fivefold increased odds of reporting depression during at least one assessment occasion.

In order to test whether sex was an effect modifier, the same regression analysis (excluding sex in the first step) was conducted for women (n=1,268) and men (n=1,192) separately. After entry of all variables in the model, low educational level (fully adjusted OR 1.93, 95% CI 1.24, 3.01 in women vs OR 1.56, 95% CI 1.02, 2.39 in men), stressful life events (OR 1.90, 95% CI 1.40, 2.59 vs OR 1.83, 95% CI 1.25, 2.68) and a history of depression (OR 4.53, 95% CI 2.95, 6.95 vs OR 5.52, 95% CI 3.38, 9.01) were significantly associated with depression for both sexes. In addition, the non-cardiovascular chronic medical conditions played a significant role in the model for women (OR 1.51, 95% CI 1.12, 2.03), while for men no other significant predictors were found (ESM Table 2).

Additional analyses in the total sample examining depression risk for each medical co-morbidity separately revealed that after correction for demographics, arthrosis (OR 1.57, 95% CI 1.26, 1.96) and rheumatoid arthritis (OR 1.57, 95% CI 1.04, 2.39) were the only significant predictors (ESM Table 3).

Baseline risk factors predicting incident and recurrent/persistent depression A multivariate logistic regression analysis identical to the model described in Table 2 was conducted to predict incident depression (range of n over all 20 datasets, 2,131–2,156; ESM Table 4). In the last step, female sex (OR 1.63, 95% CI 1.20, 2.21), low education (OR 1.62, 95% CI 1.12, 2.36) and self-reported history of depression (OR 3.27, 95% CI 2.05, 5.22) were all associated with incident depression, while microvascular disease, other chronic conditions and stressful life events increased the odds of depression by 25–33%, but did not reach statistical significance (p=0.14, 0.18 and 0.14, respectively). Repeating the analysis (excluding entry of history of depression in the last step) in the group of patients reporting no history of depression and no M_0 depression (range of n, 1,967–1,992) yielded similar results (data not shown). After splitting by sex, self-reported history of depression was associated with a three- to four-fold increased odds of incident depression in both men and women (Table 3). Low education increased the odds, but was not significant (p=0.09 and 0.06 in men and women, respectively).

Self-reported history of depression was the only significant predictor of recurrent/persistent depression (range of n, 304–329; OR 2.54, 95% CI 1.23, 5.23). Similar results were found when examining results separately for men and women (women: OR 2.69, 95% CI 1.06, 6.82; men: OR 2.76, 95% CI 0.64, 11.88), but failed to reach statistical significance in men (p=0.18; ESM Tables 5 and 6).

Discussion

Depression (defined as a high level of depressive symptoms) appeared to be a common co-morbid health problem in primary care patients with type 2 diabetes, with one in four patients suffering from depression at least once during a 2.5 year period. New occurrences of depressive symptoms

Table 2 Multivariate logistic regression analysis predicting any depression (EDS score ≥12 at M_0, M_1 and/or M_2) by baseline demographic factors, medical co-morbidities, stressful life events and self-reported history of depression (n=2,460)

Variable	Model 1	Model 2	Model 3	Model 4
Demographic factors				
Female sex	1.86 (1.51, 2.29)	1.87 (1.51, 2.31)	1.82 (1.47, 2.25)	1.74 (1.39, 2.17)
Age	1.00 (0.99, 1.01)	0.99 (0.98, 1.00)	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)
Low education level	1.66 (1.25, 2.22)	1.65 (1.24, 2.19)	1.66 (1.24, 2.23)	1.75 (1.28, 2.38)
Being single	1.28 (0.98, 1.68)	1.27 (0.97, 1.68)	1.19 (0.90, 1.57)	1.18 (0.88, 1.56)
Medical co-morbidities				
Cardiovascular disease[a]		1.13 (0.91, 1.40)	1.12 (0.90, 1.39)	1.10 (0.88, 1.38)
Microvascular disease[b]		1.25 (0.97, 1.60)	1.24 (0.96, 1.60)	1.25 (0.96, 1.62)
Other chronic conditions[c]		1.50 (1.19, 1.87)	1.44 (1.15, 1.82)	1.36 (1.07, 1.73)
Stressful life events			1.90 (1.51, 2.40)	1.86 (1.46, 2.38)
History of depression				4.90 (3.53, 6.82)

Values are OR (95% CI)

Model 1: demographic factors; Model 2: model 1+medical co-morbidities; Model 3: model 2+stressful life events; Model 4: model 3+history of depression

[a] Myocardial infarction, bypass/angioplasty, stroke and/or arterial disease

[b] Retinopathy, micro-/macroalbuminuria

[c] Kidney disease, asthma/COPD, cancer, arthrosis and/or rheumatoid arthritis

were frequently observed among those with no symptoms at baseline (14%). Once present, depressive symptoms tended to be recurrent/persistent over time in two-thirds of all cases.

The cross-sectional prevalence estimates of our study (13–16%) were slightly lower than the figure reported in a previous meta-analysis (18%) [1], but did slowly increase over time. This may reflect cohort ageing and the ensuing development of additional co-morbidities and accompanying functional limitations. In line with the results of a previous study [17], expanding the time frame from cross-sectional analyses (point prevalence) to a total estimate across successive assessments ('any depression') revealed a higher prevalence rate in a 2.5 year period, suggesting that prevalence estimates taken at one point in time underestimate the true scope of the problem.

The onset of depression in diabetes has been examined several times before, but most of these studies (including ours) have defined incident depression as the presence of depression at a distinct follow-up time point in those without baseline depression, rather than also taking incident cases during the whole follow-up period into account [12]. This definition does not allow for a correction for variable follow-up length across studies by calculating annual incidence rates, as studies with longer follow-up periods are likely to miss more incident cases and as a consequence would substantially underestimate true yearly incidence rates.

Our finding that depressive symptoms have a high rate of recurrence and chronicity in diabetes patients is in line with previous research showing that approximately half of all patients experiencing depressive symptoms at baseline also reported depression 1 to 5 years later [15, 16]. Furthermore, over 40% of diabetes patients with elevated depressive symptoms appear to develop major depression within 2 years [30]. However, to our knowledge, only two previous studies have examined the course of depressive symptoms over more than two assessments. In one study, 20% of all participants obtained scores ≥16 on the Center for Epidemiological Studies—Depression questionnaire at least twice [17]. A second study among 245 diabetes patients (65% with type 2 diabetes) measured depressive symptoms at the beginning and end of a 1 week diabetes education program and at 6 month follow-up. While the authors concluded that only 13% of their total sample was persistently depressed (i.e. exceeded the criterion for depression symptoms at all three time points), recurrent depression (depressed at least once during follow-up) was found in two-thirds of the patients depressed before the start of the programme [14]. Even though this study included a psycho-educational intervention program incorporating coping skills training, the results were roughly comparable with those from our study.

With regard to prognostic factors, female sex, a low educational level, non-cardiovascular chronic medical conditions, stressful life events and a self-reported history of depression were associated with the presence of any depression. Previous cross-sectional studies have shown an association between prevalent depression and the presence of co-morbid chronic diseases in diabetes patients [8, 9] and have suggested that a large number of general life stressors, in addition to more diabetes-specific distress, can contribute to

Table 3 Multivariate logistic regression analysis predicting incident depression by baseline demographic factors, medical co-morbidities, stressful life events and self-reported history of depression, examined separately for men and women

Variable	Model 1	Model 2	Model 3	Model 4
Men (range n=1,081–1,096)				
Demographic factors				
Age	1.01 (0.99, 1.03)	1.00 (0.98, 1.02)	1.00 (0.98, 1.03)	1.00 (0.98, 1.03)
Low education level	1.56 (0.96, 2.54)	1.51 (0.92, 2.48)	1.54 (0.93, 2.54)	1.56 (0.94, 2.60)
Being single	1.11 (0.58, 2.14)	1.11 (0.57, 2.13)	1.08 (0.56, 2.07)	0.99 (0.50, 1.95)
Medical co-morbidities				
Cardiovascular disease[a]		1.42 (0.87, 2.31)	1.42 (0.87, 2.31)	1.43 (0.87, 2.34)
Microvascular disease[b]		1.30 (0.79, 2.12)	1.30 (0.80, 2.14)	1.35 (0.82, 2.20)
Chronic conditions[c]		1.28 (0.76, 2.15)	1.24 (0.74, 2.09)	1.20 (0.71, 2.04)
Stressful life events			1.40 (0.82, 2.39)	1.38 (0.81, 2.36)
History of depression				3.99 (1.98, 8.04)
Women (range n=1,042–1,064)				
Demographic factors				
Age	1.01 (0.99, 1.03)	1.01 (0.98, 1.03)	1.01 (0.99, 1.03)	1.01 (0.99, 1.03)
Low education level	1.59 (0.95, 2.68)	1.59 (0.94, 2.68)	1.59 (0.94, 2.68)	1.69 (0.99, 2.88)
Being single	1.14 (0.75, 1.74)	1.12 (0.73, 1.72)	1.10 (0.71, 1.69)	1.11 (0.72, 1.70)
Medical co-morbidities				
Cardiovascular disease[a]		0.92 (0.61, 1.39)	0.92 (0.61, 1.38)	0.91 (0.60, 1.37)
Microvascular disease[b]		1.35 (0.83, 2.19)	1.34 (0.82, 2.19)	1.34 (0.81, 2.20)
Chronic conditions[c]		1.35 (0.94, 1.93)	1.34 (0.93, 1.92)	1.27 (0.88, 1.84)
Stressful life events			1.24 (0.83, 1.86)	1.24 (0.82, 1.88)
History of depression				2.93 (1.64, 5.26)

Values are OR (95% CI)

Model 1: demographic factors; Model 2: model 1+medical co-morbidities; Model 3: model 2+stressful life events; Model 4: model 3+history of depression

[a] Myocardial infarction, bypass/angioplasty, stroke and/or arterial disease

[b] Retinopathy, micro-/macroalbuminuria

[c] Kidney disease, asthma/COPD, cancer, arthrosis and/or rheumatoid arthritis

depressive symptoms [8]. However, the logistic regression analysis predicting incident depression in the subgroup with no baseline depression limited the results to female sex, low education and history of depression, while recurrent/persistent depression in those patients with baseline depression left only depression history as a significant predictor in the model.

Two previous studies aiming to identify baseline predictors of 'persistent' depressive symptoms reported conflicting results. In one study, low level of education, the presence of multiple complications and treatment without insulin significantly predicted persistent depression [14], while the other described an important role for more psychologically orientated factors, including baseline severity of depression, emotional problems due to diabetes and the extent to which depression disrupted the patient's quality of life [15]. Even though vascular complications are often cited as an important determinant of disease burden in diabetes, macro- and microvascular conditions were not associated with depression in any of the present analyses. One possible explanation may lie in the fact that our study focused on baseline and pre-baseline factors as potential predictors of depression. However, the onset or progression of medical conditions and cardiovascular procedures during follow-up are likely candidates to trigger new cases of depression or hamper recovery from already existing emotional problems. This hypothesis is partly supported by a study in which coronary procedures during follow-up (but not incident macro- and microvascular complications) were associated with major depression at the 5 year follow-up [16]. Alternatively, rather than examining the mere presence of any macro- or microvascular conditions, it could be that having multiple (vascular) co-morbidities (and probably accompanying functional limitations) is what particularly increases the odds of depression [8–10].

Self-reported history of depression was the only factor that consistently identified those individuals who had increased odds of experiencing any kind of depression during a period of 2.5 years, even after controlling for demographics, medical co-morbidities and stressful life events. These

results are valuable for primary care, as they clearly show that a simple self-report question is highly predictive of future depression. Additional monitoring may be required in patients who report a history of depression.

Some limitations of the present study need to be mentioned. First, depression was assessed by means of a self-report questionnaire, while the gold standard for a diagnosis of depression is a standardised psychiatric diagnostic interview. Although 30–40% of patients with an increased level of depressive symptoms are clinically depressed [11, 31], self-reported depressive symptoms have been shown to predict the development of major depression [30] and adverse health outcomes [5] in diabetes patients. Second, a more accurate measurement of incident depression can be achieved in studies also covering the time period(s) between separate measurement occasions, for example by using handheld computers for the assessment of depression. In case researchers do not want or are not able to use these devices, other authors have argued that fluctuating course types are best studied in designs with at least three measurements [32]. Third, although we aimed to study the course of depression in this cohort, no information was available on either pharmacological or psychotherapeutic treatment of depression during the study. However, this potential source of bias is most likely restricted to a minority, as depression often goes unrecognised and untreated in patients with diabetes [33]. Fourth, while interpreting our results, it has to be borne in mind that 27% of all demographic, clinical and psychological data needed for the analyses were missing and imputed using multivariate imputation techniques. However, several authors have argued that multiple imputation is preferred over other missing data approaches, including complete case analysis, in the case of complex incomplete data problems [27, 29]. Finally, the vast majority of individuals in our sample (97%) were white, which may not be representative of other diabetes populations. The strengths of the study include the large sample of primary care patients with type 2 diabetes, the prospective observational design with multiple depression assessments and the policy to verify self-reported medical diagnoses by inspection of medical records.

In sum, our results show that as many as one in four primary care patients with type 2 diabetes are confronted with depression during a 2.5 year period. Once present, depression often becomes a chronic/recurrent condition in this group. Monitoring of emotional well-being/depression seems warranted and does not necessarily have to be very elaborate, but should be embedded in collaborative care approaches [34]. Moreover, given that a considerable number of patients do not benefit from the current pharmacological and psychotherapeutic treatment modalities, future research efforts are required to further optimise depression outcomes for depressed patients with type 2 diabetes [34]. Web-based treatment of depression in diabetes appears to be effective and can be employed to help to battle this common problem in patients with diabetes with low costs [35].

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