Diabetologia (2017) 60:60–68
DOI 10.1007/s00125-016-4123-0

ARTICLE

Trajectories of depression in adults with newly diagnosed type 1 diabetes: results from the German Multicenter Diabetes Cohort Study

Hanna Kampling[1] · Frank Petrak[2,3] · Erik Farin[1] · Bernd Kulzer[4,5] · Stephan Herpertz[2] · Oskar Mittag[1]

Received: 1 April 2016 / Accepted: 31 August 2016 / Published online: 27 October 2016

Abstract
Aims/hypothesis There is a paucity of longitudinal data on type 1 diabetes and depression, especially in adults. The present study prospectively analysed trajectories of depressive symptoms in adults during the first 5 years of living with type 1 diabetes. We aimed to identify distinct trajectories of depressive symptoms and to examine how they affect diabetes outcome.
Methods We reanalysed data from a prospective multicentre observational cohort study including 313 adults with newly diagnosed type 1 diabetes. At baseline and in annual postal surveys over 5 consecutive years, we gathered patient characteristics and behavioural and psychosocial data (e.g. Symptom Checklist-90-R [SCL-90-R]). Medical data (e.g. HbA_{1c} levels) was obtained from the treating physicians. We applied growth mixture modelling (GMM) to identify distinct trajectories of depression over time.
Results Five years after diagnosis, 7.8% ($n=20$) of patients were moderately depressed and 10.2% ($n=26$) were severely depressed. GMM statistics identified three possible models of trajectories (class 1, 'no depressive symptoms'; class 2, 'worsening depressive symptoms that improve after 2 years'; class 3, 'worsening depressive symptoms'). Severity of depression symptoms at baseline (subscale of the SCL-90-R questionnaire) significantly predicted membership of classes 2 and 3 vs class 1. After 5 years, higher HbA_{1c} values were detected in class 3 patients (mean = 8.2%, 66 mmol/mol) compared with class 1 and class 2 (both: mean = 7.2%, 55 mmol/mol).
Conclusions/interpretation We identified distinct trajectories of depressive symptoms that are also relevant for diabetes outcome. Patients with worsening depressive symptoms over time exhibited poor glycaemic control after the first 5 years of living with diabetes. They also exhibited a reduced quality of life and increased diabetes-related distress.

Keywords Adults · Depression · Growth mixture modelling · Longitudinal data · Onset cohort · Psychological outcomes · Type 1 diabetes

Electronic supplementary material The online version of this article (doi:10.1007/s00125-016-4123-0) contains peer-reviewed but unedited supplementary material, which is available to authorised users.

✉ Hanna Kampling
hanna.kampling@uniklinik-freiburg.de

[1] Section of Health Care Research and Rehabilitation Research, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Hugstetterstr. 49, 79106 Freiburg, Germany

[2] Department of Psychosomatic Medicine and Psychotherapy, LWL-University Clinic Bochum – Ruhr-University Bochum, Bochum, Germany

[3] Center for Psychotherapy Wiesbaden, Wiesbaden, Germany

[4] Diabetes Center Mergentheim, Germany; Research Institute of the Diabetes Academy Mergentheim, Bad Mergentheim, Germany

[5] Department of Clinical Psychology and Psychotherapy, Otto-Friedrich-University of Bamberg, Bamberg, Germany

Abbreviations

CBT	Cognitive behaviour therapy
DIMD	Diagnostic Interview for Mental Disorders
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders IV
DQoL	Diabetes-related quality of life
FBD	Alltagsbelastungen bei Diabetes (German questionnaire on diabetes-related distress)
GMDC	German Multicenter Diabetes Cohort (study)
GMM	Growth mixture modelling

improveD	Class 2 (patients with worsening depressive symptoms that improve after 2 years)
LQD	Lebensqualität bei Diabetes (German Quality of Life with Diabetes questionnaire)
noD	Class 1 (patients with no depressive symptoms)
PFSQ-R	Perceived Family Support and Communication Questionnaire
RRR	Relative risk ratio
SCL-90-R	Symptom Checklist-90-R (questionnaire)
worseD	Class 3 (patients with worsening depressive symptoms)

Introduction

In adult patients with type 1 diabetes, there is a high prevalence of comorbid mental disorders such as depression, anxiety, dysthymia, panic disorder and social phobia [1, 2]. Next to anxiety, depression constitutes the greatest problem, with much higher prevalence (4.6–13.6% [1, 3–7]) compared with reference groups (2.7–3.2% [5, 7]). The increased presence of depression in patients with type 1 diabetes might be partly attributable to a biological link (e.g. circulating cytokines [8]), or other shared mechanisms (e.g. dysregulation of the hypothalamic–pituitary–adrenal axis [9]). When present in patients with type 1 diabetes, depression is associated with fear of hypoglycaemia [10], complications [4, 11, 12], diabetes-related distress [13, 14], impaired quality of life [15], female sex [4], low socioeconomic status [4] and physical inactivity [13, 16]. One of the most important diabetes-related problems connected to depression is inadequate glycaemic control (high HbA_{1c} levels). Recent research questions such a general association with type 1 diabetes because data were often retrieved from type 2 or mixed (types 1 and 2) diabetes cohorts. Studies focusing solely on type 1 diabetes have yielded inconsistent results. While depression was linked to poorer glycaemic control in some studies [16–19], in others it was not [2, 20, 21].

What is the course of depression following diabetes onset? When does it occur for the first time? Studies reporting the prevalence of depression tend to do so at a random time point during a patient's disease. Longitudinal data can help us better understand the course of depression over time, and also unravel the relationship between depression and diabetes-related problems (e.g. poor glycaemic control).

While longitudinal data on type 2 diabetes has been available since 2008 [22], and data on the course of depression in type 2 diabetes has been available since 2012 [23], there is very little longitudinal data on type 1 diabetes, especially concerning adults.

A recent study by Rassart and colleagues presents longitudinal data concerning psychological functioning and glycaemic control on emerging adults [20]. Here, patient's beliefs and perceptions about their diabetes were linked to diabetes-related problems (including depressive symptoms) 5 years later, but not to changes in glycaemic control. There is no longitudinal data on an onset cohort of adults with type 1 diabetes dealing with mental comorbidities.

In summary, there is a lack of research considering the natural incidence, as well as the trajectory, of depression after the diagnosis of type 1 diabetes in adults. Additionally, the predictors of depression in this group of patients are unknown. Hence, the aim of our study was to answer the following research questions: What is the long-term course (trajectory) of depressive symptoms over a period of 5 years? Is it possible to identify distinct classes of patients that develop or do not develop depression? If so, what are predictors of these trajectories of depressive symptoms? Finally, are there differences in outcome according to different depression classes or trajectories?

Methods

Two of this paper's authors (F. Petrak, B. Kulzer) conducted a prospective, multicentre, longitudinal observational study on a cohort of adult inpatients with newly diagnosed type 1 diabetes (the German Multicenter Diabetes Cohort [GMDC] study). Study inclusion criteria were a recent diagnosis of type 1 diabetes (not more than 12 weeks prior to study enrolment), age between 17 and 40 years, and sufficient German language skills to complete the questionnaires. While the lower age limit was chosen to include adults only, we chose the upper age limit to avoid the unintentional enrolment of type 2 diabetes patients misdiagnosed with type 1 diabetes. Recruitment took place at 12 different hospitals: five acute care, five rehabilitation and two university hospitals. In total, 347 patients were eligible for inclusion; of these, 313 patients agreed (provided written informed consent) to participate. After 5 years, data was available for 258 patients (for a more detailed description of the study sample, see [5]).

At baseline (i.e. time of recruitment at the hospital) and at five consecutive yearly postal surveys, we collected data on patient characteristics, as well as behavioural and psychosocial data (e.g. coping styles, quality of life, disease distress), via questionnaires. Medical data, such as the type of treatment, HbA_{1c} level or complications, were obtained from the treating physicians. See electronic supplementary material (ESM) Methods for further details.

The baseline prevalences of mental disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [24] were obtained using the Diagnostic Interview for Mental Disorders (DIMD short version) [25].

To assess the severity of depression, we used the Symptom Checklist 90-R (SCL-90-R) questionnaire [26]. Scores were transformed into sex-adjusted T-scores: $T < 60$, not depressed; $60 \leq T < 70$, moderately depressed; $T \geq 70$, severely depressed [26]. Diabetes-related distress in daily life and diabetes-related quality of life (DQoL) were measured using the German Alltagsbelastungen bei Diabetes (FBD) and Lebensqualität bei Diabetes (LQD) questionnaires [27, 28]. The latter provides three scales of DQoL in type 1 diabetes: strain, satisfaction and strain due to blood glucose level. The adequacy of perceived familial support was measured by the revised Perceived Family Support and Communication Questionnaire (PFSQ-R) [29]. See ESM Methods for further details.

In order to explore the potential advantages of more advanced statistical methods and to 'establish the best classification based on the longitudinal pattern of change' [30], we applied growth mixture modelling (GMM) using Mplus version 7.3 statistical software to identify typical trajectories of depressive symptoms over time in a cohort of adults with newly diagnosed type 1 diabetes. Across different time points, GMM determines whether meaningful trajectories underlie the data to describe distinct (latent) classes. See ESM Methods for further details.

To gain a better understanding of the trajectories, we also sought distinctive characteristics that might characterise the final classes (outcomes at 5 year follow-up), or predict class membership (predictors at baseline or 1 year follow-up). To do this, data was analysed descriptively using one-way ANCOVA, χ^2 and multinomial logistic regression (backward elimination) using IBM SPSS Statistics software version 22.0.

Predictors at baseline or 1 year follow-up for class membership We made a distinction between baseline characteristics (sex, age, years of formal education, marital status, severity of depression [SCL-90-R], major depression [DIMD] and anxiety disorder [DIMD]) and those characteristics that might change after a diagnosis of type 1 diabetes (marital status, BMI, severity of depression [SCL-90-R] and DQoL [LQD], diabetes-related distress in daily life [FBD], and adequacy of perceived familial support [PFSQ-R]). Hence, multinomial logistic regression was either conducted with potential predictors measured at baseline (baseline characteristics), or at 1 year follow-up (sensitive to change). In addition, we checked whether patients had ever undergone psychotherapy during the 5 years of follow-up and whether this might predict class membership. Table 1 provides an overview on potential predictors (at baseline and 1 year follow-up) for depression class membership.

Outcomes at 5 year follow-up We tested medical outcomes such as HbA_{1c} level, long-term complications, hypoglycaemia and type of treatment, as well as diabetes-related psychological outcomes such as DQoL, adequacy of perceived familial support and diabetes-related distress in daily life; the latter three would only be tested for class differences if they were unable to predict class membership. Table 1 gives an overview of observed outcomes at the 5 year follow-up.

Results

In total, 313 patients with newly diagnosed type 1 diabetes were included in our analyses at baseline. Because of dropouts, our patient sample comprised 291 patients for the 1 year follow-up, 267 patients for the 2 year follow-up, 267 patients for the 3 year follow-up, 254 patients for the 4 year follow-up and 258 patients for the 5 year follow-up. Figure 1 provides details about patients who dropped out completely and did not participate in any of the follow-ups. The dropouts included significantly more men (76.4%, $n = 42$) than women (23.6%, $n = 13$) compared with the sample that continued participation (men, 59.3%, $n = 153$; women, 40.7%, $n = 105$; $\chi^2_{(1)} = 5.62$, $p = 0.018$). Those who dropped out were also significantly younger at baseline (mean 26.4 years) than those who continued (mean 28.6 years, $F_{(1,312)} = 5.71$, $p = 0.017$). There were

Table 1 Overview of potential predictors (at baseline and 1 year follow-up) for depression and outcomes at the 5 year follow-up

Baseline: potential predictors for depression class membership (baseline characteristics)	1 year follow-up: potential predictors for depression class membership (sensitive to change)	Observed outcomes at 5 year follow-up
Sex	Marital status	HbA_{1c} level
Age	BMI	Long-term complications
Years of formal education	Severity of depression (SCL-90-R)	Hypoglycaemia
Marital status	DQoL (LQD)	Type of treatment
Severity of depression (SCL-90-R)	Diabetes-related distress in daily life (FBD)	DQoL (LQD)
Major depression (DIMD)	Adequacy of perceived familial support (PFSQ)	Diabetes-related distress in daily life (FBD)
Anxiety disorder (DIMD)		Adequacy of perceived familial support (PFSQ)

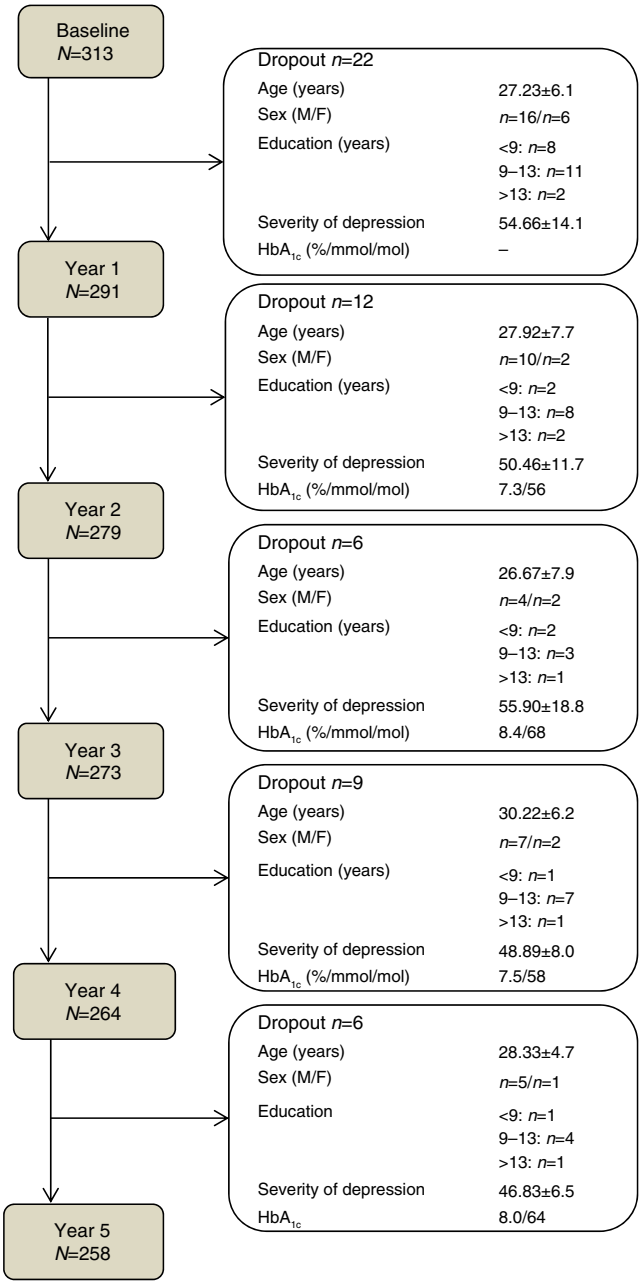

Fig. 1 Flow chart showing the number of complete dropouts at various follow-ups (this does not take into consideration missing follow-ups but dropouts at the final time point). Data includes dropout number, patient characteristics, information on severity of depression and HbA_{1c} levels. One value is missing for education (years) of dropouts prior to1 year follow-up. Data are number, mean ± SD, or mean. Subsequent analysis (displayed in the main text) was carried out on participants who took part at the point of measurement, of which there were 291 at the 1 year follow-up, 267 at the 2 year follow-up, 267 at the 3 year follow-up, 254 at the 4 year follow-up and 258 at the 5 year follow-up

no differences in years of formal education. At baseline, the average disease duration was 5.6 weeks (1 year follow-up, 63.5; 2 year follow-up, 120.0; 3 year follow-up, 176.4; 4 year follow-up, 231.9; 5 year follow-up, 288.6) and the mean age was 28.2 years. This sample comprised far more men than women, unmarried people, people living with a partner (and child[ren]) and people with a higher educational background. Diseases other than diabetes, complications and medication other than insulin were uncommon. Patient BMI ranged from underweight to obese. Detailed information on patient characteristics is found in Table 2.

At baseline, 5.8% of patients were diagnosed with a major depressive episode and 7.7% with an anxiety disorder, according to DSM-IV. In total, 12.5% of patients were diagnosed with at least one mental disorder. A detailed description of the prevalence of mental disorders at baseline was previously reported [5].

Trajectories of depressive symptoms

The mean scores for depressive symptoms (T ± SD) were 51.0 ± 11.2 at baseline, 49.0 ± 11.6 at 1 year follow-up, 49.0 ± 11.7 at 2 year follow-up, 48.8 ± 11.9 at 3 year follow-up, 48.5 ± 11.3 at 4 year follow-up and 48.8 ± 12.0 at 5 year follow-up. However, at 5 year follow-up 7.8% ($n = 20$) of patients were classified as moderately depressed ($60 \leq T < 70$), and 10.2% ($n = 26$) as severely depressed ($T \geq 70$). We applied GMM to better understand the individual trajectories of depressive symptoms.

GMM statistics allowed for three possible trajectory models, but the two-class and five-class models were rejected because of higher clinical relevance of the three-class model (see Figure 2). See ESM for each class's individual trajectories (ESM Figures 1–3).

Class 1 comprises the majority of patients ($n = 250$, 79.9%), and incorporates those with no depressive symptoms at any time. Classes 2 and 3 identified those patients with (highly) relevant depressive symptoms. Class 3 ($n = 43$, 13.7%) comprises those with worsening symptoms over a 5 year period (mean ± SD: baseline, 61.4 ± 13.4, $n = 43$; 5 year follow-up, 73.8 ± 6.0, $n = 36$). The smallest class, class 2 ($n = 20$, 6.4%), incorporates those patients whose baseline depression score was close to the cut-off score, worsened over a period of 2 years and later improved (5 year follow-up, 53.3 ± 7.8, $n = 18$).

In short, class 1 comprises those patients with 'no depressive symptoms' (noD), class 2 those with 'worsening depressive symptoms that improve after 2 years' (improveD), and class 3 those with 'worsening depressive symptoms' (worseD).

We next investigated the probability of each individual belonging to a specific class. The average latent class probabilities for the most likely latent class membership were very high: worseD, 91%; improveD, 89%; and noD, 96%. However, estimated class membership was very imprecise for two patients (e.g. probability of being in worseD, 45%; probability of being in improveD, 21%; and probability of being in noD, 34% for one patient) and questionable for another four (e.g. probability of being in noD, 46%; probability of being in improveD, 51%; probability of being in noD, <1% for one patient). We removed

Table 2 Patient demographics and clinical characteristics at baseline and the 5 year follow-up

Characteristic	Baseline ($N=313$)				5 year follow-up ($N=258$)			
	Total	noD	improveD	worseD	Total	noD	improveD	worseD
Age	28.2 ± 6.3	28.3 ± 6.2	27.0 ± 7.7	28.2 ± 6.3	33.6 ± 6.4	33.7 ± 6.3	32.2 ± 8.0	33.6 ± 6.5
Disease duration (weeks)	5.6 ± 4.3	5.6 ± 4.3	4.0 ± 3.3	6.0 ± 5.0	288.8 ± 33.1	286.9 ± 28.8	291.5 ± 46.7	297.3 ± 44.8
BMI	22.9 ± 3.4	23.0 ± 3.4	22.8 ± 3.8	22.6 ± 2.9	24.7 ± 4.0	24.9 ± 4.1	24.7 ± 4.1	23.3 ± 2.4
Sex								
Male	195 (62)	151 (60)	13 (65)	31 (72)	153 (59)	115 (57)	11 (61)	27 (73)
Female	118 (38)	99 (40)	7 (35)	12 (28)	105 (41)	88 (43)	7 (39)	10 (27)
Marital status								
Unmarried	203 ± 65	161 ± 64	13 ± 65	29 ± 67	119 ± 47	86 ± 43	10 ± 56	23 ± 62
Married	95 ± 30	79 ± 32	7 ± 35	9 ± 21	109 ± 43	94 ± 47	6 ± 33	9 ± 24
Divorced, separated or widowed	15 (4.8)	10 (4.0)	–	5 (11.6)	26 (10.2)	19 (9.5)	2 (11.1)	5 (13.5)
Years of education								
< 9	76 (24.9)	62 (25.5)	3 (15.0)	11 (26.2)	55 (21.5)	43 (21.4)	2 (11.1)	10 (27.0)
9–13	198 (64.9)	157 (64.6)	13 (65.0)	28 (66.7)	161 (62.9)	126 (62.7)	12 (66.7)	23 (62.2)
> 13	31 (10.2)	24 (9.9)	4 (20.0)	3 (7.1)	40 (15.6)	32 (15.9)	4 (22.2)	4 (10.8)
Complications	4 (1.3)	4 (1.6)	–	–	9 (3.6)	6 (3.0)	1 (5.9)	2 (5.9)

Data are means ± SD or *n* (%)

Missing values at baseline: BMI, $n=2$; years of education, $n=8$

Missing values at 5 year follow-up: BMI, $n=5$; marital status, $n=4$; years of education, $n=2$, complications, $n=10$

these six patients from further analyses because their class membership was considered uncertain (new $N=307$: worseD, $n=42$; improveD, $n=18$; noD, $n=247$).

Predictors at baseline and 1 year follow-up

For explanatory purposes, we applied multinomial logistic regression models (backward elimination) despite the low class frequency of improveD. The reference category was noD. At baseline and 1 year follow-up, only severity of depression significantly predicted class membership of either improveD or worseD vs noD (see Tables 3 and 4).

In total, 34 patients received psychotherapy. Receiving psychotherapy significantly predicted class membership of worseD and noD, favouring worseD (worseD, 35.7%; noD, 4.5%; $b=2.6$, Wald $\chi^2_{(1)}=32.0$, $p<0.001$). Although improveD was not significantly predicted, it is notable that 44.4% ($n=8$) of this class received psychotherapy.

Class membership for worseD and improveD was not predicted by any characteristics measured at baseline or 1 year after diagnosis of type 1 diabetes, nor by undergoing psychotherapy within 5 years.

Outcomes at 5 year follow-up

Although we observed no difference between depression classes for glycaemic control at 1 year follow-up (HbA_{1c} level [mean ± SD]: worseD, 6.5 ± 1.1%, 48 mmol/mol; improveD,

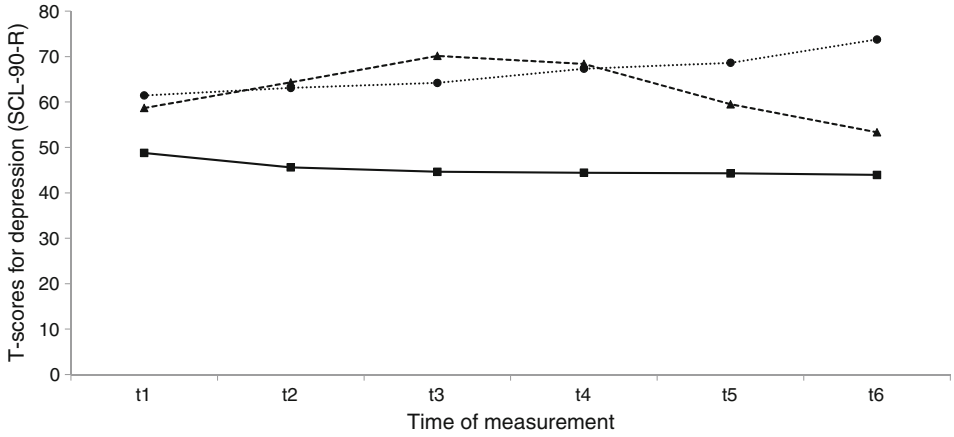

Fig. 2 GMM of trajectories of depression based on the depression subscale of the SCL-90-R. Solid line and square, class 1 (noD); dashed line and triangle, class 2 (improveD); dotted line and circle, class 3 (worseD)

Table 3 Covariates assessed at baseline for predicting depression class membership at 5 year follow-up: multinomial logistic regression models

Covariates	improveD ($n = 18$)	worseD ($n = 42$)
Sex (forced entry)	0.85 (0.30, 2.35)	1.38 (0.63, 3.02)
Age (forced entry)	0.97 (0.90, 1.05)	1.02 (0.96, 1.08)
Severity of depression	1.08 (1.04, 1.12)***	1.10 (1.07, 1.13)***

$N = 240$; data are adjusted relative risk ratio (RRR) (95% CI)

Reference category: noD

Excluded from the model: years of formal education, marital status, diagnosis of major depression, diagnosis of any anxiety disorder

***$p < 0.001$

6.4 ± 1.1%, 46 mmol/mol; noD, 6.5 ± 1.3%, 46 mmol/mol; $F_{(2,\ 260)} = 0.23$, $p = 0.793$, adjusted for sex and age), we did detect significant differences at the 5 year follow-up. Here, worseD had the higher HbA_{1c} values (see also Table 5). For DQoL, we found significant class differences for strain, strain due to blood glucose and satisfaction (see also Table 5). For DQoL, patients classified as worseD class experienced a significantly higher strain, as well as lower satisfaction compared with those classified as improveD and noD. As with the higher strain due to blood glucose, differences were only significant between patients classified as worseD and as noD. Here, patients classified as worseD demonstrated higher strain due to blood glucose than those classified as noD.

Although neither diabetes-related distress nor adequacy of perceived familial support predicted depression class membership, we identified significant differences in these scores between classes at 5 years after the first diagnosis of type 1 diabetes (see also Table 5). Patients classified as worseD exhibited more diabetes-related distress compared with those classified as improveD or noD, and experienced less adequate familial support than those classified as noD (see also Table 5).

Only about 6% of patients suffered any long-term complications during the 5 year follow-up period. There were no significant between-class differences in the number of hypoglycaemic events experienced within the last 5 years or the type of treatment (conventional, intensive, insulin pump; see also Table 5).

Table 4 Covariates assessed at 1 year follow-up for predicting depression class membership at 5 year follow-up: multinomial logistic regression models

Covariate	improveD ($n = 16$)	worseD ($n = 26$)
Sex (forced entry)	0.69 (0.20, 2.41)	1.52 (0.50, 4.58)
Age (forced entry)	0.97 (0.89, 1.07)	0.98 (0.91, 1.06)
Severity of depression	1.17 (1.10, 1.25)***	1.12 (1.07, 1.18)***
Adequacy of perceived familial support	1.16 (0.44, 3.07)	0.49 (0.24, 1.01)

$N = 166$; data are adjusted RRR (95% CI)

Reference category: noD

Excluded from the model: marital status, BMI, DQoL, diabetes-related distress in daily life

***$p < 0.001$

Discussion

We present long-term (5 year) data on the course of depressive symptoms in adults with newly diagnosed type 1 diabetes. Taken together, this population proved to be relatively healthy with average depression scores that did not become clinically significant at any time point. Also, although the diabetes burden was high in some individuals, the overall burden was considerably low. This is surprising, as one would expect that a disease with lifelong implications in terms of medication and lifestyle, and with a potential risk of secondary complications, would have a stronger impact.

However, 5.8% of patients were initially diagnosed with major depression; this percentage is more than twice as high as the percentage in a comparison group of a national representative sample without diabetes (2.7%) [5].

In addition to their increased prevalence of major depression, a small sample of our diabetes cohort became continuously more depressed over time (about 14%). These patients exhibited worse glycaemic control and less satisfaction with DQoL, received less perceived familial support, and exhibited more diabetes-related distress, strain on DQoL and strain due to blood glucose levels on DQoL. In all, 18.0% (46 out of 255) of patients exhibited depressive symptoms 5 years after diagnosis; 26 of those (10.2%) had severe depressive symptoms. While depressive symptoms themselves require therapy, they also contribute negatively to diabetes-related medical, social and psychological outcomes, and therefore need to be addressed.

However, when is the appropriate time to screen for depression and start treatment? Our analyses of depression trajectories revealed that the majority of non-depressed patients at the time of diagnosis did not become depressed. The strongest predictors for distinguishing patients with worsening symptoms or those with initially worsening and steadily improving symptoms of depression from those who did not become depressed was an increase in the severity of depression (as measured by a subscale of the SCL-90-R). Clinicians may benefit from this knowledge. Depression could and probably should be targeted as soon as an initial diagnosis of type 1 diabetes is made, especially as depression treatments such as cognitive behavioural therapy (CBT) or pharmacotherapy (sertraline) are known to be effective in patients with type 1 diabetes [31]. There is evidence for positive effects of psychotherapy including mindfulness-based cognitive therapy [32] and CBT [32–34] (the latter often combined with a diabetes self-management intervention [34]), of pharmacotherapy [32, 33], and of collaborative care approaches [34] on depressive

Table 5 Outcomes at 5 year follow-up: differences between three classes

Outcomes at 5 year follow-up	One-way ANCOVA[a] or χ^2 test	*p* value	Total	noD	improveD	worseD
HbA_{1c}, %	$F_{(2,258)} = 4.81$	0.009	7.4 ± 1.7	7.2 ± 1.4	7.2 ± 2.2	8.2 ± 2.5
HbA_{1c}, mmol/mol			57	55	55	66
DQoL						
Strain	$F_{(2,248)} = 43.70$	0.000	1.1 ± 0.6	0.7 ± 0.5	1.0 ± 0.6	1.7 ± 0.7
Strain due to blood glucose levels	$F_{(2,248)} = 11.60$	0.000	1.5 ± 0.8	1.2 ± 0.8	1.6 ± 0.8	1.8 ± 0.8
Satisfaction	$F_{(2,248)} = 37.66$	0.000	3.0 ± 0.5	3.3 ± 0.5	3.1 ± 0.5	2.5 ± 0.4
Diabetes-related distress	$F_{(2,248)} = 56.10$	0.000	1.0 ± 0.6	0.6 ± 0.5	0.9 ± 0.7	1.5 ± 0.7
Adequacy of perceived familial support	$F_{(2,201)} = 11.73$	0.000	3.9 ± 0.7	4.2 ± 0.7	3.9 ± 0.7	3.5 ± 0.7
Hypoglycaemic events						
1 event	$\chi^2_{(4)} = 7.64$	0.11	53 (23.7)	40 (22.3)	7 (43.8)	6 (20.7)
> 1 event			25 (11.2)	19 (10.6)	–	6 (20.7)
Type of treatment						
Conventional	$\chi^2_{(4)} = 3.94$	0.41	14 (5.5)	10 (5.0)	–	4 (10.8)
Intensive			212 (82.8)	169 (84.1)	15 (83.3)	28 (75.7)
Insulin pump			30 (11.7)	22 (10.9)	3 (16.7)	5 (13.5)

Data are means (SD) or *n* (%)

[a] Adjusted for sex and age

symptoms in mixed samples comprising patients with type 1 and type 2 diabetes. Time- and cost-effective screening instruments such as the Patient Health Questionnaire (PHQ)-2 [35] could be routinely applied by physicians at the start of diabetes treatment, and patients could be encouraged to seek a proper diagnosis and treatment by psychologists or psychiatrists when required. However, there is limited potential for detecting depression early via positive screening results, especially when they are not followed by clear treatment pathways (also compare [31]).

In all, 11% of our total sample and over a third of patients with worsening depressive symptoms received psychotherapy during the 5 year follow-up period, suggesting a need to consider depressive symptoms (at least partially) in patients with type 1 diabetes. However, although psychotherapy can alleviate depressive symptoms, patients in the worseD trajectory tended to express worsening depressive symptoms. This raises the question of whether patients with type 1 diabetes have special requirements that need to be addressed for treating their depression appropriately, and indeed whether diabetes-specific treatment approaches might be more beneficial. However, this proposal should be interpreted cautiously because our sample sizes are small.

Irrespective of depression, glycaemic control should be closely monitored because patients exhibited much better glycaemic control at 1 year after initial diagnosis than at 5 years. Glycaemic control was worst in patients with worsening depressive symptoms. Hence, routine check-ups should always monitor glycaemic control, especially if the patient presents symptoms of depression.

This study had several limitations. Patients were recruited consecutively from January 1996 to May 1999, thus our data is not recent. As a history of depression was not assessed at baseline, there is no way of telling whether a patient's depression preceded or co-occurred with the diagnosis of type 1 diabetes. Also, we did not investigate possible interaction effects between predictors. While acceptable for GMM, our study sample was still quite small for statistical analysis. This became more obvious when looking at the class frequencies of trajectories: WorseD consisted of 43 and improveD of only 20 patients. This is an important consideration in general, but even more so when interpreting multinomial regression models. We tolerated our model's lack of statistical robustness with the aim of identify tendencies that might guide further research. Further, two of our assessment instruments (LQD, FBD) remain to be validated. This should also be considered when interpreting our results.

Conclusion

The prevalence of major depression in patients newly diagnosed with type 1 diabetes is more than twice as high as that in reference groups. We were able to model three trajectories of depressive symptoms in which a majority of patients remaining undepressed (class 1) and the others had either worsening depressive symptoms over a 2 year period, improving steadily thereafter (class 2), or became more depressed over time (class 3). Severity of depression symptoms at baseline (subscale of the SCL-90-R questionnaire) significantly predicted whether

patients remained undepressed during the 5 years of follow-up or if they either worsened continuously during that time or got worse at first and improved after two 2 years. We found significant differences in outcome between trajectories at the 5 year follow-up: those patients with worsening depressive symptoms exhibited poorer scores for glycaemic control, DQoL and adequacy of perceived familial support, as well as more diabetes-related distress. This study has shown that longitudinal data can enhance our understanding of the underlying mechanisms of depression development in patients with type 1 diabetes.

Acknowledgements We are sincerely grateful to all patients and clinicians who supported the GMDC trial.

Funding The study was funded by the German Diabetes Association (DDG), Johannes Gutenberg-University Mainz, Novo Nordisk and Berlin-Chemie (all German institutions).

Duality of interest statement The authors declare that there is no duality of interest associated with this manuscript.

Contribution statement FP was the principal investigator of the GMDC study and designed the study design; BK and SH collected the data; EF and OM advised on the statistical analysis; HK analysed the data; HK, EF and OM interpreted the data; HK wrote the manuscript with contributions from FP and OM; EF revised the methods sections; BK, FP, OM and SH reviewed and edited the manuscript; and all authors approved the version to be published. FP is responsible for the integrity of the work as a whole.

References

1. de Ornelas Maia AC, Braga Ade A, Paes F et al (2014) Psychiatric comorbidity in diabetes type 1: a cross-sectional observational study. Rev Assoc Med Bras 60:59–62
2. Berge LI, Riise T, Hundal O, Odegaard KJ, Dilsaver S, Lund A (2013) Prevalence and characteristics of depressive disorders in type 1 diabetes. BMC Res Notes 6:543
3. Roy T, Lloyd CE (2012) Epidemiology of depression and diabetes: a systematic review. J Affect Disord 142:8–21
4. Trief PM, Xing D, Foster NC et al (2014) T1D exchange clinic network. depression in adults in the T1D exchange clinic registry. Diabetes Care 37:1563–1572
5. Petrak F, Hardt J, Wittchen HU et al (2003) Prevalence of psychiatric disorders in an onset cohort of adults with type 1 diabetes. Diabetes Metab Res Rev 19:216–222
6. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ (2001) The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care 24:1069–1078
7. Barnard KD, Skinner TC, Peveler R (2006) The prevalence of co-morbid depression in adults with type 1 diabetes: systematic literature review. Diabet Med 23:445–448
8. Korczak DJ, Pereira S, Koulajian K, Matejcek A, Giacca A (2011) Type 1 diabetes mellitus and major depressive disorder: evidence for a biological link. Diabetologia 54:2483–2493
9. Moulton CD, Pickup JC, Ismail K (2015) The link between depression and diabetes: the search for shared mechanisms. Lancet Diabetes Endocrinol 3:461–471
10. Nefs G, Bevelander S, Hendrieckx C et al (2015) Fear of hypoglycaemia in adults with type 1 diabetes: results from Diabetes MILES – The Netherlands. Diabet Med 10:1289–1296
11. Gendelman N, Snell-Bergeon JK, McFann K et al (2009) Prevalence and correlates of depression in individuals with and without type 1 diabetes. Diabetes Care 32:575–579
12. Zoffmann V, Vistisen D, Due-Christensen M (2014) A cross-sectional study of glycaemic control, complications and psychosocial functioning among 18-to 35-year-old adults with type 1 diabetes. Diabet Med 31:493–499
13. Lloyd CE, Pambianco G, Orchard TJ (2010) Does diabetes-related distress explain the presence of depressive symptoms and/or poor self-care in individuals with type 1 diabetes? Diabet Med 27:234–237
14. Tanenbaum ML, Gonzalez JS (2012) The influence of diabetes on a clinician-rated assessment of depression in adults with type 1 diabetes. Diabetes Educ 38:695–704
15. de Ornelas Maia AC, Braga Ade A, Paes F (2013) Comorbidity of depression and anxiety: association with poor quality of life in type 1 and 2 diabetic patients. Clin Pract Epidemiol Ment Health 12:136–141
16. Melin EO, Thunander M, Svensson R, Landin-Olsson M, Thulesius HO (2013) Depression, obesity, and smoking were independently associated with inadequate glycemic control in patients with type 1 diabetes. Eur J Endocrinol 168:861–869
17. Bot M, Pouwer F, de Jonge P, Tack CJ, Geelhoed-Duijvestijn PH, de Snoek FJ (2013) Differential associations between depressive symptoms and glycaemic control in outpatients with diabetes. Diabet Med 30:e115–e122
18. Roy MS, Roy A, Affouf M et al (2007) Depression is a risk factor for poor glycemic control and retinopathy in African-Americans with type 1 diabetes. Psychosom Med 69:537–542
19. Pouwer F, Geelhoed-Duijvestijn PH, Tack CJ et al (2010) Prevalence of comorbid depression is high in out-patients with type 1 or type 2 diabetes mellitus. Results from three out-patient clinics in the Netherlands. Diabet Med 27:217–224
20. Rassart J, Luyckx K, Berg CA, Bijttebie P, Moons P, Weets I (2015) Psychosocial functioning and glycemic control in emerging adults with type 1 diabetes: a 5-year follow-up study. Health Psychol 34:1058–1065
21. Strandberg RB, Graue M, Wentzel-Larsen T, Peyrot M, Rokne B (2014) Relationships of diabetes-specific emotional distress, depression, anxiety, and overall well-being with HbA_{1c} in adult persons with type 1 diabetes. J Psychosom Res 77:174–179
22. Golden SH, Lazo M, Carnethon M et al (2008) Examining a bidirectional association between depressive symptoms and diabetes. JAMA 299:2751–2759
23. Nefs G, Pouwer F, Denollet J, Pop V (2012) 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. Diabetologia 55:608–616
24. American Psychiatric Association (1994) American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn. DSM-IV. American Psychiatric Press, Washington DC
25. Margraf J (2015) Diagnostic interview for mental disorders short version handbook. Springer, Berlin [published in German]
26. Franke GH (1995) Die symptom-checkliste von derogatis – deutsche version. Beltz test Gesellschaft, Göttingen [published in German]
27. Waadt S, Duran G, Herschbach P (1995) Klinische diagnose psychosozialer belastungen: der fragebogen zu alltagsbelastungen bei diabetes mellitus. In: Kohlmann CW (ed) Diabetes und psychologie:

diagnostische ansätze. Verlag Hans Huber, Bern, pp 17–33 [published in German]
28. Hirsch A, Bartholomae C, Volmer T (2000) Dimensions of quality of life in people with non-insulin-dependent diabetes. Qual Life Res 9:207–218
29. Aymanns P (1992) Krebserkrankung und familie: zur rolle familialer unterstützung im prozess der krankheitsbewältigung. Huber, Bern [published in German]
30. Uher R, Muthén B, Souery D et al (2010) Technical appendix: methods and results of growth mixture modelling. – supplement to: trajectories of change in depression severity during treatment with antidepressants. Psychol Med 40:S1–S13
31. Petrak F, Herpertz S, Albus C et al (2015) Cognitive behavioral therapy versus sertraline in patients with depression and poorly controlled diabetes: the Diabetes and Depression (DAD) study: a randomized controlled multicenter trial. Diabetes Care 38:767–775
32. Baumeister H, Hutter N, Bengel J (2012) Psychological and pharmacological interventions for depression in patients with diabetes mellitus and depression. Cochrane Database Syst Rev, Issue 12, Art no.:CD008381. doi:10.1002/14651858
33. Tovote KA, Fleer J, Snippe E et al (2014) Individual mindfulness-based cognitive therapy and cognitive behavior therapy for treating depressive symptoms in patients with diabetes: results of a randomized controlled trial. Diabetes Care 37:2427–2434
34. van der Feltz-Cornelis CM, Nuyen J, Stoop C et al (2010) Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a systematic review and meta-analysis. Gen Hosp Psychiatry 32:380–395
35. Petrak F, Baumeister H, Skinner TC, Brown A, Holt RI (2015) Depression and diabetes: treatment and health-care delivery. Lancet Diabetes Endocrinol 3:472–485