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Research: Educational and Psychological Issues

Longitudinal relationship between diabetes-specific emotional distress and follow-up HbA_{1c} in adults with Type 1 diabetes mellitus

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Abstract

Aim To examine whether diabetes-specific emotional distress was related to follow-up glycaemic control in adults with Type 1 diabetes mellitus.

Methods Adults with Type 1 diabetes mellitus completed the Diabetes Distress Scale and reported sociodemographic information when attending a clinical consultation at a university endocrinology unit. Blood samples to determine baseline HbA_{1c} were taken during consultations. All respondents' HbA_{1c} measurements registered from January 2009 to December 2011 were collected from medical records. The relationship between baseline diabetes-specific emotional distress and HbA_{1c} was examined with linear mixed-effects models in 175 patients with complete data.

Results After controlling for confounders, baseline diabetes-specific emotional distress and glycaemic control were significantly associated (fixed-effect coefficient 0.40, $P < 0.001$) and the regimen-related distress subscale had the strongest association with glycaemic control (fixed-effect coefficient 0.47, $P < 0.001$). The two-item measure of diabetes-specific distress had a weaker but still significant association with glycaemic control (fixed-effect coefficient 0.31, $P < 0.001$). None of these relationships was significant after adjusting for the baseline HbA_{1c}.

Conclusions People with elevated baseline diabetes-specific emotional distress are at risk of prolonged suboptimum glycaemic control; therefore, elevated diabetes-specific emotional distress, especially regimen-related distress, might be an important marker for prolonged suboptimum glycaemic control, and might indicate a need for special attention regarding patient self-management.

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Introduction

Diabetes-specific emotional distress can be defined as the experience of emotional problems related to living with diabetes and its treatment [1,2]. People with diabetes mellitus face considerable demands in maintaining a healthy lifestyle and adhering to the treatment regimen in the context of family, social environment and the healthcare system [1–3]. Diabetes-specific emotional distress is seen to be associated with poor glycaemic control in people with Type 1 diabetes mellitus [4,5]. To date, most studies investigating the relationship between diabetes-specific emotional distress and glycaemic control have used either a cross-sectional methodology [4–7] and/or have studied samples of people with Type 2 diabetes mellitus [2,3,8–12]. A recent systematic review of diabetes self-care highlights the lack of longitudinal studies investigating the association between physical and emotional health in order to improve interventions in diabetes care [13]. In cross-sectional analyses of adults with Type 1 diabetes, depression, anxiety and overall well-being were not significantly related to glycaemic control, whereas

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What's new?

- In adults with Type 1 diabetes, elevated baseline diabetes-specific emotional distress is associated with worse glycaemic control over a 1–3-year period and regimen-related distress had the strongest association with subsequent glycaemic control.
- Baseline diabetes-specific emotional distress is associated with the stable component of glycaemic control and does not account for within-individual change in glycaemic control over 1–3 years.
- Elevated diabetes-specific emotional distress may be an important marker for risk of prolonged suboptimum glycaemic control.

diabetes-specific emotional distress was significantly associated with glycaemic control [5]. Better understanding of the longitudinal relationship between diabetes-specific emotional distress and glycaemic control could contribute important knowledge for use in clinical consultations. The aim of the present study, therefore, was to examine whether diabetes-specific emotional distress is related to subsequent glycaemic control in adults with Type 1 diabetes mellitus.

Patients and methods

Patients and setting

A total of 319 people aged 18–69 years with Type 1 diabetes, attending an outpatient endocrinology unit at a university hospital in Norway between October 2008 and the end of January 2009, were invited to participate in this study, and 235 (74%) agreed to participate. The patients completed self-reported questionnaires either at the outpatient clinic or at home, in addition to providing sociodemographic and clinical information (Table 1). The study was approved by the Western Norway Committee for Medical and Health Research Ethics (19580/865).

Measures

Follow-up HbA_{1c} was handled as a continuous variable, and constituted the dependent variable in all analyses. The baseline HbA_{1c} of each patient was measured during the initial clinical consultation at which consent was obtained, and follow-up HbA_{1c} values, obtained from clinical consultations between January 2009 and December 2011, were recorded from the patients' medical records. The date each patient was invited to participate was registered as the baseline date, and the time variable for each HbA_{1c} measurement was calculated as months from baseline.

The Diabetes Distress Scale (DDS) was used to assess the baseline level of diabetes-specific emotional distress. The questionnaire consists of 17 items with a six-point Likert scale [1], and includes four subscales: regimen-related distress (five items); emotional burden (five items); interpersonal-related distress (three items); and physician-related distress (four items). The DDS has shown good reliability

Table 1 Baseline descriptive information of 175 respondents included and 60 respondents excluded in the linear mixed-effect models

	(a) Included respondents*	(b) Excluded respondents*	*P*
Mean (SD) age†, years	39.4 (13.5)	37.6 (14.1)	0.356
Men, *n* (%)	97 (55)	38 (63)	0.295
Mean duration†, years	19.0 (11.7)	17.6 (12.8)	0.437
Mean baseline HbA_{1c}, mmol/mol [HbA_{1c}% (SD)]	67 [8.3 (1.7)]	61 [7.7 (1.2)]	0.011
Presence of one or more late complications: yes, *n* (%)‡	73 (42)	8 (31)	0.392
Education‡, *n* (%)			0.560
> 4 years higher education	21 (12)	9 (17.0)	
≤ 4 years higher education	50 (29)	17 (32.1)	
High school	81 (46)	23 (43.4)	
Primary school (9 years)	23 (13)	4 (7.5)	
Living with a partner: yes, *n* (%)‡	112 (64)	34 (58.6)	0.531
Insulin regimen, *n* (%)‡			0.110
1–3 insulin injections per day	13 (7.5)	9 (15.3)	
Multi-injections	117 (67.2)	32 (54.2)	
Insulin pump	44 (25.3)	18 (30.5)	
Mean (SD) DDS total score§,¶	2.0 (0.8)	2.0 (0.8)	0.996
DDS emotional burden§,¶	2.3 (1.1)	2.3 (1.1)	0.854
DDS regimen-related distress§,¶	2.2 (1.1)	2.1 (1.0)	0.694
DDS interpersonal-related distress§,¶	1.7 (0.9)	1.6 (0.8)	0.674
DDS physician-related distress§,¶	1.5 (0.7)	1.6 (1.0)	0.464
DDS2§,¶	2.3 (1.2)	2.2 (1.1)	0.637

DDS, Diabetes Distress Scale; DDS2, two-item Diabetes Distress scale.
*175 respondents included and 60 respondents excluded from the linear mixed-effect models as a consequence of complete case analyses.
†Age and duration at baseline date
‡Number of cases in column (b) for late complications: 26; education: 53; living with a partner: 58. Insulin regimen not included in analyses models, $n = 174$ in column (a) and $n = 59$ in column (b).
§1–6 scales: the DDS, the emotional burden subscale, the regimen-related distress subscale, the interpersonal-related distress subscale, the physician-related distress subscale, and the DDS2.
¶Cronbach's α, $n = 235$/ $n = 175$: DDS total: 0.917/0.919, emotional burden subscale: 0.877/0.880, regimen-related distress subscale: 0.841/0.848, interpersonal-related distress subscale: 0.811/0.829, physician-related distress subscale: 0.829/0.782, DDS2: 0.706/0.722.

and validity across cultures in Type 1 diabetes [1,4,14]. A validated Norwegian version was used [14]. The two-item measure of diabetes-specific distress, the DDS2, proposed by Fisher *et al.* [15] was used in parallel analyses. The DDS2 consists of the following items: 'feeling overwhelmed by the demands of living with diabetes', and 'feeling that I am often failing with my diabetes regimen'. Scores ranging from 1 to 6 (highest possible distress level) were calculated for the DDS total score, each of the four DDS subscales and the DDS2. The means of valid items were used if ≥ 50% of the items had valid responses. If > 50% of items were missing, the scale score is missing. DDS scores were also dichotomized into ≥ 3.0 for severe distress, based on the high distress group of the three distress categories found in Fisher *et al.* [9].

Data analyses

Histograms and descriptive information from the diabetes distress scales were inspected to examine the distribution. Those with missing values on any analytical variable were excluded from analyses (60 respondents, 26%), resulting in a sample of 175 patients for the primary analyses (Fig. 1).

Attrition analyses were performed using independent *t*-tests and exact chi-squared tests to compare: (a) respondents (n = 235) with non-respondents (n = 84); (b) the 21 cases that were excluded because no follow-up HbA_{1c} registrations were available with the remaining 214 cases; (c) the 175 cases included in the linear mixed-effect models with the 60 excluded cases.

The follow-up course of HbA_{1c} (every follow-up HbA_{1c} counted individually) was assessed according to the proportion of patients who had a > 0.3-unit (HbA_{1c} %) change in either direction from baseline to the last follow-up in glycaemic control; also assessed were the proportions that had neither a 0.3-unit (HbA_{1c} %) increase nor decrease and the proportion that had both. There is no widely accepted, empirically established value of clinically meaningful difference in HbA_{1c}; however, the difference that is accepted as evidence of non-inferiority is 0.3 units (HbA_{1c} %) [16]. This corresponds to a difference of ~ 0.2 standard deviations of the baseline HbA_{1c} in the present study, a difference that corresponds to the upper limit of a 'small' effect size [17].

The primary analyses used linear mixed-effect models to examine whether baseline level of diabetes-specific emotional distress was associated with glycaemic control during subsequent follow-up. A total of 652 follow-up HbA_{1c} observations was included in the primary analyses (mean number of observations per case 5.45, range 1–16). Follow-up HbA_{1c} constituted the dependent variable in the linear mixed-effect models, and these were clustered within patient. Baseline HbA_{1c} was not included in the dependent variable.

Four sets of analyses were conducted with 1) the DDS total score, 2) the four DDS subscales, 3) the DDS2 and 4) the binary threshold (DDS ≥ 3) for severe distress as explanatory

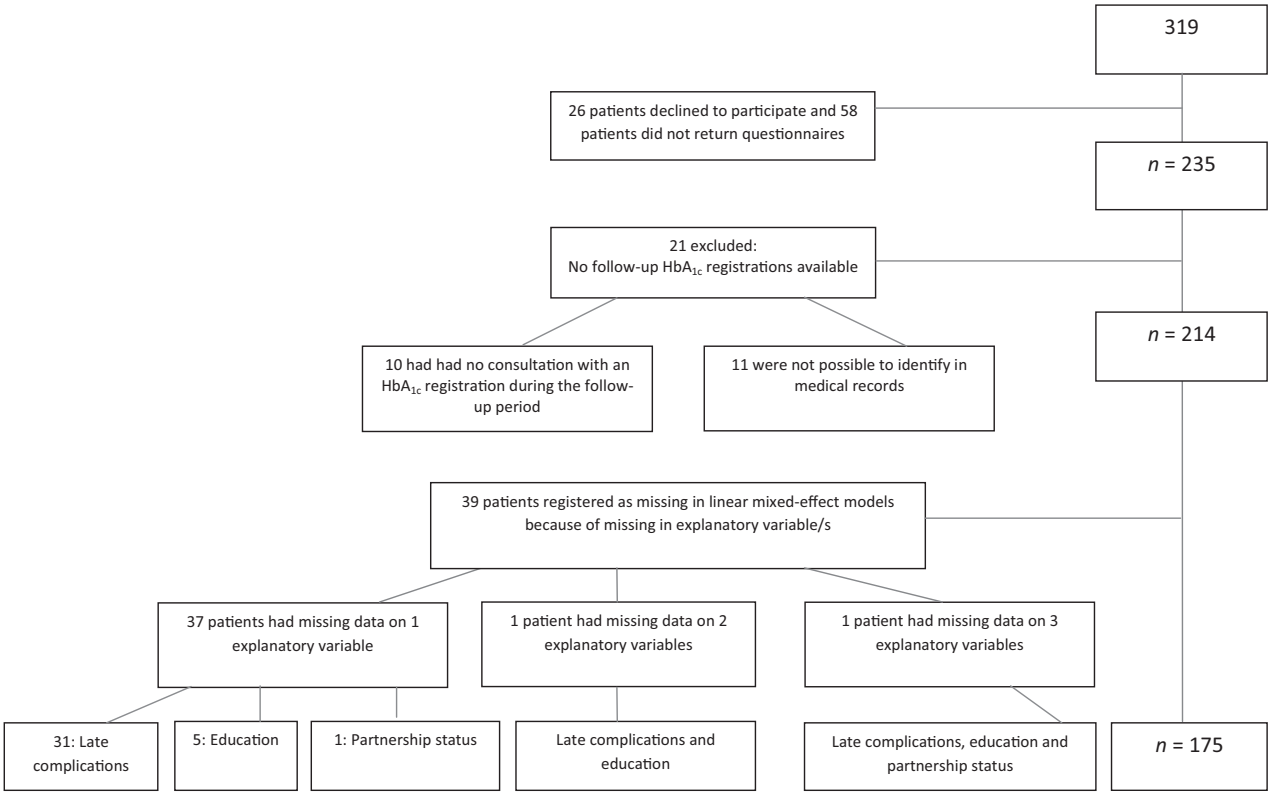

FIGURE 1 Flow chart of attrition from the 319 patients invited to the 175 patients included in the linear mixed-effect models.

variables. In analyses of the DDS subscales, separate models were performed for each subscale. Fisher *et al.* [15] showed that items from the regimen-related distress and the emotional burden subscales seem to capture most of the distress that the DDS was assessing; therefore, a model containing these two subscales was also estimated. The first model in each set of analyses adjusted for potential confounders (age, gender, education, late complications, and partnership status; these potential confounders were not of primary interest in this study, and are therefore not presented in the Tables). The second model in each set of analyses also adjusted for time to follow-up HbA_{1c} measurement and baseline HbA_{1c}. Random effects included intercept and time slope in all models adjusted for time, otherwise random intercept only was used.

Multiple imputation with 150 imputed datasets was used [18] to examine whether the results from the complete case analyses were replicated on the models for DDS total score, for the combination of regimen-related distress and emotional burden subscales, and for the DDS2. The imputation models, clustered on the 214 patients (because of missing data on the dependent variable for 21 cases), included time from baseline, HbA_{1c}, baseline HbA_{1c}, DDS, age, gender, living alone, late complications, education, DDS scales in each analysis model, and a uniform random draw (because a level one variable had to be included for technical reasons). Burn-in was 5000 Gibbs sampling iterations, and the number of iterations between each imputed dataset was 1000.

The R (The R Foundation for Statistical Computing, Vienna, Austria) package NLME was used for mixed effects models, REALCOM IMPUTE [19] was used for multiple imputation, and SPSS 21/22 (IBM Corp., Armonk, NY, USA) was used for other analyses.

Results

The attrition analyses showed that there were: (a) no significant differences between the 235 respondents and the 84 non-respondents in mean age (39 vs. 38 years; $P = 0.535$), gender (57 vs. 66% men; $P = 0.244$), or baseline HbA_{1c} [65 vs. 68 mmol/mol (HbA_{1c} 8.1 vs. 8.4%); $P = 0.285$]; (b) no significant differences between the 21 excluded cases because no follow-up HbA_{1c} registrations were available and the 214 remaining cases in the examined variables (HbA_{1c}, age, duration, DDS total score, DDS subscales, DDS2, gender, late complications, partnership status; all P values ≥ 0.211); (c) no significant differences in the tested variables between the 175 included respondents and the 60 respondents excluded from the linear mixed-effect models (Table 1), except for a significant difference between the two groups in baseline HbA_{1c} [67 vs. 61 mmol/mol (HbA_{1c} 8.3 vs. 7.7%); $P = 0.011$], indicating that the excluded cases had significantly better glycaemic control than those included in the linear mixed-effect models.

Descriptive analyses of proportion of patients that had a change of > 0.3 units (HbA_{1c} %) from the baseline value during the follow-up course showed that 98 patients (46%) had an increase of > 0.3 units, 66 patients (31%) had a decrease of > 0.3 units, 27 patients (13%) did not have either an increase or decrease of > 0.3 units (i.e. had stable glycaemic control within the limit of 0.3 units change from baseline), and 23 patients (11%) had both an increase and a decrease of > 0.3 units during follow-up (total does not sum to 100% because of rounding). Note that 24 patients only had one follow-up measurement, and it was not possible for them to have both an increase and a decrease in this analysis.

Results from the main analyses are shown in Table 2. In the first set of analyses (including DDS total score), the first model (not adjusted for time and baseline HbA_{1c}) showed that diabetes-specific emotional distress was significantly related to follow-up glycaemic control (fixed-effect coefficient 0.40, $P < 0.001$). In the second model (adjusted for time and baseline HbA_{1c}) diabetes-specific emotional distress was not significant ($P = 0.314$).

In the second set of analyses (the DDS subscales), the results were as follows. The separate analyses of each DDS subscale, adjusted for potential confounders (but not time and baseline HbA_{1c}), showed that glycaemic control was significantly related to the regimen-related distress (fixed-effect coefficient 0.47, $P < 0.001$) and emotional burden subscales (fixed-effect coefficient 0.17, $P = 0.023$), but not the interpersonal-related distress or physician-related distress subscales ($P = 0.359$ and 0.125, respectively). When examining the regimen-related distress and the emotional burden subscales together (data not shown), both were significant ($P < 0.001$ and $P = 0.009$, respectively); while the regimen-related distress subscale still had a positive relationship (fixed-effect coefficient 0.64) with glycaemic control, the coefficient for the emotional burden subscale changed to negative (fixed-effect coefficient -0.24), possibly as a result of multicollinearity. The second model (regimen-related distress and emotional burden subscales adjusting also for time and baseline HbA_{1c}) showed no significant relationship for either measure of distress (both $P \geq 0.309$).

In the third set of analyses (the DDS2), a significant relationship was apparent with glycaemic control (fixed-effect coefficient 0.31, $P < 0.001$), but not when controlling for time and baseline HbA_{1c} ($P = 0.140$). The fourth set of analyses (threshold for distress ≥ 3) followed the similar pattern, where diabetes-specific emotional distress was significantly related to follow-up HbA_{1c} (distress ≥ 3: fixed-effect coefficient 1.01, $P < 0.001$), but not when adjusting for baseline HbA_{1c} and time ($P = 0.228$).

Baseline HbA_{1c} was significantly related to follow-up glycaemic control (fixed-effect coefficients 0.43–0.45, all P values < 0.001) in models adjusted for baseline HbA_{1c} (Table 2). Of the covariates, educational level and having late complications were significantly related to follow-up glycaemic control in models not adjusted for HbA_{1c} baseline

Table 2 Diabetes-specific emotional distress [Diabetes Distress Scale (DDS) total score, DDS subscales, DDS2 and DDS non-severe vs. severe distress] as explanatory variables of follow-up glycaemic control in adults with Type 1 diabetes

	Not adjusted for time and baseline HbA_{1c}*,†			Adjusted for time and baseline HbA_{1c}*,†		
Explanatory variables	Coefficient‡	CI	*P*	Coefficient‡	CI	*P*
Diabetes-specific distress total score§	0.40	0.19 to 0.60	<0.001	0.09	−0.08 to 0.26	0.314
Months from baseline¶	–	–	–	−0.02	−0.05 to 0.01	0.182
Baseline HbA_{1c}	–	–	–	0.45	0.37 to 0.53	<0.001
	Each DDS subscale in separate analysis:			The DDS subscales together:		
Regimen-related distress§,**	0.47	0.33 to 0.61	<0.001	0.10	−0.10 to 0.30	0.309
Emotional burden§,**	0.17	0.02 to 0.32	0.023	−0.02	−0.18 to 0.14	0.829
Interpersonal-related distress§,**	0.09	−0.10 to 0.27	0.359	–	–	–
Physician-related distress§,**	0.18	−0.05 to 0.42	0.125	–	–	–
Months from baseline¶	–	–	–	−0.02	−0.05 to 0.01	0.176
Baseline HbA_{1c}	–	–	–	0.43	0.33 to 0.52	<0.001
DDS2§,**	0.31	0.17 to 0.44	<0.001	0.09	−0.03 to 0.20	0.140
Months from baseline¶	–	–	–	−0.02	−0.05 to 0.01	0.180
Baseline HbA_{1c}	–	–	–	0.44	0.36 to 0.52	<0.001
Diabetes-specific distress ≥ 3**	1.01	0.48 to 1.55	<0.001	0.27	−0.17 to 0.71	0.228
Months from baseline¶	–	–	–	−0.02	−0.05 to 0.01	0.196
Baseline HbA_{1c}	–	–	–	0.45	0.37 to 0.53	<0.001

DDS, Diabetes Distress Scale; DDS2, two-item Diabetes Distress scale.
*652 HbA_{1c} observations clustered in 175 respondents.
†Controlled also for age, gender, education, late complications, and partnership status (coefficients not shown).
‡Fixed-effect coefficients.
§Scored on 1–6 scale.
¶Coefficients and CIs per 3 months' change.
**Regimen-related distress subscale, emotional burden subscale, interpersonal-related distress subscale, physician-related distress subscale, DDS2, and threshold for severe distress at ≥ 3.

and time, and education remained significant when adjusting for the baseline HbA_{1c} and time in all models.

Results from the multiple imputation analyses were consistent with the results from the complete case analyses. Estimates were generally close to the estimates calculated by complete case analyses, but a few coefficients differed notably; the largest difference was for DDS total score, where the coefficient decreased from 0.40 in complete case analysis to 0.35 in multiple imputation. The standard errors were generally somewhat smaller.

Discussion

Elevation of diabetes-specific emotional distress was significantly associated with follow-up HbA_{1c} when the baseline level of glycaemic control was not controlled for, and the regimen-related component of distress showed the strongest relationship with follow-up HbA_{1c}. The baseline value of HbA_{1c} was related to follow-up glycaemic control, and no measure of diabetes-specific emotional distress was significantly associated with follow-up glycaemic control when adjusting for baseline HbA_{1c}. These results parallel those of Aikens *et al.* [20] who showed that, in people with Type 2 diabetes, the relationship between depression and glycaemic control became insignificant when adjusting for baseline HbA_{1c}.

It is argued that HbA_{1c} levels are stable over time [21], and deVries *et al.* [22] concluded that persistent poor glycaemic control is a common and serious problem in Type 1 diabetes mellitus. Descriptive analyses in the present study showed that only 13% sustained within the limits of 0.3 HbA_{1c} units change of increase or decrease from the baseline value. The fact that 46% had a > 0.3-unit increase and 31% had a > 0.3-unit decrease during the follow-up indicates that there is some variability in the within-patient glycaemic trajectory; however, this variability was mainly in one of the directions, as only 11% of patients experienced both an increase and a decrease during follow-up.

Peyrot *et al.* [23] argued that glycaemic control consists of stable and labile components: an individual's mean level over time (stable component), and within-person variability over time (labile component), which might be one explanation of why the association between diabetes-specific emotional distress and glycaemic control became insignificant when adjusted according to the baseline HbA_{1c} and time. An increasing number of studies have found that baseline diabetes-specific emotional distress is associated with baseline glycaemic control [2,4,5,12], but neither Fisher *et al.* [2]

nor Hessler *et al.* [12] found a prospective relationship between baseline diabetes-specific emotional distress and follow-up HbA_{1c} in adults with Type 2 diabetes, a result replicated in the present study for adults with Type 1 diabetes. More importantly, using time-varying analysis, Hessler *et al.* [12] found that a decrease in regimen-related distress was significantly associated with a decrease in HbA_{1c} in terms of within-person change, even though mean aggregate follow-up HbA_{1c} was not significantly different from baseline. The present results are consistent with an interpretation that baseline diabetes-specific emotional distress (including the regimen-related component) is related to the stable component of glycaemic control, not the labile component (i.e. within-patient variability in the glycaemic trajectory), and possibly conversely, within-patient variability in the glycaemic trajectory is related to within-patient variability in diabetes-specific emotional distress (i.e. the labile component of distress); however, to test this interpretation in Type 1 diabetes would require follow-up measures of diabetes-specific emotional distress and glycaemic control.

Fisher *et al.* [15] proposed that the DDS2 is suitable for an initial screening of high diabetes-specific emotional distress in clinical consultations, and showed that DDS2 was significantly associated with HbA_{1c} levels. The DDS2 consists of items from the regimen-related distress and emotional burden subscales [15] and a recent study found that items of regimen-related distress and emotional burden loaded on the same factor [24]. In the present study the DDS2 showed a significant relationship with follow-up HbA_{1c}, but not when adjusting for baseline glycaemic control.

The present study has some limitations. Although the response rate was 74%, the study included a rather limited number of patients, partly because 26% of volunteers were excluded from the analyses as a result of missing values for variables used in the main analyses. There were few significant differences, however, in baseline variables between the included and excluded respondents, and there were no significant differences in relevant variables between the cases excluded from the longitudinal data ($n = 21$) and the remaining cases ($n = 214$). In addition, replication of the complete case analyses by multiple imputation showed mostly the same pattern. Furthermore, the diabetes distress scales were found to be right-skewed. We did not have information about changes in prescribed treatment regimen during the follow-up period, which could have biased the results. Also the lack of follow-up data on diabetes-specific emotional distress precluded time-varying analyses to examine the association of changes in distress with changes in glycaemic control. To gain insight into the causal dynamics of diabetes-specific emotional distress and glycaemic control we would recommend cohort studies in newly diagnosed people with Type 1 diabetes.

The present study highlights that diabetes-specific emotional distress might be a marker for risk of poor glycaemic control. Our data do not allow us to say whether relieving this distress will affect glycaemic control, but suggest that diabetes-specific emotional distress can be used to identify high-risk patients for more intensive intervention. A recent study investigating the use of the DDS2 to facilitate conversation about psychological concerns in clinical consultation, found that a dialogue tool might make it easier to address psychological issues, but emphasized the importance of a short tool and the importance of using the tool in a flexible manner in clinical consultations [25]. Ease of use favours the two-item DDS2 over the full 17-item DDS, but the DDS2 does not have as strong a relationship with glycaemic control as the longer version; however, the five-item regimen distress scale is shorter than the full DDS, and has a stronger association with follow-up glycaemic control. As people with Type 1 diabetes do not have the ability to produce insulin, variations in regimen adherence can have major consequences for glycaemic control [23]. Perhaps high levels of distress related to the diabetes treatment reflect problems with the regimen [26], which could hinder the ability to implement the behaviours needed to manage the demands of the disease and achieve good glycaemic control. As regimen-related distress accounts for most of the relationship between diabetes-specific emotional distress and glycaemic control, it might be the best measure of distress to identify people at risk of prolonged poor glycaemic control.

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Competing interests

None declared.

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