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Levels of personality functioning and not depression predict decline of plasma glucose concentration in patients with type 2 diabetes mellitus

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ABSTRACT

Aims: Psychosocial variables influence chronic diseases, such as type 2 diabetes mellitus. While there is evidence for a negative impact of depression, much less is known about stable, personality oriented factors. Aim of the study was to assess the impact of depression and personality functioning on glucose regulation in patients with type 2 diabetes.
Methods: Seventy-five adult individuals with a first diagnosis of type 2 diabetes were consecutively recruited in an outpatient medical practice. Plasma glucose (HbA1c) was measured at initial contact, and after three and six months of a standardized disease management program. Depression was assessed by self-report (Patient Health Questionnaire, PHQ-D), levels of personality functioning with the screening version of the Operationalized Psychodynamic Diagnosis structure questionnaire (OPD-SQS).
Results: Using mixed regression models, OPD-SQS scores were associated with lower baseline levels of HbA1c, but a less steep decline over time. PHQ-D scores were neither associated with intercept nor with slopes of HbA1c.
Conclusions: In type 2 diabetes, levels of personality functioning but not depression predicted decline in plasma glucose during the first six months of a standardized disease management program. Personality functioning may be especially important in chronic diseases that demand a high level of compliance and lifestyle change.

1. Introduction

Diabetes mellitus is a common, chronic, and impairing disease that affects about 9% of men and 7.9% of women worldwide [1]. With increasing incidence rates and lower age of onset, it has been called an epidemic by some researchers. About 90% of the individuals suffering from diabetes are diagnosed with type 2 diabetes mellitus. Although there is no known cure to type 2 diabetes, some of its risk factors, symptoms and subsequent long-term damage can be managed

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through life-style changes or compliance to an evidence-based treatment [2]. Because of the chronicity of type 2 diabetes, adherence to life-style changes or medication have to be maintained life-long. This adherence depends on the subjects' emotional and cognitive abilities, which are influenced by the patients' personality and might be impaired due to mental disorders. As in other chronic diseases, the prevalence for mental disorders is higher in individuals with diabetes than in the general population [3]. This is also true for depression and type 2 diabetes [4,5]. Individuals with type 2 diabetes [6] have higher levels of depressive symptoms, which might be similar to diabetes-specific distress [7]. The direction of the association is likely to be bi-directional: The burden of a diagnosis of and coping with type 2 diabetes can increase the risk of developing a sub-clinical or clinical depression. Similarly, depressive symptoms can increase the risk of developing type 2 diabetes via changes in lifestyle and health-behaviour, as well as endocrinological changes [8,9]. While some studies indicate a rather linear effect of depression severity on type 2 diabetes [10], others point towards the relevance of assessing subclinical levels of depression as well [11]. This is of relevance, as a diagnosis of depression has been linked to poor outcome [12,13], low medication adherence and adverse health behaviour in type 2 diabetes [14]. In contrast, in type 1 diabetes depression does not seem to be related to long term outcome of glycemic control [15].

However, while depression is a common psychiatric condition, others, such as personality disorders, pose a higher burden of disease on the individual as well as society due to its chronicity [16].

Common comorbid conditions of depression are personality disorders (PDs) [17]. Personality disorders (PDs) describe enduring maladaptive patterns of emotion, cognition, regulation and behaviour. Patients suffering from a PD are significantly impaired in their psychosocial functioning, which includes difficulties in interpersonal relations as well as self-regulation. PDs pose a high burden on the individual as well as society, and are sometimes experienced as 'difficult to treat', especially outside of specialized psychotherapy settings [16,18,19]. While there is some evidence for an association between specific forms of PDs and diabetes [20], research on the impact of PDs in diabetes is rare. This is somewhat surprising, as PDs are a significant risk-factor for complications or hospitalizations of patients with diabetes [21]. In one study, a diagnosis of a comorbid borderline personality disorder was related to several disease-specific parameters [22]. In another study, social and relationship functioning, which are key variables for PDs, were interrelated with markers of inflammatory processes in a sample of 200 individuals with type 2 diabetes [23].

Personality variables not directly related to a diagnosis of PD, but to five-factor models of personality, may influence patterns of glycemic control, with mixed findings [24,25]. To sum up, PDs may be especially harmful in the context of type 2 diabetes via changes in health-behaviour and a resulting lack of compliance. Current models of assessment of PDs stress the importance of capturing the impact of subsyndromal alterations in a subjects´ personality functioning as well, as those might already interfere with its capacity to implement and maintain behavioural changes, such as dietetic restrictions in type 2 diabetes. The Alternative Model for the Assessment of Personality Disorders (AMPD) of the Diagnostic and Statistical Manual for Mental Disorders of the American Psychiatric Association (DSM-5) [26] and the mental disorder section of the WHO ICD-11 [27] propose a dimensional model of PD diagnosis that focuses on levels of personality functioning regarding the self and relationships. This approach is in line with empirical data from similar research traditions [28], helps to assess subthreshold conditions, and allows for the development of screening instruments [29,30].

Therefore, it is reasonable to ask if alterations in personality functioning on a subsyndromal level outside of PDs also have an impact on the course in a chronic disease such as diabetes type 2, possibly due to the subjects' impairment in regulatory capacities. Consequently, the current study addresses the research question if levels of personality functioning are predictive of severity and course of patients with a first diagnosis of type 2 diabetes talking part in an evidence-based disease management program over and above the impact of depression symptoms. To be more precise, the study aims at the question if depression, personality function, or both will have major impact on changes of HbA1c during a standardized treatment program in diabetes type 2 patients.

2. Subjects, materials and methods

2.1. *Study sample*

The study was approved by the institutional review-board of the Medical Association Northrhine, Germany (Id.-Nr.: 2012422). Over a period of 36 months, all patients with a first diagnosis of a type 2 diabetes of a GP outpatient setting were invited to participate in a naturalistic, longitudinal observational study with three measurement time-points (T0 = first type 2 diabetes diagnosis, T1 = three months follow-up, and T2 = six months follow-up). Exclusion criteria were high age (>80 years), substance dependency, or another medical or psychiatric condition that demanded immediate attention.

2.2. *Intervention*

All patients were treated according to a standardized disease management program (DMP) in Germany. The DMP for type 2 diabetes was designed by health-care professionals and health-care insurances for routine care. It provides disease- and health-related information for patients and GPs, standardizes diagnostic procedures as well outcome evaluation, and establishes routines for evidence-based treatment decisions.

2.3. *Assessments*

At all time-points, plasma glucose concentration (*HbA1c*) was assessed via standardized laboratory measurements. Furthermore, *Body Mass Index* (BMI) was assessed at all time-points as well.

Levels of personality functioning was assessed with the screening version of the *OPD-2 Structure Questionnaire* at T0 [30]. The OPD-SQS is a 12 item questionnaire that measures

levels of personality functioning according to the Levels of Structural Integration Axis (LSIA) of the Operationalized Psychodynamic Diagnosis (OPD-2) [31]. The LSIA is conceptually and empirically closely related to the DSM-5 Levels of Personality Functioning Scale [28,32]. The long version of the OPD-SQS, the OPD-Structure Questionnaire (OPD-SQ) [29], correlates with the interview-based expert-rating to r = 0.62 [33]. The OPD-SQS was developed as a screening version of the OPD-SQ by means of exploratory and confirmatory factor analysis [30]. Consistent with the recommendations of the authors, we used the overall score, which has a range from zero to 48. A higher score of the OPD-SQS reflects impaired personality functioning of an individual with greater problems in personal relationships, affect regulation, impulse control and interpersonal communication.

Depression was measured at T0, T1 and T2 using the German version of the depression module (PHQ-9) of the *Patient Health Questionnaire* [34], with scores ranging from zero to 27. Scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe and severe levels of depressive symptoms [35].

2.4. *Statistical analyses*

Due to the data structure including the dependency of HbA1c measures over time, we applied multilevel regression modelling to predict intercept and slope of HbA1c over the three measurement points by variables measured at T0. This approach is especially suited for questions regarding patient features that can be assessed as risk-factors before the beginning of treatment. We entered PHQ-D and OPD-SQS as centered values as level 2, and modelled time as a linear slope at level 1 of the model. Intercept and slope were set as random with variance components as covariance structure. All analyses were controlled for gender, age, and BMI at T0. As available data on the effect of disease management programs for type 2 diabetes before begin of the study was mixed [36–38], we conservatively estimated a possible low to medium effect of the intervention on our primary outcome variable HbA1c of d = 0.35, resulting in a minimum required sample size of N = 67 (difference between matched pairs, with $\alpha = 0.05$, $1 - \beta = 0.80$, two-tailed, [39] to detect a significant change in HbA1c over time).

3. Results

Recruitment took place between January 1st 2013 and July 30th 2015. During this period, 78 patients were newly diagnosed with a type 2 diabetes, all of them meeting the study criteria. Seventy-five patients (96.2% of the sample) gave their informed written consent, five individuals dropped out over the course of the intervention, resulting in 70 subjects with complete data (89.7% of the initial sample). 45.7% of the participants were female (N = 32), with a mean age around 60 years. Most of the subjects were in a stable partnership and lived in the same household (N = 60, 85.7%). For further information about the sample, see Table 1.

Mean weight of the participants at T0 was 101.15 ± 22.26 kg, indicating overweight. Mean PHQ-9 scores indicated low to mild levels of depression, with six patients experiencing moderately severe levels of depression (PHQ-9 ≥ 10), and 31 patients experiencing moderate levels of depressive symptoms (4 < PHQ-9 > 9). The mean OPD-SQS score was in the lower range as well. PHQ-9 and OPD-SQS at T0 correlated at r = 0.53 (p < .001; Pearson, two-tailed).

Six months later the BMI of the subjects dropped in a small, but significant way (two sample dependent *t*-test t = 5.11, p < .001), but still remained on a level of adipositas grade 1. Levels of depressive symptoms remained stable at 4.54 ± 2.87 after 6 months (t = 1.21, p = .23) (see Table 1).

HbA1c changed from 7.12 ± 1.18% (range 6.2–12.9) [54.93 ± 13.07 mmol/mol (44–117)] at T0 to 6.38 ± 0.76% (range 5.4–11.0) [46.29 ± 8.39 mmol/mol (36–97)] at T1, and to 6.35 ± 0.60% (range 5.1–8.7) [45.93 ± 6.58 mmol/mol (32–72)] at T2 (see Table 1), indicating a medium effect size of d = 0.67 from the first to the least measurement. According to the clinical cut-off score of <6.5%, which is aimed for by the DMP, only 25 (35.7%) subjects had a score >6.5% after 6 months of treatment, while at T0 it had been 60 subjects (80%).

Concerning the key study question, which factors might influence the outcome of a standardized diabetes treatment measured as change in HbA1c after three and six months, multilevel modelling showed a main effect of time on HbA1c-values, indicating a significant decline of plasma glucose concentration during the six months period. In the full model, OPD-SQS was associated with lower levels of HbA1c, but also less steep decline of plasma glucose levels (interaction time × OPD-SQS). In other words, subjects with lower personality functioning (indicated by higher OPD-SQS scores) showed less decline in their HbA1c scores during 6 months than subjects with higher levels of personality functioning. Severity of depressive symptoms were neither associated with levels nor slope of HbA1c over time. No covariate was associated with a higher overall level of HbA1c. Age, gender and even BMI at T0 were not associated with level or decline of HbA1c (see Table 2, Figs. 1 and 2).

4. Discussion

In a sample of 70 patients with a first diagnosis of type 2 diabetes, a standardized, evidence based disease-management program resulted in a significant decrease of HbA1c over a period of 6 months. Lower levels of personality functioning, but not depression, were related to a less steep decline of HbA1c. To our best knowledge, this is the first longitudinal study to simultaneously test the impact of both depression and personality functioning on HbA1c during a standardized intervention in this patient group.

Compared to other data from German DMPs, the results on HbA1c change were large. In a representative evaluation of insurance data published after the completion of our study, the effect size 12 months after the beginning of the intervention was d = 0.28 in patients of 51–60 years of age, and d = 0.22 in patients of 61–70 years of age [40]. Concerning our main hypothesis, we did not find any association between depression and HbA1c. While depression can be related to type 2 diabetes in general [41], other studies also found just a minimal impact on HbA1c specifically [42]. It therefore may be understood as a more distal risk-factor on type 2 diabetes

Table 1 – Participants characteristics (N = 70) at T0 and follow-up.

Variables	T0 (Mean ± SD or N (%))	T2 (Mean ± SD)	t-score (df) (one-sample t-test)
Age (years)	60.24 ± 10.54		
Sex			
Female	32 (45.7)		
Male	38 (54.3)		
Education level			
Less than high school diploma	43 (61.4)		
High school diploma	18 (25.7)		
College degree	3 (4.3)		
Graduate school or degree	6 (8.6)		
OPD-SQS	13.29 ± 6.79		
HbA1c (%)	7.12 ± 1,18	6.35 ± 0.60	5.86 (69)***
BMI (kg/m^2)	33.93 ± 6.56	32.81 ± 6.4	5.11 (69)***
PHQ-9	4.75 ± 3.11	4.54 ± 2.87	1.21 ns

PHQ-9 = Depression dimension of Patients Health Questionnaire; BMI = Body Mass Index; HbA1c = Hemoglobine A1c; OPD-SQS = Screening version of the OPD-2 Structure Questionnaire; T0 = time point prior Intervention; T2 = 6 months after Intervention; ns = not significant.
*** = p < .001.

Table 2 – Predicting HbA1c by depression and levels of personality functioning (Mixed-Model).

Variables	Model I			Model II		
	Coeff.	t-score	df	Coeff.	t-score	df
Level 1						
Time	−0.41	−6.79**	140	−0.40	−6.83***	139
Level 2						
PHQ-9	−0.001	−0.30	205	0.07	1.32	203
PHQ-9 * Time	0.02	0.86	140	−0.01	−0.58	139
OPD-SQS	–			−0.06	−2.54*	203
OPD-SQS * Time	–			0.03	2.50*	139
Covariates at Level 2						
Age	−0.01	−1.28	66	−0.01	−1.30	65
BMI	0.01	0.79	66	0.01	0.68	65
Gender	0.01	0.08	66	0.01	0.13	65
AIC	564.66			571.79		

Note. ***p < .0001; **p < .01; *p < .05. Time = linear slope T0-T1-T2; PHQ-9 = Depression score of the Patient Health Questionnaire; OPD-SQS = OPD-Structure Questionnaire Screener; BMI = Body Mass Index, AIC = Akaike information criterion. All predictors and covariates were measured at T0. Degrees of freedom are presented as rounded numbers of a Satterthwaite approximation used by SPSS.

[14,43]. However, depression itself is associated with lower levels of psychosocial functioning in diabetes [44], and due to high levels of comorbidity between depression and PDs [45], it is reasonable to assume that in a number of studies on the relationship between depression and type 2 diabetes, the effects are at least partly attributable to the impact of personality disorders. In our sample of diabetes patients, the severity of depressive symptoms was relatively low with a mean score of 4.7, and only 8.7% of the patients fulfilling the full-blown diagnosis of depression. Therefore, one could argue that in a sample of diabetes patients with higher levels of comorbid depression, the impact of depressive symptoms might be more pronounced than in our sample. At the same time, according to the incidence of depression in diabetes patients in a GP setting in general [46], our sample represents a rather typical sample from the German health-care system. While it is still important to screen for comorbid depression in diabetes patients [47] to offer adequate treatment, personality functioning might influence the subjects' compliance as well. The impact of personality functioning on a slower decline of plasma glucose in our sample may be attributed to lower levels of trust, compliance, less self-regulatory control, or other behavioural factors such as dysfunctional life style and eating behaviour typically associated with personality disorders [48]. This relates to a recent study on 'brittle diabetes', where Pelizza and Pupo [49] found a higher percentage of personality dysfunction in these glycemically instable patients compared to a sample with stable diabetes.

The effect of a generally lower HbA1c in patients with lower level of personality functioning in comparison to patients with higher level at T0 is somewhat surprising. In accordance to the above mentioned negative impact of psychological factors on the course of diabetes it might be expected that subjects with low levels of compliance, self-

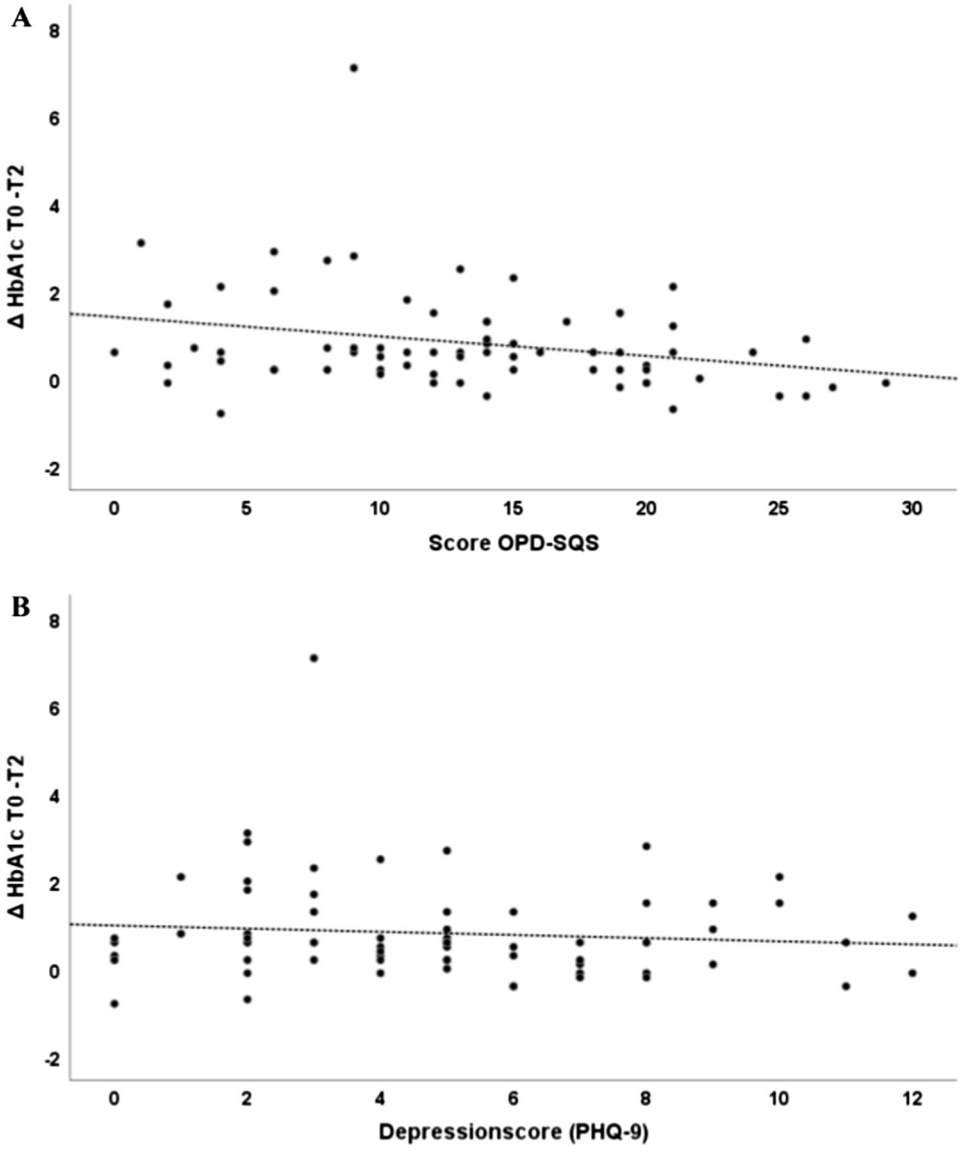

Fig. 1 – Correlation of the amount of HbA1c decline (Δ) after 6 months with level of functioning (OPD-SQS) (A), and amount of depression (B). T0 = admission; T2 = after 6 months; OPD-SQS = OPD-Structure Questionnaire Screener; PHQ-9 = Depression score of the Patient Health Questionnaire.

regulatory control, and self-efficacy should have a higher risk of diabetes in general due to dysfunctional behaviour or a higher percentage of stressful live-events. However, other studies found patients with higher levels of neuroticism to have a lower risk for type 2 diabetes [50], possibly related to a positive impact of more disease-specific worry. Therefore, as in many disorders with a multifactorial aetiology, psychological factors can worsen the course of a chronic organic disorder, but might serve as a protective factor under certain conditions as well. In addition, personality functioning can also be understood as related to other psychological variables such as self-efficacy, alexithymia, or attachment disorganization [51], which can have an impact in a variety of disease conditions [52–54]. Unfortunately, these questions remain to be at the focus of future studies.

Strengths of the study are a clinically relevant sample, three measurement points, low drop-out rates, and a disease management program that makes the intervention comparable across patients. Similarly, we kept the treatment setting constant by just including patients from one GPs office to reduce variance. Multilevel modelling allowed testing the possible impact of depression and levels of personality functioning on HbA1c intercept and slope, while controlling for covariates such as gender, age, or weight. Multilevel modelling is especially suited to simultaneously test the influence of depression and levels of personality functioning over time, which seems reasonable, as both variables correlate with each other.

There are also some limitations to the study. First and foremost, the results need replication in a larger sample. Although the sample size was adequate to detect a change in HbA1c (The adjusted effect of the intervention, with HbA1c values from T0 to T3 correlating at $r = 0.31$, was at a medium level ($d = 0.67$), which resulted in an actual power ($1 - \beta$)

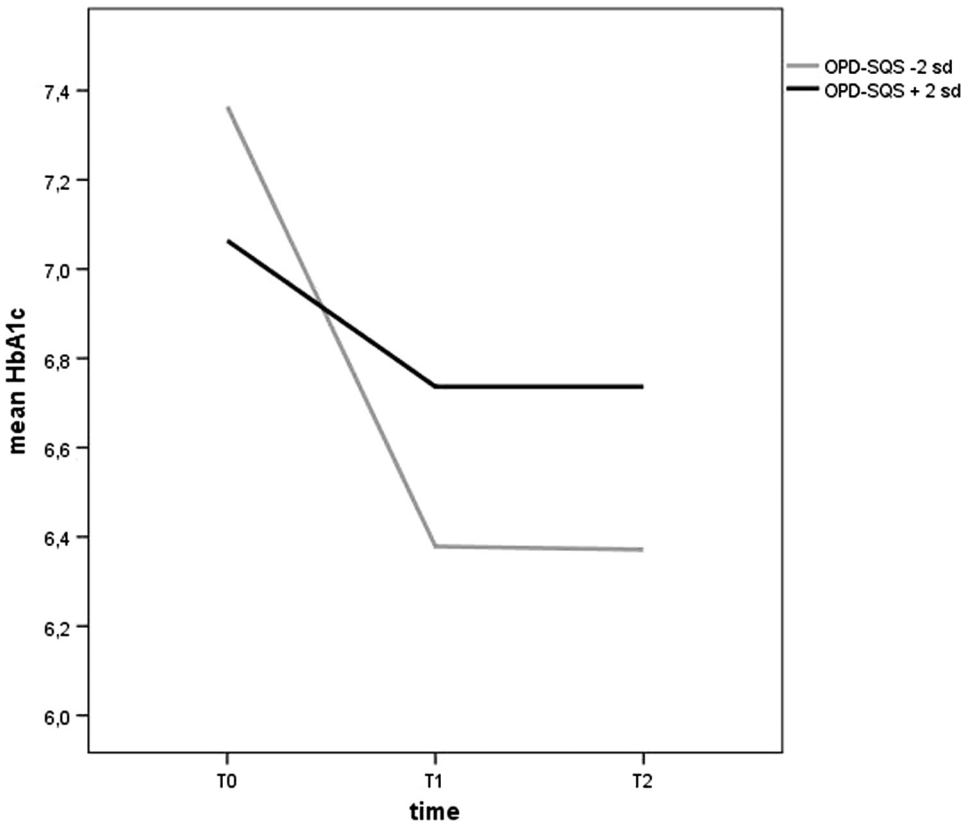

Fig. 2 – HbA1c over time depending on levels of personality functioning. Black line depicts subjects with lower level of functioning, grey line subjects with higher level of functioning. OPD-SQS = OPD-Structure Questionnaire Screener; T0 = admission, T1 = +3 months, T2 = +6 months. To make the effect easier to interpret, the y-axis starts at a value of six instead of zero.

= 0.99.), it would be helpful to include patients with a wider range of depressive symptoms and personality dysfunction. According to PHQ-9 cut-off scores [35], just a small percentage of our sample had a high risk of a major depressive disorder, and the mean value of the OPD-SQS was comparable to other non-clinical samples [30]. In addition, compliance to medical treatment and reduction of risk factors should be measured to understand the less favourable decline of HbA1c in patients with lower levels of personality functioning.

We tentatively conclude that levels of personality functioning may be a variable that deserves further attention in diabetes patients, not only from a research-perspective, but also for GPs. Current dimensional models from DSM-5 and ICD-11 help to screen for subthreshold impairment which can still impact compliance and health-behaviour. This bears the potential to detect a special group of difficult-to-treat patients who are at risk for adherence problems and may benefit from psychotherapeutic support to improve their medical outcome.

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Declaration of interest

None.

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