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Health related quality of life in patients with type I diabetes mellitus: generic & disease-specific measurement

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Background & objectives: An ideal instrument for the assessment of health related quality of life (HRQOL) in patients with diabetes mellitus type I (T1DM) should incorporate the benefits of both generic and disease-specific instruments. The objective of this study was to investigate the responsiveness and the ability to provide information about diabetes-specific associations with HRQOL, of two generic instruments, in comparison with two diabetes-specific instruments, in patients with T1DM.

Methods: In a Dutch cohort of 234 patients with T1DM we longitudinally assessed HRQOL using both generic and diabetes-specific instruments. We investigated the responsiveness, the associations with diabetes-specific variables and the identification of specific patients by the instruments used.

Results: The generic RAND-36 was able to detect statistically significant and clinically relevant changes in HRQOL over time. Moreover, the RAND-36 was associated with (changes in) diabetes-specific variables. The generic and diabetes-specific instruments partly identified different patients with lowest HRQOL.

Interpretation & conclusion: The RAND-36 was highly responsive to changes in HRQOL in patients with T1DM and revealed diabetes-specific associations with HRQOL. A low correlation between the generic and diabetes-specific instruments and partly different identification of patients with lower HRQOL support the complementary use of these instruments in patients with T1DM.

Diabetes mellitus type I (T1DM) permanently changes a person's life. Patient's self care, consisting of daily insulin injections and self-monitoring of blood glucose, has an impact on health related quality of life (HRQOL). Moreover, the acute and long-term complications which might develop will also affect a person's HRQOL[1]. Many different instruments have been developed to measure the physical, psychological and social aspects of HRQOL[2-6]. One can distinguish between generic and disease-specific HRQOL instruments[7,8]. Generic instruments are applicable to healthy people as well as to persons with diseases, and thereby enable comparisons to be made between various groups of patients and general population samples. Moreover, the general public has valued different health states, provided by some generic questionnaires, which makes economic evaluations possible[9-11]. Disease-specific instruments focus on a population with a specific disease and are expected to be more sensitive to treatment effects and changes over time than generic instruments[7,8]. The limitation of these instruments, however, is that the scores such instruments generate remain specific for the affliction studied. Many cross-sectional studies, using different instruments of both types have shown that in TIDM older and female patients, patients without a partner, patient with a lower education, and patients with complications are at risk for a decrease in HRQOL[12-28].

An ideal instrument for the assessment of HRQOL in T1DM should incorporate the benefits of both generic and diabetes-specific instruments. It should be sensitive for changes, provide information about diabetes-specific associations with HRQOL, enable comparisons between various groups of patients or general population samples and make economic evaluations possible.

The aim of this study was to investigate these properties of two generic instruments in the assessment of HRQOL in T1DM. In addition, the feasibility of these instruments and the clinical relevance of their results were also investigated.

We therefore examined whether the generic instruments used in our study are capable of measuring (clinically relevant) changes in HRQOL in patients with T1DM and whether these generic instruments can identify diabetes-specific associations with HRQOL. An additional aim was to examine whether diabetes-specific and generic instruments identify the same patients, when low HRQOL scores are assessed.

Material & Methods

Patients: In 1995 a total of 293 consecutive T1DM patients seen at the outpatient clinic of the Isala Clinics in Zwolle, the Netherlands, were invited to participate in the study. Of these, 281 patients agreed and were investigated from 1995 onwards on a yearly basis. T1DM was defined as starting insulin therapy within six months after the first signs of diabetes mellitus and before the age of 30 yr, or the absence of C-peptide secretion. Ethics committee approval was obtained from the Hospital Scientific and Ethics Committee. Informed consent was obtained from all patients.

Health related quality of life (HRQOL): Two different, frequently applied generic instruments, the RAND-36 and the EuroQol, which have both been translated and validated for the Dutch situation were used. In addition, two different diabetes-specific instruments (Problem Areas In Diabetes, Fear of Hypoglycamia Scale) were used to measure some diabetes-specific aspects of HRQOL and to make comparisons possible with the generic assessments[9,29-31].

These four instruments were sent to the patient's home address in one package. Patients were asked

to fill in the questionnaires at home. At the next visit to the outpatient clinic the patients returned the completed questionnaires to the diabetes specialist nurse. Patients who did not return the completed questionnaires when visiting the clinic were asked to send their completed questionnaires afterwards. The RAND-36 is a self-administered, generic questionnaire containing 36 items involving eight different subscales. For each subscale, scores are transformed to a scale from 0 (worst health) to 100 (best health)[30,32]. In addition, physical and mental component summary scores can be determined (PCS/MCS)[33]. The questionnaire takes about ten minutes to complete. The instrument has been translated into Dutch[34] and validated for the Dutch population[35]. The RAND-36 was assessed yearly.

The Euroqol (EQ): The EuroQol was developed by a multidisciplinary group of researchers from five European countries to describe and value health states[9]. It is a generic, multidimensional measure, consisting of two parts, and takes about 2 min to complete by the patient.

The first part consists of five questions covering 5 dimensions (EQ-5D). Each dimension is divided into 3 levels: 'no problem', 'some/ moderate problems' and 'extreme/ unable to'. A respondent's health state is defined by combining one level from each of the 5 dimensions. A total of 243 possible health states can be defined in this way. Valuations of these health states have been made, by the U.K. general public, using time trade-off[36]. The set of possible values has a range of -0.594 to 1, where 1 is the value of perfect health, 0 is the value of death and –0.594 indicates the worst possible health state, which is viewed by the general public as considerably worse than death.

The second part, a single overall score, can be gained from a "thermometer": a self-rated health status using a graduated (0-100) visual analogue scale (EQ-VAS), in which 0 indicates worst HRQOL and 100 best possible HRQOL. The EuroQol has been validated for the Dutch situation[37]. The EQ was assessed in 1995 through 1998, and in 2001.

The problem areas in diabetes survey (PAID): The PAID was developed as a new measure of psychosocial adjustment to diabetes. It is a diabetes-specific, unidimensional instrument. The instrument can be scored quickly, in 3-5 min, by the patient. Its primary aim is to tap the breadth of emotional responses to diabetes[31,38]. The PAID is a 20-item questionnaire in which each item represents a unique area of diabetes-related psychosocial distress. The items are divided over four areas. A total score, hypothesised to reflect the overall level of diabetes-related emotional distress, is computed by summing the 20 item responses. It is scored on a scale of 0 to 100, with higher PAID scores indicating greater emotional distress. Reliability and validity are good[31,38] and the PAID has been validated for the Dutch situation[39]. The PAID was assessed in 1998 and 2001.

The fear of hypoglycaemia scale (FHS): The FHS was developed as a research and clinical tool measuring the degree of fear experienced with respect to hypoglycaemia[29]. Worries about hypoglycaemia as well as behaviour designed to avoid hypoglycaemia are examined. It is a diabetes-specific, unidimensional measure. The scale consists of 23 items: 13 items concerning worry and fear and 10 items concerning behaviour or avoidance. The 13 worry items can be summed to a Worry subscale, while the 10 behaviour items can be summed to a Behaviour subscale. Together, the two subscales can be summed to create the total FHS-score, a higher score indicating greater fear for hypoglycaemia[40]. Various studies support the validity and the reliability of the FHS[29,40]. We only used the Worry subscale, since at the time of the study the validity of the behaviour subscale was discussed[40,41]. The Worry subscale was assessed in 1997 and 2001.

Clinical data: Socio-demographic data including sex, age, marital status and level of education were recorded. Therapy-specific data were recorded and included pen-/ pump use, frequency of insulin injections and number of blood glucose control measurements per week. Metabolic control was assessed by measuring glycosylated haemoglobin A1c (HbA1c). The acute complications of the therapy were also recorded; patients recorded all hypoglycaemic events during the three months preceding the outpatient visit. Patients were asked to report whether they had one or more of six different hyperglycaemic complaints during the previous three months (yes/ no): tiredness, weight loss, pruritus, thirst, polyuria and polydipsia.

Using a list of 26 chronic diseases/ diagnoses the patients could indicate which other diseases they had besides diabetes[42]. When they indicated one or more chronic diseases, apart from diabetes mellitus, they were scored as having comorbidity.

Chronic complications

Microvascular complications-Patients with retinopathy, neuropathy or nephropathy were categorised as having microvascular complications.

Retinopathy-The ophthalmologist examined all patients annually. The degree of diabetic retinopathy was assessed by fundoscopy in mydriasis. The classification of diabetic retinopathy used was based on de Jong[43]: no retinopathy (=0), background retinopathy (=I), preproliferative (=II) and proliferative diabetic retinopathy (=III). Retinopathy was scored positive when any type of retinopathy was present in either eye. When the degree of retinopathy was different in two eyes, the highest degree was scored.

Neuropathy-Sensitivity was tested by the Semmes-Weinstein pressure aesthesiometer[44]. At five

dorsal and plantar sites on the foot (left and right) sensibility was tested with six different monofilaments. When the monofilament 5.07 was not felt at one of the ten test sites, patients were considered to have neuropathy.

Nephropathy-The 24 h urinary excretion of albumin (UAER) was measured annually. UAER was considered abnormal when it was >30 mg/24 h. Micro-albuminuria was defined as 30-300 mg/ 24 h and macro-albuminuria as >300 mg/24 h. All patients with micro-albuminuria or macro-albuminuria were defined as having nephropathy[45-47]. At the Isala clinics, patients with micro-albuminuria >100 mg/24 h received an angiotensin converting enzyme inhibitor (ACE-inhibitor) in 1995. We included ace-inhibitor users, even with normalbuminuria, as having nephropathy, when treatment was initiated for micro-albuminuria at an earlier stage.

Macrovascular complications-The clinician recorded the status of macrovascular complications. Patients were classified as having macrovascular complications when one or more of the following diagnoses was present: angina pectoris, myocardial infarction, intermittent claudication, transient ischaemic attack (TIA), or a cerebrovascular accident (CVA).

Statistical analysis-Responsiveness of the RAND-36 and the EuroQol was investigated in patients with T1DM, to answer the question whether these generic instruments are sensitive for changes in HRQOL. Although responsiveness is considered to be an essential property of an evaluative instrument, the methodology of assessing reponsiveness tends to be less well understood[48].

In this study three methods were applied to investigate responsiveness of the generic instruments

used in our cohort. Firstly, we investigated the ability to detect, longitudinally, statistically significant changes in HRQOL over time (1998-2001) using paired sample T-tests. Since the diabetes-specific instruments were assessed only in 1998 and 2001, we used this time interval.

Secondly, we investigated whether the observed changes were also clinically relevant. The developers of the RAND-36 and the EuroQol do not provide cut-off points for clinically important changes in HRQOL scores. However, changes of >2-5 points for the RAND-subscales and >1 point for the RAND summary scores are sometimes considered as the smallest clinically significant changes[32,49,50]. For the EQ-5D and the EQ-VAS, 0.05 points and five points can be used as a rough guide although formally the EuroQol Group has not published any minimally significant values.

Finally, we investigated whether the generic instruments assessed changes in HRQOL when changes were expected on the basis of changes in diabetes-specific clinical characteristics. We

Table I. Personal and disease-specific characteristics of the study population (n=234)

	1995	1998	2001
Gender (men)	134 (57.3%)	134 (57.3%)	134 (57.3%)
Age (yr)	38.2 11.5)	41.2 (11.5)	44.2 (11.5)
Duration of diabetes (yr)	16.5 (10.1)	19.5 (10.1)	22.5 (10.1)
Married/ cohabiting	207 (90.8%)	194 (89.4%)	189 (87.9%)
High level of education	76 (33.6%)	72 (34.0%)	76 (35.5%)
Systolic blood pressure (mm Hg)	138.9 (17.8)	131.1 (19.4)	131.5 (19.2)
Diastolic blood pressure (mm Hg)	83.0 (8.4)	79.4 (10.2)	77.8 (10.4)
Body mass index (kg/m^2)	24.8 (3.2)	25.6 (3.6)	26.1 (4.0)
HbA1c (%)	8.1 (1.9)	7.9 (1.3)	7.6 (1.1)
Insulin pump	63 (26.9%)	76 (32.6%)	102 (43.6%)
Insulin pen	171 (73.1%)	157 (67.4%)	132 (56.4%)
Frequency of insulin pen injections (per day)			
1-3	24 (14.0%)	22 (14.0%)	19 (14.4%)
4	147 (86.0%)	128 (81.5%)	108 (81.8%)
>4	0 (0.0%)	7 (4.5%)	5 (3.8%)
No. of control measurements (per wk)	12.0 (11.3)	18.2 (14.4)	20.0 (15.2)
Patients with:			
Hypoglycaemic events last 3 months	185 (80.8%)	180 (84.9%)	173 (87.4%)
Hyperglycaemic complaints last 3 months	122 (53.3%)	105 (50.5%)	116 (58.3%)
Comorbidity (at least one comorbid condition)	133 (58.1%)	130 (62.5%)	107 (52.7%)
Patients with diabetic complications			
Microvascular	104 (45.8%)	111 (58.1%)	119 (65.7%)
Retinopathy	79 (34.6%)	88 (44.9%)	99 (48.5%)
Nephropathy	43 (18.4%)	33 (16.7%)	45 (23.0%)
Neuropathy	24 (10.4%)	32 (15.2%)	23 (12.2%)
Macrovascular	10 (4.3%)	- -	23 (9.8%)

Values are number of patients (with valid percentages between parentheses) or means (with standard deviation between parentheses)

expected a decrease in HRQOL for the patients who developed microvascular complications between 1998 and 2001 and compared the means of the patients who developed microvascular complications and of the patients who did not (using the Mann Whitney test).

To investigate whether the generic instruments can provide information about diabetes-specific influences on HRQOL, we did multivariate stepwise regression analyses to investigate cross-sectional associations of HRQOL scores with several demographic and disease-specific patient characteristics (in 2001). The different HRQOL scales were the dependent variables and all the personal and disease specific variables (Table I) were the independent variables. We used the adjusted R^2 (result of the multivariate regression analysis) to describe the degree of variance in HRQOL explained by the model.

To investigate whether diabetes-specific and generic instruments identify the same patients, we calculated correlations between the different instruments using Spearman rank correlation coefficients. Moreover, for each instrument the 10 per cent lowest and 10 per cent highest scores (in 2001) were defined and the patients, thus identified by the different instruments, were compared. Finally, we described several feasibility characteristics of the instruments, to provide practical information for the use of these instruments.

Relationships were considered statistically significant with $P<0.05$. Data were analysed using SPSS for Windows, version 10.0.

Results

A total of 281 adult patients with type I diabetes mellitus entered the study in 1995.

The dropout rate over these six years was 16.7 per cent (n=47). Dropouts were more frequently women (59.6 vs. 42.7%, *P*=0.04), more often single (24 vs. 9.2%, *P*=0.01), had a longer disease-duration (20.6 vs.16.5 yr, *P*=0.05), and a higher HbA1c (9.0 vs. 8.1, *P*=0.007) and reported a lower baseline HRQOL.

Personal and disease-specific characteristics of the patients who completed the study period of six years are shown in Table I (n=234). Data are shown for the years 1995, 1998 and 2001. Mean age at entry

Table II. Health related quality of life in 1998 versus 2001

	1998	2001	*P* value
RAND-36:			
Physical functioning	91.0 (15.8)	87.3 (19.0)	0.004
Role physical	81.2 (33.3)	76.2 (37.8)	0.070
Bodily pain	87.5 (19.9)	83.6 (20.2)	0.016
General health	66.8 (18.9)	64.4 (20.3)	0.015
Vitality	68.3 (19.8)	61.6 (20.0)	<0.001
Social functioning	86.5 (18.6)	84.2 (20.3)	0.086
Role emotional	83.0 (35.5)	83.5 (32.6)	0.913
Mental health	79.9 (15.9)	77.1 (16.1)	0.004
Physical summary score	51.5 (7.6)	49.8 (9.1)	0.006
Mental summary score	51.7 (9.5)	50.9 (9.3)	0.176
EuroQol:			
EQ-5D	0.87 (0.18)	0.85 (0.19)	0.191
EQ-VAS	77.1 (14.4)	76.0 (13.5)	0.054
PAID:			
Diabetes related	13.8 (11.8)	14.9 (12.0)	0.073
Treatment related	1.7 (2.7)	2.2 (2.9)	0.030
Food related	2.5 (2.7)	2.4 (2.6)	0.862
Social support related	1.1 (1.9)	1.1 (1.8)	0.808
Total score	19.5 (17.2)	20.5 (17.5)	0.254
Hypoglycaemia fear:			
Worry subscale	10.9 (8.4)[*]	10.7 (8.0)	1.000

Values are means with standard deviations between parentheses
P values are based on paired sample T-Tests
HRQOL data in this table are based on 213-220 patients, resulting in 204-213 paired samples
Worry subscale was assessed in 1997
EQ-5D, EuroQol utility index; EQ-VAS, EuroQol Visual Analogue Scale; PAID, Problem Areas in Diabetes

was 38.2 yr, and 57.3 per cent were men. The percentage of patients using a pump increased from 26.9 per cent in 1995 to 32.6 per cent in 1998 (*P*=0.002) to 43.6 per cent in 2001 (*P*<0.001). The therapy was intensified over the six-year study period. An increased number of control measurements per week, a lower HbA1c and rise in body mass index were observed over this period. The percentage patients with hypoglycaemic events did not increase significantly between 1995 and 2001. The percentage of patients with microvascular complications increased from 45.8 per cent in 1995 to 58.1 per cent in 1998 (*P*=0.005) and later to 65.7 per cent in 2001 (*P*=0.248). In 1995 the percentage of patients with macrovascular complications was 4.3 per cent and in 2001 9.8 per cent (*P*<0.001).

Ability to detect change in HRQOL over time: RAND-36. Five subscales of the RAND-36 and the PCS showed a statistically significant decrease in HRQOL over time. The subscales role physical and social functioning and the mental component summary tended to decrease, whereas the subscale role emotional remained stable between 1998 and 2001. Seven RAND-subscales and the PCS showed a clinically relevant change over time within this study period. The subscale role emotional and the

MCS did not show a clinically relevant change in HRQOL over time (Table II).

EuroQoL: The EQ-5D as well as the EQ-VAS tended to decline between 1998 and 2001. This decline was not statistically significant and/ or clinically relevant. In both years the percentage of patients with the highest possible EQ-5D score was high (52.3 and 46.6% respectively).

PAID: The problems related to treatment increased after 3 yr follow up (*P*=0.03). The diabetes related problems and the total score tended to increase, whereas the problems related to food and social support remained stable over time.

Hypoglycaemia fear: The degree of worry was not increased after the 3 yr period (Table II).

Ability to detect real changes in the concept being measured: The patients, who developed microvascular complication(s) between 1998 and 2001 reported a faster decrease in MCS and EQ-5D than the patients without new microvascular complication(s) [MCS -4.85 vs+0.26, *P*=0.006 and EQ-5D -0.09 vs. +0.02, *P*=0.013)].

Table III. Results of the multivariate regression analysis of health related quality of life scores in 2001

	PCS	MCS	EQ-5D	EQ-VAS	PAID-total	Worry subscale
R²	0.243 (n=180)	0.075 (n=192)	0.180 (n=177)	0.157 (n=177)	0.083 (n=184)	0.038 (n=201)
Intercept	55.4	54.6	0.96	82.9	14.4	19.77
HbA1c						-1.29 (*P*=0.014)
Hyperglycaemia	- 4.71 (*P*<0.001)	-5.03 (*P*<0.001)	-0.09 (*P*<0.001)	-6.80 (*P*<0.001)	10.85 (*P*<0.001)	
Co-morbidity	- 2.78 (*P*=0.018)		-0.05 (*P*=0.033)			
Macrovascular complications	-10.03 (*P*<0.001)		-0.135 (*P*=0.002)	-11.6 (*P*=0.001)		

R², Adjusted R square; Intercept, mean value of the population; PCS, physical component summary; MCS, mental component summary; EQ-5D, EuroQol utility index; EQ-VAS, EuroQol Visual Analogue Scale; PAID, problem areas in diabetes

Ability to provide information about diabetes-specific associations with HRQOL: Table III shows the results of the multivariate stepwise regression analyses. The explained variance in HRQOL varied from 3.8 (Worry scale) to 24.3 per cent (PCS). Only four characteristics showed a statistically significant association with a HRQOL scale; the presence of hyperglycaemic complaints, co-morbidity and macrovascular complications were all negatively associated with HRQOL. A lower HbA1c was associated with more worries about hypoglycaemia (P=0.014). Both generic instruments revealed a negative association between the presence of comorbidity and HRQOL (PCS and EQ-5D).

The presence of macrovascular complications had the most pronounced negative association with HRQOL; these patients reported a lower PCS, EQ-5D, EQ-VAS. Patients with hyperglycaemic complaints also had a lower HRQOL (PCS, MCS, EQ-5D, EQ-VAS) and reported more diabetes related emotional distress (PAID).

Identification of specific patients: Table IV shows the Spearman rank order correlations between the different instruments.

Generic/generic - the PCS showed a strong correlation with the EQ-5D and a moderate correlation with the EQ-VAS. The MCS was

Table IV. Spearman rank order correlations between the different quality of life scales

	PCS	MCS	EQ-5D	EQ-VAS	PAID-total	Worry subscale
PCS	-					
MCS	0.071 (P=0.303)	-				
EQ-5D	0.643 (P<0.001)	0.409 (P<0.001)	-			
EQ-VAS	0.531 (P<0.001)	0.557 (P<0.001)	0.613 (P<0.001)	-		
PAID	-0.263 (P<0.001)	-0.457 (P<0.001)	-0.293 (P<0.001)	-0.432 (P<0.001)	-	
Worry subscale	-0.219 (P=0.002)	-0.402 (P<0.001)	-0.281 (P<0.001)	-0.296 (P<0.001)	0.627 (P<0.001)	-

PCS, physical component summary; MCS, mental component summary; EQ-5D, EuroQol utility index ; EQ-VAS, EuroQol Visual Analogue Scale; PAID, problem areas in diabetes

Table V. Percentage of patients with 10 per cent lowest HRQOL identified by both instruments

	PCS	MCS	EQ-5D	EQ-VAS	PAID	Worry subscale
PCS	-	9.5	50.0	60.0	19.1	20.0
MCS	9.5	-	33.3	38.9	42.1	30.0
EQ-5D	58.8	29.4	-	72.2	23.5	25.0
EQ-VAS	41.4	24.1	46.4	-	26.7	21.4
PAID	21.1	42.1	33.3	47.1	-	55.6
Worry subscale	17.4	26.1	21.1	28.6	43.5	-

PCS, physical component summary; MCS. mental component summary; EQ-5D, EuroQol utility index; EQ-VAS, EuroQol Visual Analogue Scale; PAID, Problem Areas in Diabetes

moderately correlated with the EuroQol scales. The PCS and MCS were not correlated, inherent to the method we chose to calculate the summary scores[33].

Diabetes-specific/diabetes-specific - the PAID was strongly correlated with the Worry subscale.

Generic/diabetes-specific - The PCS and EQ-5D correlated only weakly with the more psychological health scales (*i.e.*, the PAID and the Worry subscale), whereas the MCS and EQ-VAS correlated moderately with the PAID and the Worry scale (MCS).

Table V shows the extent to which the instruments identified the same patients within the 10 per cent lowest HRQOL range. The percentage of agreement was highest between the PCS, the EQ-5D and EQ-VAS. For example, of the patients with the 10 per cent lowest PCS scores, 60 per cent reported lowest EQ-VAS scores. Of the patients with the highest hypoglycaemia worry scores, only a quarter

was found in the lowest MCS-score category (26.1%). Patients reporting most diabetes-related emotional distress had in 42.1 per cent lowest MCS scores.

Table VI shows that of the patients with the 10 per cent highest Worry and PAID scores, here defined as having the least worries about hypoglycaemia and problems about diabetes, only 15.8 and 26.7 per cent of the patients, respectively had highest MCS scores.

Feasibility: Table VII shows several feasibility data of the instruments used in our cohort. All four instruments led to very high percentages of valid scores.

Discussion

In our study we followed a Dutch cohort of 234 patients with T1DM for three years. We used both generic and diabetes-specific HRQOL instruments to assess HRQOL.

Table VI. Percentage of patients with 10 per cent highest QOL identified by both instruments

	PCS	MCS	EQ-5D	EQ-VAS	PAID	Worry subscale
PCS	-	9.1	63.6	25.0	30.0	18.2
MCS	9.5	-	47.6	38.0	40.0	15.0
EQ-5D	14.6	10.4	-	15.6	17.4	12.8
EQ-VAS	25.0	40.0	75.0	-	42.1	35.0
PAID	20.0	26.7	53.3	27.6	-	31.0
Worry subscale	21.1	15.8	66.7	35.0	56.3	-

PCS, physical component summary; MCS, mental component summary; EQ-5D, EuroQol utility index; EQ-VAS, EuroQol Visual Analogue Scale; PAID, problem areas in diabetes

Table VII. Several feasibility data of the different instruments used in the cohort

	No. of subscales	No. of items	Total score	Completion time in min	Suitable for self-assessment	Valid scores (1998)
RAND-36	8	36	Yes	10	Yes	92.3-93.6%
EuroQol	5	6	Yes	2	Yes	93.2-93.6%
PAID	4	20	Yes	3-5	Yes	89.7-92.7%
HFS	2	23	Yes	3	Yes	92.7%*

PAID, problem areas in diabetes; HFS, hypoglycaemic fear survey; *based on worry subscale

A central question was how well the generic RAND-36 and EuroQol capture changes in HRQOL in patients with T1DM and whether they provide information about diabetes-specific associations with HRQOL. Moreover we examined the feasibility and the clinical relevance of their results. Could these generic instruments replace the diabetes-specific instruments in the assessment of HRQOL in T1DM?

The responsiveness of the generic RAND-36 was good: it was sensitive to changes in HRQOL over three years and the changes could also be considered clinically relevant. Moreover, the RAND mental summary score (MCS) was associated with a change in a diabetes-specific characteristic. The onset of microvascular complications was associated with a decrease in MCS, which we can explain by the fact that the knowledge of having a microvascular complication will negatively influence mental health. Very likely the PCS will be influenced negatively later, when the severity of the microvascular complications is increased, and the complications become symptomatic. These symptoms will influence patient's functioning and thereby HRQOL indirectly[51].

The responsiveness of the EQ was limited. The mean observed changes in EQ between 1998 and 2001 were neither statistically significant nor clinically relevant. Moreover, this instrument showed a considerable ceiling effect, in that half of the patients reported the best possible HRQOL. This inability of the EQ to differentiate between small differences in the highest HRQOL ranges has previously been described[52,53]. Nevertheless, the EQ-5D decreased when microvascular complications developed.

Patients reported more treatment related problems in 2001 than in 1998. Earlier studies provided support for the responsiveness for changes of the PAID[54]. Indeed therapy was intensified during that period. No associations were found between PAID scores and objective factors of intensified therapy (*i.e.*, pump use/ more than 4 times daily pen injection, higher frequency of self monitoring blood glucose, lower HbA1c) or the possible side effects of an intensified therapy (weight gain and more hypoglycaemic events) and PAID scores. The PAID scores purely reflected patient's subjective self-report and evaluation of problems concerning treatment. The Worry subscale did not show changes over time. Although the HbA1c declined significantly, the number of patients that reported hypoglycaemic events did not increase significantly, which might explain this result.

We therefore conclude that the generic RAND-36 was highly responsive to changes in HRQOL over time and to changes in a diabetes-specific variable.

Both the RAND-36 and the EuroQol provided information about diabetes-specific influences on HRQOL. Hyperglycaemia and the presence of macrovascular complications were associated with a lower HRQOL. The generic instruments showed a lowered HRQOL in the presence of non-diabetic morbidity (co-morbidity), whereas the diabetes-specific instruments did not. Woodcock *et al*[55] reported in a general practice T2DM population the negative influence of co-morbidity on generic measured HRQOL and used this finding to support the complementary use of generic and disease-specific instruments.

Although the PCS is a generic measure, the model used to explain variance in PCS resulted in the largest percentage explained variance (*i.e.*, 24.3%). This percentage was much lower for the MCS, the EuroQol, the Worry subscale of the HFS and the PAID. This suggests that it is easier to explain variance in the more physical aspects than in the more mental aspects of HRQOL. The RAND-36 is multidimensional and approaches HRQOL as broadly

as possible, including physical, psychological and social aspects. In contrast, the HFS worry scale and the PAID are uni-dimensional and focus on a small though important portion of the concept HRQOL of patients with T1DM[56].

We can state that the generic RAND-36, and the EQ in a less degree, gave information about diabetes-specific influences on HRQOL. This information was partly different from that provided by the diabetes-specific, uni-dimensional instruments used in our study[2,4,38,56,57].

The low correlations between the generic and diabetes-specific instruments used in our study suggest that these instruments measure different aspects of health. Indeed, rather different aspects, ranging from problems with one's job ('did you have any problem with your work as result of your physical health?' RAND-36) to fear for hypoglycaemia ('do you worry about passing out in public?' HFS) are assessed[2]. When instruments have a low correlation, a complementary use of these instruments can give additional information.

The generic and diabetes-specific instruments in our study only partly identified the same patients with the lowest or highest HRQOL. When a clinician wishes to identify and select patients who are at greatest risk of a worsening in HRQOL, the choice of the instrument will influence which patients will be identified. For example, for patients showing poor glycaemic control, a clinician can wonder whether these patients are more afraid of hypoglycaemic events than others, since this fear can lead to non-compliance and poor glycaemic control. This specific question should lead to a carefully considered choice of instrument, and in this case, the HFS would be the most appropriate choice.

Although the RAND-36 questionnaire consists of more items and takes longer to complete than other instruments, this did not lead to a lower response rate or a lower percentage of valid scores. Apparently, the length of this instrument and the longer completion time were not a problem in this group of patients.

In conclusion, the generic RAND-36 appears to be very sensitive to changes in HRQOL in a cohort of patients with T1DM. Although the RAND-36 is a generic instrument, it provides information about diabetes-specific associations with HRQOL. The generic and diabetes-specific instruments show low correlations and identify for the most part different patients with the lowest HRQOL. We recommend the use of the RAND-36 for assessing HRQOL in patients with T1DM. The complementary use of a diabetes-specific measure like the PAID and the HFS will give additional information about the psychological status of patients with T1DM.

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