Impact of monitoring health-related quality of life in clinical practice in children with type 1 diabetes mellitus

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Accepted: 9 August 2017
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Abstract

Purpose To test whether the systematic monitoring of health-related quality of life (HRQOL) in clinical practice in Spanish pediatric patients with T1DM helps improve their daily life in a multicenter longitudinal study.

Methods One hundred thirty-six patients participated, recruited from five centers in Barcelona, Spain (72 girls, mean age 13.4 years). Complete data were collected for 119 patients (85%). Pediatricians were randomly assigned to the HRQOL intervention ($n = 70$), or control group ($n = 49$). The intervention group discussed the results of HRQOL face to face with the physician, quarterly over a year. The control group received care as usual. HRQOL was assessed using KIDSCREEN-27 collected online. Standardized mean differences (effect size, ES) and generalized estimating equation (GEE) were computed to compare group differences between baseline and follow-

up, taking into account sociodemographic and clinical variables.

Results Statistically significant higher scores were seen in the intervention group at follow-up for the dimensions of Psychological well-being ($ES = 0.56$), School environment ($ES = 0.56$), and the KIDSCREEN-10 index ($ES = 0.63$). No differences were found in the control group. GEE analysis showed an improvement in HRQOL at follow-up with statistically significant association of the intervention on Psychological well-being ($B = 4.32$; $p 0.03$ for the interaction of group by follow-up) and School environment ($B = 4.64$; $p 0.02$ for the same interaction term).

Conclusions Routine assessment and face-to-face patient-physician discussion of HRQOL results improved HRQOL scores after a year of follow-up, especially in Psychological well-being and school environment. The results support the routinary use of HRQOL assessment in clinical practice.

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Keywords Adolescents · Children · Health-related quality of life · Pediatric · Type 1 diabetes

Introduction

Type 1 diabetes mellitus (T1DM) is a chronic disease that affects all aspects of the patient's life, especially psychologically [1, 2], which in turn has a direct influence on the care and management of the disease [3, 4]. On the other hand, hormonal and psychosocial changes that occur during puberty make this stage a difficult time with high metabolic instability [5, 6]. Health-related quality of life (HRQOL) assessment has become an important outcome measure in patients with chronic conditions [7–9]. Current clinical guidelines recommend the assessment of HRQOL in children and adolescents with T1DM as well as adult population [7, 10]. A systematic review on the impact of T1DM on HRQOL showed similar HRQOL compared to healthy peers, and a negative impact of diabetes was found on daily functioning, and some diabetes-related worries [11]. In Spain, to our knowledge, only one descriptive study on children and adolescent with T1DM has been published showing that the most affected dimension was anxiety/depression, mainly in older adolescents [12].

Information and communication technologies (ICT), such as Internet, are increasingly used in a variety of pediatric chronic conditions [13, 14] to assess health outcomes [15], as well as to facilitate patient-physician communication [16]. For example, a web-based application to systemically monitor HRQOL problems in clinical practice in children with juvenile idiopathic arthritis showed its effectiveness in increasing awareness of psychosocial topics in both the patient and the patient's family [17]. Moreover, monitoring HRQOL is increasingly advocated to be included in routine care, although with difficulties for implementation [18].

Few experiences to date have been published on the use of HRQOL questionnaires in daily clinical practice in children and adolescents with T1DM [19]. A study carried out in the Netherlands, showed an improvement in self-esteem and satisfaction with care after a year of routine assessment in the intervention group, whose HRQOL had been assessed and discussed as part of periodic consultations, and no significant changes were found on metabolic control. Authors also found that the positive effect disappeared after a year of the end of the study, returning to the baseline scores [20]. It is necessary to confirm these results in other contexts and to increase knowledge about the use of technologies to assess health outcomes in routine pediatric clinical practice.

The objective of the study was to assess whether the systematic monitoring of HRQOL via Internet in clinical

practice in Spanish pediatric patients with T1DM helps improve their daily life with diabetes. It was hypothesized that continued use of KIDSCREEN and discussion on HRQOL among patients and their physicians at each routine check-up would result in a better HRQOL on psychosocial dimensions at follow-up in the intervention group, compared with the control group. It was not expected to find significant differences in metabolic control between groups, but the intervention group may have fewer decompensations than the control group.

Methods

This is a longitudinal study in a cohort of children and adolescents with T1DM, which analyzed the routine assessment of HRQOL through internet using generic instruments, and compared the results with a control group.

Participants and procedures

Patients were consecutively recruited from a list of 205 potential candidates (104 girls) with T1DM attending outpatient pediatric endocrinology of 5 hospitals in the Barcelona province area, Spain (all 7 pediatric endocrinologists from these hospitals participated in the study), between July and December 2014. Mean age was 13.6 years (standard deviation [SD] 3.0, range 8–21), the average time of diabetes duration was 5 years. Exclusion criteria were less than 6 months from diagnosis of T1DM, less than 8 years old at the time of recruitment, cognitive problems that prevented comprehension of the questionnaires, and patients who declined to participate in the study.

Families that fulfilled inclusion criteria and agreed to participate were provided with a letter explaining the characteristics of the project and the need to access to digital questionnaires 48 h before the follow-up visits. After agreeing to participate in the study, parents answered a paper questionnaire administered during this visit.

Seven pediatric endocrinologists were randomly assigned to either the HRQOL intervention or the control group. There were four pediatricians in the intervention group and three in the control group. Pediatrician randomization was used rather than patients', to avoid contamination at pediatricians' level. During the 12-month study period all patients were visited quarterly at the outpatient clinics, and at each visit different clinical variables related to the T1DM were collected. All patients completed the self-administered questionnaire, including the online version of KIDSCREEN at home, within 48 h before visit

1 and 4, while the intervention group completed the HRQOL assessment before every visit. Those patients without Internet at home completed the questionnaire at the hospital during the waiting time for the visit. The web-version of the questionnaires was developed through a generic internet tool, using Ruby on Rails applications and a MySQL database (<http://rubyonrails.org>).

Study variables

Sociodemographic variables were collected from parents, clinical variables came from clinical records, and HRQOL, mental health, and adherence to treatment came from the self-administered online questionnaire.

Sociodemographic variables were: age, sex, the highest family level of education (primary, secondary or university degree); family origin (native vs immigrant if both parents and/or the patient was born in a developing country); family type (single-parent vs bi-parental family), and hospital. The Family APGAR questionnaire was collected to determine family dysfunction, stratified as family dysfunction (score ≤ 6) vs family function (score 7–10) [21]. The Family Affluence Scale (FAS), a self-reported socioeconomic indicator, was collected into eight categories ranging from 0 to 7, which were recoded into 3 groups in the analysis (low [0–3], intermediate [4, 5], and high [6, 7] FAS level) [22].

Clinical variables analyzed at each visit were: time since diagnoses (in years), type of insulin therapy (multiple daily injections [MDI] or pump therapy, the latter received only by three patients); and use of insulin bolus calculator or not. Decompensation in the last 3 months was assessed as significant hypoglycemia (<60 mg/dl) with decreased level of consciousness requiring glucagon or the help of others to be reversed and significant hyperglycemia (>400 – 450 mg/dl) which required intervention of professionals. The HbA1c was used as a measure of metabolic control by determination in capillary blood (DCA 2000 Bayer/Siemens®) or serum in an analytical laboratory (HPLC). Weight, height, and body mass index (BMI, Z score) were also collected [23].

The self-reported KIDSCREEN-27 was assessed by its 5 dimensions: physical well-being (5 items), psychological well-being (7), autonomy and relationships with parents (7), social support and relationship with friends (4), and school environment (4). Responses were categorized into 5-option Likert scales, with a recall period of 1 week in most questions. The scores are standardized to a mean of 50 and SD = 10, according to a reference sample of 22,000 European children and adolescents that allows to compare with the reference population norms. Higher scores mean better HRQOL. The KIDSCREEN-10 index that is embedded within the KIDSCREEN-27 was also

included as a summary measure [24]. The Spanish and Catalan online versions of the questionnaire have demonstrated acceptable reliability and validity [25].

Adherence to treatment in the month prior to the visit was assessed by two questions: frequency of glucose level control (3 or more times per day vs fewer times), and frequency of blood sugar check within 2–3 h after a meal (3 or more times a week vs less than 3 times). Patients were categorized into high adherence if they answered positively to both questions.

Children's mental health status was assessed using the Strengths and Difficulties Questionnaire (SDQ), a brief behavioral screening questionnaire for children and adolescents that asks about their mental health symptoms and positive attitudes [26]. The Total Difficulties Score, ranging from 0 (no problems) to 40 (maximum problems) was computed; higher scores indicate more problems. The Spanish and Catalan versions have been shown to be reliable and valid [27].

Intervention

The HRQOL intervention consisted of discussing the HRQOL scores between the doctor and the patient at each visit from visit 1 to visit 3, emphasizing those points where the result was worse. The scores are reflected in a few simple graphics which the doctor showed the patient on a computer screen.

The KIDSCREEN-27 results were displayed with the numerical value of each dimension, and then with similar colors to a traffic light, marking green if this was good (mean score >55), yellow for medium (between 45 and 55), and red for a poor outcome (<45). Evolutionary results were displayed in the case of visits 2, 3, and 4 to make a comparison with previous visits. At each visit, pediatricians invited the patients to comment and discuss the results, identified those dimensions in the low value scores, explored possible solutions and actions, and reviewed these actions over time with these advices. Before the intervention, patients were asked whether they preferred their parents to be present during the consultation. Before starting the study, pediatricians in this group had received a standardized training in the use and interpretation of HRQOL questionnaires supervised by a psychologist.

Control group

This group of patients completed several online questionnaires 48 h before each visit like in the intervention group, and they answered the HRQOL questionnaires only before visit 1 and visit 4. In the consultation, these patients received the usual care without commenting on the results of the questionnaires.

Fig. 1 Flow diagram of the participants through each stage of the study

Ethics

The study was approved by the ethics committee of participant hospitals in accordance with national and international guidelines (code of ethics, Helsinki Declaration) as well as legislation on data confidentiality (Organic Law 15/1999 of December 13 Data Protection character staff). Signed consent to participate was requested from parents and children over 12 years. The collection and transfer of data was carried out according to strict security and data encryption.

Statistical analysis

Mean KIDSCREEN-27 and KIDSCREEN-10 Index scores and their 95 percent confidence interval (95%CI) were computed and compared between groups at baseline and follow-up visits. Changes in KIDSCREEN-27 and KIDSCREEN-10 Index scores were calculated using standardized mean differences (effect size, ES) [28]. A commonly accepted interpretation of the ES is: none (<0.2), low (0.2 – 0.5), moderate (0.51 – 0.80), and high (>0.8). A negative effect size means that scores were lower (worse HRQOL) at follow-up than at baseline. To

determine whether KIDSCREEN scores changed significantly over time and by group, generalized estimating equations (GEE) with identity link and normal distribution and an exchangeable working correlation matrix were estimated, and model-based standard errors were used [29]. These models are often used to analyze longitudinal and other correlated response data. Dependent variables were the KIDSCREEN-27 and KIDSCREEN-10 dimension scores assessed at baseline and follow-up. The independent variables included in the models were the time period (baseline or follow-up score), age at baseline, sex, FAS, the highest family level of education, and clinical variables at baseline such as HbA1c, mental health (SDQ), and adherence to treatment also at baseline. Interaction terms were included in the model to assess whether the intervention group showed any differences from the control group at follow-up.

The sample size estimation was based on previous studies, taking into account an interconglomerate correlation ($\rho = 0.006$) and accepting an alpha risk of 0.05 and a beta risk of less than 0.2 in a bilateral contrast, and concluded that 63 patients in each group (126 in total) were required to detect a difference equal to or greater than 5 units ($1/2$ standard deviation) on the standardized

Table 1 Baseline characteristics of participants with complete data at follow-up

Sociodemographic variables	Baseline data of participants w/completed follow-up					
	Total		Intervention group		Control group	
	<i>N</i>	<i>M</i> (SD) or %	<i>N</i>	<i>M</i> (SD) or %	<i>N</i>	<i>M</i> (SD) or %
Age at baseline						
Mean	119	13.4 (2.8)	70	13.3 (2.9)	49	13.5 (2.8)
8–11 years	33	27.7	20	28.6	13	26.5
12–19 years	86	72.3	50	71.4	36	73.5
Sex						
Boys	58	48.7	33	47.1	25	51
Girls	61	51.3	37	52.9	24	49
Type of family						
Biparental	100	85.5	60	88.2	40	81.6
Monoparental	17	14.5	8	11.8	9	18.4
Highest family level of education						
Primary school	45	38.5	23	33.8	22	44.9
Secondary school	49	41.5	30	44.1	19	38.8
University degree	23	19.7	15	22.1	8	16.3
Origin						
Native	112	94.1	66	94.3	46	93.9
Immigrant	7	5.9	4	5.7	3	6.1
Family function (Apgar)						
Acceptable function	79	66.4	42	60**	37	75.5
Disfunction	40	33.6	28	40	12	24.5
Family affluence scale						
Low	67	56.3	47	67.1*	20	40.8
Middle	47	39.5	21	30	26	53.1
High	5	4.2	2	2.9	3	6.1
Clinical variables at baseline						
Time w/diagnoses (years)	119	5.1 (3.7)	70	5.23 (3.8)	49	4.91 (3.6)
>5 years	48	59.7	28	60	29	59.2
≤5 years	71	40.3	42	40	20	40.8
BMI (Z score)	119	0.3 (0.9)	70	0.24 (0.8)	49	0.37 (0.9)
HbA1c	119	7.5 (1.07)	70	7.69 (1.1)	49	7.42 (1.0)
>7.5% (58 mmol/mol)	58	48.7	37	52.9	21	42.9
≤7.5%	61	51.3	33	47.1	28	57.1
Mental health						
SDQ	119	10.7 (5.3)	70	10.9 (5.1)	49	10.4 (5.5)
Adherence						
High	59	49.6	28	40*	31	63.3
Low	60	50.4	42	60	18	36.7
Changes during the last 3 months						
No changes on treatment	98	83.1	54	78.3	44	89.8
Changes on diet/nutrition	14	11.9	12	17.4	2	4.1
Bolus calculator	6	5.1	3	4.3	3	6.1
Hypoglycemia						
Yes	3	2.5	2	2.9	1	2
No	116	97.5	68	97.1	48	98
Hyperglycemia						
Yes	8	7.2	7	10	1	2

Table 1 continued

Sociodemographic variables	Baseline data of participants w/completed follow-up					
	Total		Intervention group		Control group	
	<i>N</i>	<i>M</i> (SD) or %	<i>N</i>	<i>M</i> (SD) or %	<i>N</i>	<i>M</i> (SD) or %
No	111	92.8	63	90	48	98

SD standard deviation, *BMI* body mass index, *HBAc1* Glycated hemoglobin, *SDQ* Strengths and Difficulties Questionnaire. Missing values: level of education (2); type of family (2); changes during the last 3 months (1)
Statistically significant differences ($p < 0.01$) are shown in bold. ** p 0.058

Table 2 Clinical variables at follow-up

	Total sample		Intervention group		Control group	
	<i>n</i>	<i>M</i> (SD)	<i>n</i>	<i>M</i> (SD)	<i>n</i>	<i>M</i> (SD)
HbA1c	117	7.9 (1.2)	68	7.9 (1.03)	49	7.89 (1.43)
>7.5% (58 mmol/mol)	68	58.1	40	58.8	28	57.1
≤7.5%	49	41.9	28	41.2	21	42.9
Difference after-before HbA1c	117	0.3 (1.06)	68	0.19 (1.13)	49	0.46 (0.95)
Mental health						
SDQ	119	9.4 (4.7)	70	9.47 (4.9)	49	9.3 (4.4.)
Diff. after-before (SDQ)	119	−1.35 (3.8)	70	−1.47 (3.6)	49	−1.18 (4.1)
Adherence						
High	50	40.8	30	42.9	20	40.8
Low	69	59.2	40	57.1	29	59.2
Changes						
No changes on treatment	89	76.1	57*	83.8	32	65.3
Changes on diet/nutrition	26	22.2	9	13.2	17	34.7
Bolus calculator	2	1.7	2	2.9	–	–
Hypoglycemia						
Yes	2	1.7	2	2.9	–	–
No	116	98.3	67	97.1	49	100
Hyperglycemia						
Yes	2	1.7	1	1.4	1	2
No	116	98.3	68	98.6	48	98

Missing value HbA1c visit4 (1); hyperglycemia (1); changes during the last 3 months (1). SD: Standard deviation; HbA1c: Glycated hemoglobin; SDQ: Strengths and Difficulties Questionnaire. Statistically significant differences ($p < 0.01$) are shown in bold

KIDSCREEN-27 dimension scores. The GEE analysis was conducted using the xtgee command in STATA version 11.0.

Results

A hundred and thirty-six patients with completed data at baseline were initially included in the study (participation rate 66.3% at baseline; the sample characteristics at baseline can be consulted elsewhere [30]). Seventeen patients were lost to follow-up during the year (1 in control group,

16 in intervention group, total response rate: 58%). No differences were found comparing participants at baseline with and without data at follow-up. The study profile is depicted in the Fig. 1. The final sample included 119 patients with complete data at the end of follow-up: 70 in the HRQOL intervention group and 49 in the control group (Table 1).

No statistically significant differences were found at baseline between HRQOL intervention and control group regarding age, sex, type of family, or the highest family education level. Control group reported higher family affluence level than the intervention group ($p < 0.01$).

Table 3 Health-related quality of life of the intervention and control groups at baseline and follow-up ($n = 119$)

	Physical well-being M (95%CI)	Psychological well-being M (95%CI)	Parents and autonomy M (95%CI)	Peers M (95%CI)	School environment M (95%CI)	KIDSCREEN-10 index M (95%CI)
Intervention group ($n = 70$)						
Baseline	45.9 (43.9–47.9)	48.9 (46.6–51.1)	50.0 (48.3–51.7)	54.4 (52.4–56.4)	51.8 (49.6–54.0)	49.3 (47.5–51.1)
Follow-up	49.7 (47.1–52.2)	54.2 (52.0–56.4)	54.1 (51.7–56.5)	56.4 (54.2–58.6)	57.3 (54.9–59.7)	55.2 (52.7–57.7)
ES*	0.38	0.56	0.46	0.22	0.56	0.63
Control group ($n = 49$)						
Baseline	47.2 (44.4–50.0)	51.1 (48.2–54.1)	50.9 (48.3–53.5)	52.1 (49.2–55.0)	52.8 (49.9–55.8)	50.7 (47.8–53.5)
Follow-up	49.0 (46.3–51.6)	52.1 (48.9–55.4)	54.4 (51.9–56.8)	53.3 (49.2–57.5)	53.7 (50.6–56.7)	53.1 (50.2–56.0)
ES*	0.18	0.09	0.38	0.09	0.07	0.23
Total sample ($n = 119$)						
Baseline	46.4 (44.8–48.1)	49.8 (48.0–51.6)	50.4 (48.9–51.8)	53.5 (51.8–55.1)	52.2 (50.5–54.0)	49.9 (48.3–51.4)
Follow-up	49.4 (47.5–51.2)	53.3 (51.5–55.2)	54.2 (52.5–55.9)	55.1 (53.0–57.3)	55.8 (53.9–57.7)	54.3 (52.4–56.2)
ES ^a	0.30	0.45	0.43	0.15	0.35	0.46

^a Standardized mean differences (effect size, ES) based on follow-up versus baseline scores. Statistically significant differences are shown in bold

Clinical variables (Tables 1 and 2)

No significant differences were found on clinical variables comparing both groups at baseline except for adherence; the control group reported higher percentage of adherence to treatment at baseline, but was similar to the intervention group at follow-up. Mean HbA1c was $7.69 \pm 1.1\%$ (61 mmol/mol) for the HRQOL intervention group and $7.42 \pm 1\%$ (58 mmol/mol) for the control group at baseline, with no difference between the groups in HbA1c changes over time.

Regarding metabolic decompensations, the HRQOL intervention group decreased the number of severe hyperglycemies (10% at baseline to 1.4%), while the control group remained unchanged during follow-up.

HRQOL results (Table 3)

Statistically significant improvement at follow-up was found in the total sample on the dimensions Parent & Autonomy (ES = 0.43) and the KIDSCREEN-10 (ES = 0.46). Statistically significant higher scores were seen at follow-up for the dimensions of Psychological well-being (ES = 0.56), School environment (ES = 0.56), and the KIDSCREEN-10 index (ES = 0.63) in the intervention group, while no differences were found in the control group. Figures 2 illustrates these key results.

Multivariate analysis (Table 4)

The GEE analysis showed an improvement in HRQOL scores at follow-up. The main results comparing the intervention and control groups at follow-up showed a positive and statistically significant impact with the intervention on Psychological well-being ($B = 4.32$; p 0.03 for the interaction of group by follow-up) and School environment ($B = 4.64$; p 0.02 for the same the interaction term).

Mental health showed a negative impact at follow-up on Psychological well-being ($B = -0.78$; $p < 0.0001$) and the KIDSCREEN-10 Index ($B = -0.65$; $p < 0.001$). Family dysfunction showed a negative impact on Psychological well-being ($B = -2.99$; $p = 0.03$) and the KIDSCREEN-10 Index ($B = -3.0$; p 0.03); while adherence showed a positive impact on Physical well-being ($B = 3.17$; p 0.02) and Psychological well-being ($B = 3.7$; $p = 0.006$).

Discussion

The results of the present study show that periodic evaluation of HRQOL as part of the routine visit of diabetic patients improves HRQOL, especially in psychological well-being and school environment. The results were also positive but at limit of statistical significance for the KIDSCREEN-10 Index, and no changes were found in metabolic control. Our study also demonstrated the feasibility, viability, and effectiveness

a Psychological well-being **b** School environment **c** KIDSCREEN-10

Fig. 2 Health-related quality of life in children and adolescents with type I diabetes. Comparison of intervention and control groups. **a** Psychological well-being. **b** School environment. **c** KIDSCREEN-10 Index

of assessing HRQOL via Internet. Online measurement in a highly prized tool for children and, especially adolescents, and can be more engaging than traditional methods. Internet has also made progress in many other aspects in the management of diabetes [31, 32]. Besides some barriers described when assessing Patient Reported Outcomes (PRO) in clinical practice, [18] most of the studies analyzing the implementation of these assessments were carried out in pediatric oncologic patients [33].

The results of the present study are consistent with similar studies that found improvement in psychological well-being in adolescent and adult patients with T1DM, and found no improvement in metabolic control [19, 34]. The fact that beneficial effects of HRQOL intervention disappear one year after withdrawing the HRQOL assessment procedure [20] should be confirmed in our context. In that case, alternatives should be considered, given the consistently positive results on patient HRQOL and the feasibility of administrating HRQOL questionnaires via Internet to patients in this age group.

The results at the follow-up confirm that the evaluation of HRQOL in pediatric diabetic patients is an important component of ongoing care, previously highlighted by the ADA [7] and ISPAD [10] guidelines' recommendations.

The present study also shows that mental health, family dysfunction, and treatment adherence are the most influential factors on HRQOL over time. The SEARCH study [35], a large cross-sectional analysis of more than 2500 US youth with T1DM, shows that in the presence of lower HRQOL a number of indicators of poor clinical functioning may be affected. The ADA guidelines also recommend a mental health screening for youth and family at diagnosis and annually [36]. The present study reinforces the need for monitoring these factors, given their negative impact on HRQOL at follow-up. Moreover, adherence is strongly related to metabolic control, and the decline in diabetes management and control could be predicted through low HRQOL scores, as Hilliard et al. previously showed [37].

Some limitations of the study deserve comment. Firstly, 35% of the initial 205 patients who did not enter the study could lead to a selection bias. Although there were no differences between these patients and those who participated in terms of age or years of disease evolution, we didn't know the metabolic control of some of them. Perhaps some had higher levels of HbA1c and therefore would not participate. On the other hand, losses to follow-up have been greater in the intervention than in the control group

Table 4 Generalized estimating equation (GEE) of baseline and follow-up assessment of health-related quality of life ($n = 119$)

	Physical well-being		Psychological well-being		Parents and autonomy		Peers		School		Kidscreen-10	
	Coeff.	<i>p</i>	Coeff.	<i>p</i>	Coeff.	<i>p</i>	Coeff.	<i>p</i>	Coeff.	<i>p</i>	Coeff.	<i>p</i>
Age	−0.13	0.1	0.02	0.79	0.07	0.29	−0.17	0.04	−0.11	0.17	−0.11	0.15
Sex	0.85	0.56	−0.36	0.77	−1.59	0.19	−0.21	0.88	−3.75	0.007	−1.45	0.25
Intervention group	−0.85	0.6	−0.62	0.7	−0.41	0.78	3.13	0.03	−0.3	0.86	−0.55	0.73
Family Apgar	−1.36	0.37	−2.99	0.03	−2.97	0.02	−0.07	0.96	−3.7	0.01	−3.0	0.03
Adherence	3.17	0.02	3.7	0.006	−0.11	0.93	0.79	0.6	−0.16	0.9	1.58	0.23
SDQ	−0.22	0.09	−0.78	0.0001	−0.47	0.0001	−0.61	0.0001	−0.43	0.001	−0.65	0.0001
Follow-up	1.74	0.26	1.01	0.5	3.44	0.01	1.67	0.11	0.84	0.59	2.4	0.1
Interaction												
Group* follow-up	2.02	0.3	4.32	0.03	0.64	0.7	0.77	0.72	4.64	0.02	3.47	0.07

Reference category: Girls; control group; acceptable family function; low adherence; baseline assessment. SDQ: Strengths and Difficulties Questionnaire. All models in the table are adjusted for Family Affluence Scale and the highest family level of education. Statistically significant differences ($p < 0.01$) are shown in bold

because one of the pediatricians from this first group carried out the intervention discontinuously due to personal problems during the fieldwork period. As a consequence, 12 patients were lost from this pediatrician, while in the rest of participants on both groups the losses were minimal (0–5). Nevertheless, it seems that these facts have not influenced the results. Reanalyzing the data excluding the pediatrician's patients who could not continuously performed the whole study, the results show similar trends with lower ES and level of statistical significance (data not shown). Secondly, patients were recruited from 5 different centers, so that personal characteristics, clinical factors, treatments, and the quality of the intervention received may vary the results, and they were not specifically evaluated. In addition, distribution of patients was not individually randomized. In order to try to minimize this bias, every hospital tried to assign a physician in charge of the control group and another physician for the intervention group. This design could be associated to biases in the sample characteristics. Nevertheless, it does not seem that these factors have influenced the results, since no significant differences were found in the multivariate models when entering the center or pediatrician (data not shown). Moreover, the control group showed better scores on some sociodemographic and clinical variables at baseline than the intervention group, which goes against the study null hypotheses. Third, the relatively small sample size may have influenced the results mainly in the control group of patients, where the sample size was slightly lower than expected and consequently there was less statistical power to detect differences (statistical power achieved was 0.79, while the theoretical power was 0.8). However, differences

found between baseline and follow-up were seen specifically in the intervention group, reinforcing the study hypotheses. Future studies should include larger samples to confirm these results. Fourth, it was not possible to confirm the hypothesis of less number of decompensations in the intervention group, as the whole group was generally very well controlled, and a minimum number of events were detected in both groups. To a certain extent, this may be due to good clinical practices and the ease of access to health services in the study population. Finally, there is a risk due to using the same questionnaire as outcome and during the intervention, and moreover it is possible that response shift may have affected the responses. Nevertheless, in this case it is unlikely to affect differently the intervention and control groups, given the high rates of data completion, the fact that both groups have answered the HRQOL questionnaire at baseline and follow-up, and other types of questionnaires have been administered simultaneously to the control group at intermediate visits.

The strengths of the study include that 87% of baseline patients completed follow-up data; all the followed patients completed HRQOL variables at visit 4, probably thanks to the use of internet and that the intervention was relatively easy and short in time; and finally the use of reliable, valid, and standardized tools for the assessment of HRQOL.

In conclusion, we found an improvement in HRQOL scores between baseline and 1-year administrations of the KIDSCREEN-27, slightly higher in the group of diabetic patients in which the HRQOL results are discussed between the physician and the patient, improving specially in psychological well-being and school environment. The results of the present study support the routinary use of

HRQOL measures in clinical practice, given its potential benefits.

Funding The study was partially financed by the Spanish Ministry of Health, contract No. PI12/01296.

Compliance with ethical standards

Conflict of interest Authors declare that they have no conflicts of interest.

Ethical approval The study was approved by the ethics committee of participant hospitals in accordance with national and international guidelines (code of ethics, Helsinki Declaration) as well as legislation on data confidentiality (Organic Law 15/1999 of December 13 Data Protection character staff).

Informed consent Signed consent to participate was requested from all parents and also children over 12 years. The collection and transfer of data was carried out according to strict security and data encryption.

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