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ORIGINAL ARTICLE

Psychometric performance of the Quality of Life in Short Stature Youth (QoLISSY) questionnaire in the Netherlands

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Abstract The European Quality of Life in Short Stature Youth (QoLISSY) questionnaire is a disease-specific instrument assessing quality of life (QoL) in children with short stature from the child and parent perspectives. In order to use the QoLISSY in Dutch samples, a translation process and psychometric testing is needed. Children diagnosed with short stature (8 to 18 years) and their parents were recruited from a Dutch growth clinic. Reliability was assessed using Cronbach's α and intraclass correlation coefficients (ICCs). Pearsons' correlations with the generic KIDSCREEN and a confirmatory factor analysis (CFA) were performed to test validity. Scales showed good internal consistency with α ranging from 0.80 to 0.94 (child report) and from 0.85 to 0.95 (parent report). Test–retest reliability (ICC) ranged from 0.15 to 0.91 (child report) and from 0.14 to 0.83 (parent report). Correlations with the KIDSCREEN in the mean range indicated criterion validity. The models' goodness of fit was confirmed by CFA results in the Dutch and in comparison with the European sample.

Conclusion: The Dutch QoLISSY is a psychometrically reliable and valid short stature-specific QoL measure. It is now available for use in clinical research and practice to evaluate well-being and possible effects of growth hormone treatment and psychological interventions in the Netherlands.

What is Known:
- *Questions in terms of the efficacy and effectiveness of psychological versus pharmacological interventions alone or in combination can be answered with a disease-specific questionnaire as a self-reported outcome measure.*
- *There is a lack of internationally available short stature-specific QoL instruments reflecting the child and parent perspectives.*

What is New:
- *The Dutch QoLISSY questionnaire is a psychometrically sound short stature-specific QoL measure reflecting the child and parent perspectives.*
- *The Dutch QoLISSY questionnaire can be used as a treatment outcome indicator in research and practice.*

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Keywords Children · Short stature · Psychometric testing · Quality of life · Growth hormone (treatment)

Abbreviations

CFA	Confirmatory factor analysis
GHD	Growth hormone deficiency
GH-T	Growth hormone therapy
ICC	Intraclass correlation coefficient
ISS	Idiopathic short stature
QoL	Quality of life
QoLISSY	Quality of Life in Short Stature Youth
SDS	Standard deviation scores

Introduction

Short stature, clinically defined as a height below −2 standard deviation scores (SDS), is a common reason for referral to pediatric endocrinologists for an evaluation of growth-inhibiting disorders [2, 21]. In addition to growth hormone deficiency (GHD) and idiopathic short stature (ISS), many other growth-related conditions are seen at growth clinics such as the Turner syndrome, skeletal dysplasia, oncological and neurological conditions impacting on growth, familiar short stature, and constitutional growth delay. We concentrated on GHD as secondary growth disorder which is treated with growth hormone replacement therapy (GH-T) as well as on ISS for which such treatment is optional. Because of an interest in the burden of disease and the QoL outcome of GH-T in these conditions, the original QoLISSY questionnaire was developed for young patients with GHD and ISS and was consequently tested in this group also in the Netherlands. Children with GHD lack growth hormone and have a low growth velocity for age or pubertal stage. The clinical approach is to accelerate growth and improve their final height through GH-T, and the majority of children who have been diagnosed with GHD are therefore treated with GH.

ISS is defined as a condition in which the height of an individual is more than 2 SDS below the mean height for age and gender in the population, without evidence of systemic, endocrine, nutritional, or chromosomal abnormalities [8]. Specifically, children with ISS have normal birth weight and are GH sufficient. While clinical effectiveness of GH treatment in ISS has been documented, the use of growth hormone for treatment of ISS has only been approved in the USA in children whose height is more than 2.25 SDS (1.2nd percentile) below the mean for age and sex [7]. The clinical effectiveness of GH treatment in ISS is well documented [1, 11, 17]. In contrast to the USA, treatment of ISS with GH is not approved by the European Medicines Agency [3], although the impact of short stature and its treatment on children's and adolescents' mental health and behavioral functioning has been documented. The effects on quality of life (QoL) have only recently been investigated. QoL is defined as the person's subjective evaluation of their health in terms of physical, psychological and social well-being [4]. It can be measured via generic and condition-specific instruments. There is however a lack of internationally available short stature-specific instruments that reflect the child and parent perspectives. Therefore, the aim of the European Quality of Life in Short Stature Youth (QoLISSY) Study Group was to develop and psychometrically test a disease-specific questionnaire for short statured children and adolescents.

The original QoLISSY project utilized a simultaneous approach to cross-cultural QoL assessment with a common conceptual development of the instrument across different European countries and languages. The international guidelines for the development of quality of life measures including focus groups, pilot testing with cognitive debriefing, and field and retesting were followed resulting in a cross-culturally valid instrument [6].

The aim of the original European QoLISSY study was to construct a psychometrically sound and cross culturally valid tool to assess the impacts of short stature on QoL in children and adolescents from their own perspective with the added perspective of their parents. This development and psychometric testing of the original QoLISSY instrument was described in previous papers [5]. The QoLISSY questionnaire was also validated in Flemish in Belgium [13]. The current paper describes the translation, adaptation and validation of a Dutch language version based on the Flemish language version for use in children/adolescents with short stature and their parents in the Netherlands.

Subjects and methods

Study design

The validation of the QoLISSY questionnaire in a Dutch population of clinically referred children and adolescents included a forward and backward translation of the existing Flemish version into Dutch, followed by a cognitive debriefing and a pilot test and finally a field test together with a retest.

The Dutch QoLISSY questionnaire was used in a pilot test and sent out to the families with a short statured child via mail together with a prepaid return envelope. Participants of the study were asked to fill out the questionnaire and for cognitive debriefing purposes, give a feedback on the questionnaire in terms of understanding, interpretation, and relevance of items. They were also asked whether any aspects related to their experience with short stature were missing and should be added.

After receiving and evaluating the feedback of the families, the QoLISSY questionnaire was adapted according to their responses. A number of 13 short statured children/adolescents from 8 to 18 years as well as at least one parent and parents of younger children (4–7 years) participated in the Dutch cognitive debriefing and pilot test phase. As a result, some items were changed in wording, where the Dutch differs from the Flemish language, but in general items were judged as applicable, important, and clear by the participating Dutch families. No additional themes emerged to be added to the questionnaire. Quantitative results show low floor and ceiling effects below 10 % and mean scale scores (possible range between 0 and 100) of 41.80 to 72.60 with standard deviations ranging from 9.03 to 22.35.

For the field test, the adapted questionnaires for short statured children and parents in the Netherlands were distributed via mail along with a prepaid return envelope. For

validation purposes, participants were asked to fill out the QoLISSY questionnaire as well as the generic KIDSCREEN questionnaire [20]. Fifty children/adolescents and 56 parents (including the children/parents from the cognitive debriefing) were invited to participate in the field test. Test–retest was to be performed with a minimum of three patients per age group and gender.

Recruitment of participating families

Patients with diagnosed short stature (ISS or GHD) aged between 8 and 18 years and their parents were asked to participate in the Dutch QoLISSY validation study. The study was conducted in the Tergooi Hospital, a general, nonacademic hospital with a special growth clinic which is consulted by about 200 new patients per year who have questions about their height (too short or too tall) and pubertal development (too early or too late). Exclusion criteria were other medical conditions (e.g., diabetes and asthma) or a multiple hormone deficiency as well as severe physical or mental conditions making participation difficult as judged by the investigators. In addition, parents of younger children (aged 4 to 7 years) were asked to participate. An informed consent (for parents) and assent (for children) was a requirement to participate in the study. The study had been approved by the local medical ethics committee of Tergooi Hospitals in Blaricum and Hilversum (kv/12.012).

Measures

Participating families completed the disease-specific QoLISSY questionnaire with a total of 53 items for children/adolescents and 66 items for parents. Three core scales constitute the total QoL score of the QoLISSY, namely *Physical*: six items—physical limitations that the child can experience in everyday life due to short stature; *Social*: eight items—refers to the way short stature interferes with the child's social life; and *Emotional*: eight items—refers to the child's feelings and emotions with regards to his short stature. These domains are supplemented by three additional scales covering *Coping* aspects (ten items—referring to the way the child copes with negative feelings or experiences due to his short stature), experiences with GH *Treatment* (14 items—referring to the child's experiences linked to growth hormone treatment), and general *Beliefs* about height (with four items—referring to the child's beliefs about stature). The parent-reported version reflects the child version in item content and is used to obtain observer report as well as to compare the QoL between child and parent perspectives. The parent report additionally includes aspects of the child's *Future* (five items—referring to the parent's worries about the future of their child in relation to his short stature) and *Effects of the child's short stature on the parents* (11 items—referring to the impact the child's growth problem has on his parent's feelings). Responses are coded on a standard five-point Likert scale ranging from "not at all/never" to "extremely/always." Missing values were substituted by the scales mean score if at least 80 % of the items per scale were completed. Within the original QoLISSY Study [18], Cronbach's alpha ranged between 0.82 (*Coping*) and 0.92 (*total QoL score*) for the child self-report and between 0.86 (*Physical*) and 0.95 (*total QoL score*) for the parent report [5, 12]. The generic KIDSCREEN questionnaire with 52 items provides detailed information on ten QoL dimensions (The KIDSCREEN Group Europe, 2006). These are *Physical Well-being*, *Psychological Well-being*, *Moods & Emotions*, *Self-Perception*, *Autonomy*, *Parent Relation & Home Life*, *Financial Resources*, *Social Support & Peers*, *School Environment*, and *Social Acceptance* (*Bullying*). Questions were answered via a similar five-point Likert scale (never to always). The KIDSCREEN was used to examine the convergent validity of the QoLISSY. Sociodemographic and clinical data on height (cm), diagnosis, treatment status, gender, and age were collected as well.

Data analysis

In the first step of the validation process, an overview of the scale distributional characteristics (mean, standard deviation, floor and ceiling effects) was obtained. Reliability analysis was performed using Cronbach's alpha as in indicator of internal consistency for each scale ($\alpha > 0.70$ can be considered as acceptable [9]). Intraclass correlation coefficients (ICCs) were calculated to examine test–retest reliability and to reflect congruency in the child–parent dyads. Differences in mean scale scores between subgroups regarding age, gender, and SDS height (> -2 SDS, ≤ -2 SDS) were analyzed via *t* tests.

To test for convergent validity, Pearson's correlations between the generic KIDSCREEN scale scores and the disease-specific QoLISSY subscales were inspected. Correlations in the mean range of $r=0.40$ to 0.60 were expected to indicate measurement of the same but not the identical content [8].

Known groups validity in terms of differences between height (> -2 SDS vs ≤ -2 SDS) was assessed by comparing scale mean scores via the Student's *t* tests. These were used to analyze differences in the QoLISSY according age and gender as well. Since only eight children received GH treatment, group comparison across treatment status (treated vs untreated) was not performed. The level of significance was reported at two thresholds, 0.05 and 0.01.

Construct validity was examined via a confirmatory factor analysis (CFA). Given the small sample size ($N=$ 49 Dutch children), indices of fit (comparative fit index (CFI), root mean square error of approximation (RMSEA), χ^2/df) were compared in a multigroup analysis investigating differences between the existing European dataset (including data from Spain, France,

the UK, Sweden, and Germany; N=268 children and N=317 parents) and the Dutch data. This procedure named "TOCO approach" (take one country out) has previously been used in the cross-cultural analysis of the QoLISSY across languages and indicated cross-cultural equivalence in psychometric performance [6].

Reference values were taken from Hu and Bentler [10] indicating a good model with χ^2/df <2 and acceptable with <3. The CFI should be >0.90 and the RMSEA should be <10.0 to be acceptable.

Results

Sociodemographic and clinical characteristics

A total of 49 children/adolescents between 8 and 18 years and 49 parents plus 8 parents of younger children between 4 and 7 years were included in this validation study. Patients' mean age was 11.82±3.18 years. A total of 23 children (age 8–12 years) as well as 26 adolescents (age 13–18 years) were included. The majority of children/adolescents were diagnosed with ISS (80.7 %), and 3 out of 49 children currently received GH treatment. About 60 % of the patients had reached normal height (> −2 SDS) at time of assessment while about 40 % were short statured (see Table 1). A total of 13 families filled in the questionnaire again about 2 weeks later (retest).

Table 1 Characteristics of the Dutch patient sample

	4–7 years[a]		8–12 years		13–18 years		Total	
	n	%	*n*	%	*n*	%	*n*	%
Sex								
Girl	3	37.5	12	52.2	10	38.5	25	43.9
Boy	5	62.5	11	47.8	16	61.5	32	56.1
Condition								
GHD	3	37.5	4	17.4	4	15.4	11	19.3
ISS	5	62.5	19	82.6	22	84.6	46	80.7
Treatment								
Untreated	5	62.,5	18	78.3	23	88.5	46	80.7
Treated	3	37.5	5	21.7	3	11.5	11	19.3
Height (*SDS*)[b]								
> −2.0	5	71.4	11	47.8	18	69.2	34	60.7
≤ −2.0	2	28.6	12	52.2	8	30.8	22	39.3

GHD growth hormone deficiency, *ISS* idiopathic short stature

[a] Only parents filled in the questionnaire

[b] Actual height is missing in some cases

Psychometric testing of the Dutch QoLISSY version

Data quality in terms of missing values for children/adolescents and their parents was acceptable. QoLISSY scale scores were calculated by mean substitution if missing values were present in less than 20 % of the items per scale. Missing data were present in five patient-reported cases and six parent reports only in the additional *Coping* subscale. Distributional characteristics and reliability (test–retest and internal consistency) of the QoLISSY scales are shown in Table 2. Mean scale scores (M) from the child report and the parent report were in the mid to upper range of the 0–100 scores. The corresponding standard deviations were high. Almost no floor and ceiling effects were present for the QoLISSY scale scores—except for the *Beliefs* scale (ceiling children 24.5 %, parents 28.1 %) and *Future* scale (ceiling 39.3 %). Internal consistency coefficients ranged between r=0.80 (*Physical*/*Beliefs*) and r=0.94 (*Treatment*/*total QoL score*) for children/adolescents and between r=0.84 (*Beliefs*) and r=0.95 (*total QoL Score*) for parents, indicating high reliability. Parent–child agreement was analyzed with the ICC. Concordance between child and parent dyads ranged from r=0.34 (*Physical*) to r=0.61 (*Coping*).

Test–retest concordance was tested with an intraclass correlation as well. The coefficient for the QoLISSY questionnaire in almost all scales ranged from r=0.15 (*Physical*) to r=0.91 (*Beliefs*) in the child self-report and similarly in the parent report (r=0.14 (*Physical*) to r=0.83 (*Future*)).

Differences according to sociodemographic characteristics were inspected for information about the potential effects of age and gender on scale scores to be taken into consideration regarding scoring and clinical interpretation in future studies. Differences in mean scale scores between age groups (8–12 and 13–18 years) were only present in the *Physical* scale of the child self-report ($t(47)$=−2.55, p=0.014, α=0.05). Younger children (M=74.49±17.84) reported more limitations in their perceived physical QoL than adolescents (M=85.58±15.57). Regarding differences between gender, results showed higher scores for emotional aspects of QoL for boys (M=85.75±15.80) than for girls (M=72.56±18.85; $t(47)$=−2.66, p=0.11). In the parent report, significant differences between boys and girls were present in the three QoL subscales as well as in the total QoL score ($t(54)$=−2.23, p=0.030). Parents of boys (M=79.58±14.84) reported their children to have a significantly better QoL than parents from girls (M=70.07±17.06).

Shorter children with a height ≤ −2 SDS reported a lower QoL in the *Physical* (p=0.007), *Social* (p=0.019), and *Coping* (p=0.026) scales of the QoLISSY questionnaire (see Table 3). Parents of shorter children only rated their children in aspects of *Coping* lower in comparison to parents of taller children (p=0.033).

Table 2 Distributional characteristics of the patient and the parent version of the Dutch QoLISSY scales in the field test

QoLISSY scales	Total sample, *N*		Mean (*M*)[a]		SD		% Floor		% Ceiling		Cronbach's alpha		ICC parent–child	*N* Retest		ICC	
	Children	Parents	Children	Parents	Children	Parents	Children	Parents	Children	Parents	Children	Parents		Children	Parents	Children	Parents
Physical	49	56	80.37	77.32	16.02	17.51	2.0	1.8	6.1	8.9	0.80	0.85	0.34	11	13	0.15	0.14
Social	49	57	78.71	75.07	18.32	17.86	2.0	1.8	6.1	7.0	0.88	0.88	0.53	10	13	0.69	0.64
Emotional	49	57	79.83	73.69	18.29	17.82	2.0	1.8	14.3	8.8	0.88	0.87	0.38	11	13	0.83	0.55
Coping	44	51	40.46	41.47	22.32	20.03	2.3	3.9	2.3	2.0	0.86	0.89	0.61	10	12	0.80	0.23
Beliefs	49	57	80.23	78.87	19.61	20.85	2.0	1.8	24.5	28.1	0.80	0.84	0.52	11	13	0.91	0.74
Treatment	8	9	55.13	67.14	28.99	18.12	12.5	11.1	12.5	11.1	0.94	0.89	0.34	–	–	–	–
Future[b]	–	56	–	87.05	–	17.76	–	1.8	–	39.3	–	0.90	–	–	12	–	0.83
Effects on parents[b]	–	56	–	83.24	–	15.16	–	1.8	–	5.4	–	0.90	–	–	13	–	0.64
Total QoL score	49	56	79.64	75.34	15.56	16.43	2.0	1.8	2.0	1.8	0.94	0.95	0.43	10	13	0.56	0.50

ICC intraclass correlation coefficient

[a] Range 0–100

[b] Only in parents' version

Table 3 Differences QoLISSY scales according to height below and above −2 SDS (at time of recruitment)

Scales	> −2*SDS*		≤ −2*SDS*		*t*	*df*	*p* value
	M	SD	*M*	SD			
Physical							
Children	85.37	11.75	73.13	18.75	2.81	47	0.007
Parents	79.70	19.44	72.92	13.47	1.42	53	0.161
Social							
Children	83.74	12.64	71.41	22.75	2.43	47	0.019
Parents	77.95	18.75	70.19	15.98	1.60	54	0.115
Emotional							
Children	81.59	15.14	77.28	22.26	0.80	47	0.423
Parents	73.53	18.74	73.46	17.02	0.01	54	0.990
Coping							
Children	33.69	20.66	48.60	21.99	−2.32	42	0.026
Parents	36.45	20.43	48.72	18.00	−2.20	48	0.033
Beliefs							
Children	80.39	19.82	80.00	19.83	0.07	47	0.947
Parents	80.51	21.80	75.38	19.34	0.90	54	0.373
Future[a]							
Parents	90.30	16.77	81.59	18.48	1.81	53	0.076
Effects on parents[a]							
Parents	83.86	16.95	81.66	12.31	0.522	53	0.604
Total score							
Children	83.57	10.47	73.94	19.80	2.22	47	0.032
Parents	77.04	18.01	72.19	13.77	1.07	53	0.289

[a] The scales "Future" and "Effects on parents" only exist in the parents' version

Significant correlations (r=0.40–0.60) between the generic KIDSCREEN and the short stature-specific QoLISSY questionnaire were present in QoLISSY core scales (*Physical*, *Social*, and *Emotional*) reflecting the child's QoL and *Moods & Emotions*, *Self-Perception*, as well as *Autonomy* (KIDSCREEN). The highest correlation was found between *Treatment* (QoLISSY) and *Autonomy* (KIDSCREEN) in the child self-report (r=0.76). In the parent report, significant correlations were present between *Self Perception* (KIDSCREEN) and nearly all parent-related QoLISSY scales except *Coping* and *Treatment*. The correlation was highest between *Emotional* (QoLISSY) and *Self-Perception* in the parent report (r=0.72), see Table 4.

To analyze the factorial structure of the QoLISSY questionnaire in the Dutch dataset, the TOCO approach was used as published recently [6]. This means to add the Dutch data to the original field test data and compare results with and without the Netherlands. In the model, the three core scales were represented by their items and are constituted as three independent dimensions of the latent construct QoL.

Table 4 Correlation coefficients (Pearson *r*) for the QoLISSY scales with subscales of KIDSCREEN-52 (child–parent)

		KIDSCREEN-52									
		Physical well-being	Psychological well-being	Mood & Emotions	Self Perception	Autonomy	Parents	Financial	Social	Schooling	Bullying
QoLISSY	Physical	−0.016/−0.031	0.020/−0.110	**0.505****/0.134	0.263/**0.496****	0.271/0.108	0.123/0.020	0.143/0.211	0.002/−0.043	0.181/0.176	**0.476****/0.216
	Social	0.158/−0.061	0.290/−0.010	**0.535****/0.144	**0.600****/**0.581****	**0.421****/0.129	**0.350***/0.053	0.202/0.074	0.226/0.106	**0.312***/**0.329***	**0.360***/0.217
	Emotional	0.209/0.062	0.334*/0.043	**0.529****/0.123	**0.562****/**0.717****	**0.445****/0.120	**0.307***/0.122	0.123/0.033	0.137/0.230	**0.300***/**0.272***	**0.295***/0.152
	Coping	**0.430****/0.282	0.217/**0.308***	−0.012/0.142	0.065/0.001	0.222/0.115	**0.376***/0.154	0.141/**0.474****	0.117/0.221	**0.317***/**0.361***	0.261/0.203
	Beliefs	0.094/−0.123	0.176/−0.052	0.292/0.038	**0.613****/**0.452****	**0.309***/−0.097	0.163/−0.017	0.141/−0.145	0.117/0.250	**0.317***/0.261	−0.091/0.036
	Treatment	0.529/0.090	0.432/**0.729***	−0.034/0.525	−0.086/0.320	**0.764****/0.165	0.646/0.667	0.513/0.132	0.380/0.249	0.607/0.625	0.295/0.298
	Future[a]	−0.152	−0.130	0.162	**0.495****	0.072	0.028	0.057	0.020	0.263	**0.288***
	Effects on parents[a]	0.111	−0.116	0.129	**0.491****	0.074	0.033	0.260	0.047	0.136	**0.340***
	QoLISSY total score	0.138/−0.010	0.251/−0.027	**0.592****/0.147	**0.432****/**0.654****	**0.300***/0.130	−10.0/0.073	0.181/0.118	0.142/0.112	**0.303***/**0.282***	**0.419****/0.229

*Significant at $p<0.05$; **significant at $p<0.01$

[a] Only parent's scale

Table 5 shows the results of the multigroup analyses to test for differences between model fit in the European sample with and without the Netherlands samples. No significant difference was found, confirming the measurement and structural invariance of the structural model across the two subsamples (with and without the Dutch data) for the child self-report as well as for the parent report.

The indices (χ^2/df, CFI, and RMSEA) show an overall acceptable fit to the dimensional structure of the QoLISSY questionnaire within the dataset.

Discussion

This validation study focused on the assessment of QoL in Dutch children with GHD/ISS from the child and parent perspectives. Pediatric endocrinologists who treat short statured children are aware of the impact the disease might have on the affected families: restrictions in physical activities especially sports, regular appointments with the clinician and problems with the GH-T.

QoL was assessed in this study with the disease-specific QoLISSY questionnaire for self-report in children aged 8–18 years and report from parents of children aged 4–18 years.

The results demonstrate that the Dutch version of the QoLISSY questionnaire is a valid and reliable instrument for the assessment of QoL in children with GHD/ISS. It shows acceptable correlations with the well-validated generic KIDSCREEN questionnaire [19] as well as good internal consistency in terms of Cronbach's alpha >0.80 and test–retest reliability ($r \geq 0.50$ for the total QoL score). Confirmation of the factorial structure examined via CFA and the TOCO approach indicated construct validity in the child self-report and in the parent's report. Results showed no differences in factorial structure between the Dutch sample and that of the original European QoLISSY study. It is important to note that this does not imply comparability of the QoLISSY mean score between countries. The Dutch population is considered the tallest population in the world [16]. If tested in a representative sample, short stature could be expected to result in lower QoL in comparison to Dutch peers or in higher QoL as compared with non-Dutch populations. Because of composition and potential selection effects, QoL of the clinical samples cannot be compared in our study [16].

High ICCs indicate agreement between child and parent judgments. Differences between smaller and taller children in physical and social aspects of QoL show that the QoLISSY is able to detect height-related differences in perceived QoL. Shorter children report a lower QoL on these subscales of the QoLISSY than taller children.

According to Wiklund et al. [20], it is well known that differences in perceived QoL exist between boys and girls. Current findings of age and gender effects on QoLISSY scale

Table 5 Comparison of the factorial structure in the European sample without (original model) and with the Netherlands (plus NL)

			Model's goodness of fit				Model comparison					
							Measurement invariance			Structural invariance		
		n	χ^2; *p*	χ^2/df	CFI	RMSEA	$\Delta\chi^2$	Δdf	*p*	$\Delta\chi^2$	Δdf	*p*
Children	Original model	263	615.35; 0.05	2.99	0.88	0.087	1.515	19	1.00	0.147	2	0.929
	Original model plus the Netherlands	312	1023.3; <0.001	2.52	0.91	0.051						
Parents	Original model	259	718.81; <0.05	3.49	0.87	0.098	5.588	19	0.999	0.036	2	0.982
	Original model plus the Netherlands	315	1150.36; <0.001	2.85	0.91	0.057						

scores suggest their inclusion as covariates in the statistical analysis plans of future studies. The main limitation of this study is the monocentric design and a limited number of study participants, especially the low number of GH-treated patients enrolled, which makes subgroup analysis difficult. A related limitation is the low number of parents of younger children aged 4–7 years, which might be due to parental reluctance to health services consultation or due to a recruitment bias. Further studies should use a controlled design (ideally a randomized clinical trial) to investigate the impact of rGH treatment on the QoL of patients with GHD or ISS. The explanation of this may be found in the fact that parents of younger children tend to wait for catch-up growth before they introduce their children to endocrinologists [20].

Although this study presents a psychometric analysis of the QoLISSY questionnaire, results identify specific problems from the children and the parent perspectives. Physical, social, and coping difficulties were found from the child perspective and problems concerning the child's future according to the parents. Given that coping is a problem, it is possible to intervene with a psychosocial group intervention to encourage coping strategies (such as with the program "op Koers" in the Netherlands [14, 15]) which could be offered to children and results might be compared with GH treatment alone or in combination, e.g., in a randomized controlled trial. Questions regarding efficacy and effectiveness of psychological versus pharmacological interventions alone or in combination with psychological intervention could thus be answered in the future.

The results of this study are encouraging that adaptation of the QoLISSY questionnaire for use in other populations is possible in that the concepts of quality of life impacts appear to be applicable to a broad range of children across cultures and languages. Additional validation studies are currently ongoing in Greece, Italy, and the USA.

In conclusion, the QoLISSY can be used as a treatment outcome indicator in research but also in clinical management to make treatment choices, understand patient and parent needs, and to enhance the well-being and functioning of children and adolescents with diagnosed short stature.

Compliance with ethical standards

Authors Contributions AR designed the study with JQ, organized the data management, performed the statistical analysis, interpreted the results, and wrote the draft manuscript. SS conducted the study, collected data, and participated in instrument translation, and in drafting the manuscript. GK provided patient access and clinical data, supervised data collection, reviewed translations, and revised the manuscript. MB revised the manuscripts, supervised study design, and conducted statistical analysis and interpretation of results. JQ participated in designing and managing the study, supervised data collection, and revised the manuscript.

All authors read and approved the final submitted manuscript.

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