Quality of life and self-esteem in children treated for idiopathic short stature

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Objective: Changes in health-related quality of life (HRQOL) and self-esteem were studied in children with idiopathic short stature (ISS) participating in a study on the effect of growth hormone treatment.

Study design: Prepubertal children (n = 36) with ISS were randomly assigned to a treatment or control group. Children with ISS, their parents, and the pediatrician completed HRQOL and self-esteem questionnaires 3 times in 2 years.

Results: At the start, children with ISS did not have lower scores than the norm population, except for social functioning HRQOL. The pediatrician reported an improvement of HRQOL in the treatment group, the parents reported no change, and the children in the treatment group reported the same, or sometimes even worse, HRQOL or self-esteem than the control group. Changes related to the child's satisfaction with height and hardly to growth itself.

Conclusion: The assumption that growth hormone treatment improves HRQOL in children with ISS could not be supported in this study. (J Pediatr 2002;140:507-15)

It is widely assumed that idiopathic short stature (ISS) can result in psychologic, social, and physical problems.[1] Children with short stature appear younger than they are and are often treated as such by adults and peers.[2,3] The physical limits they meet in sports and play with peers could make them the subject of ridicule.[3] Nevertheless, some studies show that

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children with short stature have unimpaired self-esteem and normal patterns of behavior, in non-referred[4,5] and also referred children.[6-8]

The approach to children with ISS has been to accelerate growth and improve the final height through growth hormone (GH) treatment. However, the mean final height increase appears modest (between 3-9 cm),[3,9,10] most studies had methodologic flaws (inadequate or absent control groups and the use of mixed diagnostic groups), and thus far, there are no accurate predictors of the growth response.[9] Furthermore, most studies have concentrated on the isolated physical, psychologic, or social consequences of being short. Such studies focus only on specific aspects of well-being. The concept of health-related quality of life (HRQOL) combines physical, psychologic, and social well-being in one outcome measure. HRQOL is defined by the person's perception of problems in health status combined with the affective responses to such problems.[11] Another relevant outcome measure is self-esteem.[1,6,7,12-14]

ANOVA	Analysis of variance
CF	Child-form
DUCATQOL	Dutch Children's AZL/TNO Quality of Life questionnaire
GH	Growth hormone
HRQOL	Health-related quality of life
ISS	Idiopathic short stature
ISSQOL	Idiopathic Short Stature Quality of Life questionnaire
PF	Parent-form
RM-ANOVA	Analysis of variance for repeated measurements
SDS	Standard deviation score
TACQOL	TNO/AZL Children's Quality of Life questionnaire
TES	Therapy evaluation scale

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Table I. Distribution of baseline characteristics

		Treatment n (%)	Control n (%)	*P**
Child's sex	Male	15 (75)	14 (70)	.72
Age (y)	5-7	9 (45)	11 (55)	
	8-12	11 (55)	9 (45)	.53
Responding parent's sex	Female	19 (95)	17 (85)	.35
Hospital	Eindhoven	8 (40)	13 (65)	
	Rotterdam	9 (45)	5 (25)	
	Amsterdam	3 (15)	2 (10)	.25
Maternal educational level	Low	8 (42)	7 (39)	
	Medium	8 (42)	11 (61)	
	High	3 (16)	0 (0)	.17
Paternal educational level	Low	9 (47)	11 (61)	
	Medium	6 (32)	3 (17)	
	High	4 (21)	4 (22)	.56

*χ^2 test.

We conducted a prospective randomized controlled GH dose-response study, preceded by an extensive biochemical characterization of GH sensitivity,[15] and investigated whether participating in the study as part of the treatment or control group would influence the well-being of the children. It was expected that if short stature is accompanied by low HRQOL or self-esteem, both should be improved by increasing height. As a result, in the treatment group, the HRQOL and self-esteem might become better than in the control group.

However, there are some factors that could disturb a straightforward relationship between growth and HRQOL or self-esteem. First, scores could be influenced by the project itself. All participants intended to undergo treatment if they were allocated a place by lot, but 50% of the children were randomly assigned to the control group. This could result in a temporary lower HRQOL or self-esteem in the control group. Furthermore, treatment with GH imposes a burden on the child and his or her parents because it requires daily injections for several years. Therefore, special attention was given to the motivations of children and parents to participate in the project and to the possible drawbacks they encountered during participation. Second, HRQOL or self-esteem could be influenced by the expectations of the participants. Because the effect of GH on ISS is not certain, disappointment (in the treatment group) or surprise (in the control group) about achieved height might prevent the treatment group from having better HRQOL or self-esteem than the control group. Therefore, the effect of growth expectations, growth achievements, and the satisfaction with current height on the changes in HRQOL and self-esteem were investigated. Because agreement between informants of HRQOL is limited,[6,16-18] we studied children's, parents', and physicians' views about the effect of GH treatment on the HRQL in children with ISS.

METHOD

Participants and Data Collection Procedures

Data were collected from 36 prepubertal children (age at start, 4-10 years) with ISS and their parents (Table I). ISS is defined as a height of >2 SD below the mean of an age and sex-specific population reference, no GH deficiency, a normal size for gestational age at birth, normal body proportions, no evidence of chronic organic disease, no psychiatric disease or severe emotional disturbance, and normal food intake.[19] The children were enrolled between 1994 and 1997 in the Dutch multicenter study on the responsiveness to short and long-term GH therapy, a prospective randomized controlled study. Most children were boys (73%). The children were randomly assigned to a GH treatment group (n = 20) and a control group (n = 20) (Figure). Table I shows the demographic data. The children of the GH treatment group had an extensive biochemical assessment to verify their GH responsiveness during the first year. High-dose GH therapy (Genotropin 2 mg/m^2 body surface per day, Pharmacia and Upjohn, Stockholm, Sweden) was started and given for at least 2 years.

Children in the treatment group visited the pediatrician 4 times per year, and the children in the control group 1 or 2 times per year. To obtain data on HRQOL and self-esteem, children were seen after randomization, but 2 weeks before treatment, or an equivalent period in the control group (T1), 1 year (T2) and 2 years (T3) after start of treatment. Children and their parents were scheduled at the same time but were interviewed independently in different rooms. The parents were seen by a developmental psychologist and the children by different psychology graduate students. The sessions took 2 hours at T1 and 1.5 hours at T2 and T3. The protocol was reviewed and approved by the medical ethics committees of the 3 participating centers in The Netherlands (Catharina Hospital Eindhoven, Sophia Children's Hospital Rotterdam, Free University Hospital Amsterdam). The parents of all children gave written consent to the study. Consent was also obtained from appropriately aged children.

Measures

TNO-AZL CHILDREN'S QUALITY OF LIFE (TACQOL) QUESTIONNAIRE. This is a 56-item instrument for assessing HRQOL of children, aged 6 years

to 12 years, in medical research and clinical trials. Two parallel questionnaires for the child's HRQOL were available: a child form (CF, scales given in Table II) and a parent form (PF, scales given in Table III), both with good measurement properties.[11] The TACQOL explicitly offers respondents the possibility of differentiating between their functioning and the way they feel about it. The final version of the TACQOL appeared in 1995. Because the first children were enrolled in 1994, an earlier version was used during the whole research period. The impact of the difference between the old and the new version was intensively tested and appeared negligible.[20] Because the previous version was used for both groups at all 3 points of measurement, this could not have influenced the comparison between groups in this longitudinal study.

IDIOPATHIC SHORT STATURE QUALITY OF LIFE (ISSQOL) QUESTIONNAIRE. This is an 8-item ISS-specific scale covering vitality. Vitality was chosen because GH treatment can improve the energy level in children and adults with GH deficiency.[2,14,16] Clinical observations of participating pediatricians and psychologists had indicated that vitality might be an important subject in children with ISS. The ISSQOL PF had a Cronbach's α of .71, the α of the ISSQOL CF was .66.

DUTCH CHILDREN'S AZL/TNO QUALITY OF LIFE (DUCATQOL) QUESTIONNAIRE. This is a 25-item generic self-report HRQOL for school-aged children (aged 5-16 years). HRQOL was defined as the children's effective evaluation of various aspects of their daily functioning. The DUCATQOL has good validity and reliability and covers the 4 domains plus a total HRQOL score (Koopman et al,[18] submitted scales given in Table II). The items use abstract faces (☺) as answer categories, with expressions from happy to sad, thus constructing a 5-point Likert scale. The faces allow this instrument to be used with children who lack writing skills.

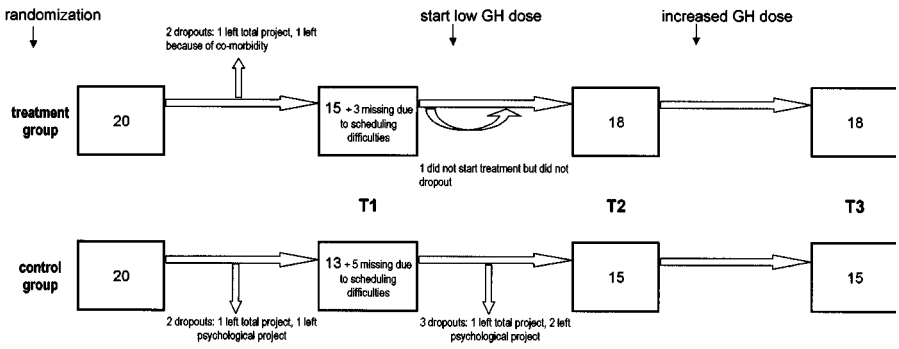

Figure. Composition of the study group over time.

SELF-PERCEPTION PROFILE. This is a 36-item questionnaire measuring self-esteem in children aged 8 years to 12 years.[12,21] The questionnaire stresses the multidimensional nature of the child's sense of competence. It contains 6 scales of 6 items each (see Table II). Statements are presented in a forced choice format and the child is asked to compare her or himself with peers.

THERAPY EVALUATION SCALE (TES). The TES was constructed by the Dutch Working Group Psychologists and Growth Hormone.[22] Perceived growth since the last year and growth expectations in the next year were obtained using a 1 to 6 categoric scale ("not" to "very much"). Other aspects were covered by open-ended questions; at T1, the TES was used to infer the motivations of children and parents to participate in the project. At T1, T2, and T3, participants were asked why they wanted to continue participation and if they could mention drawbacks of the project.

JUDGEMENT OF THE PEDIATRICIAN: GLOBAL HRQOL OF THE CHILD. This instrument contained 3 questions: (1) seriousness of present medical situation, (2) distress of the child from current physical situation (ie, short stature), and (3) distress of the child from participating in the research program. The questions used a 1 to 7 point Likert scale ("not serious at all" to "very serious").

CHILDREN'S AND PARENTS' CHARACTERISTICS. Questions about the children's and parents' characteristics included general information such as parental education. Changes in height were measured by the pediatrician and expressed in centimeters and as standard deviation scores (SDS).[23]

Data Analysis

Dutch reference data were available for the TACQOL-CF, Self-Perception Profile, and DUCATQOL concerning children aged 8 years to 12 years, and on the TACQOL-PF concerning children aged 6 years to 12 years. The children's instruments are allowed to be read aloud when children lack sufficient reading skills. Therefore, we used the instruments with children up to 1 year younger than the available reference groups. Differences between children within and outside the reference data's age ranges were tested with multivariate analysis of variance (ANOVA). Because differences between children within and outside these age ranges were not significant in this study group (data not shown), reference data of the nearest age group were used to calculate standardized scores of children outside the age ranges. All scale scores were obtained by adding item scores within scales and transforming crude scale scores linearly to a 0 to 100 scale, with higher scores indicating better HRQOL or better self-esteem. Raw scores were

Table II. Child's perception: Health-related quality of life and self-esteem at all measurements

	T1		T2		T3		Longitudinal changes†		
	Treatment M	Control M	Treatment M	Control M	Treatment M	Control M	*P* time	*P* group	*P* time × group
TACQOL-CF (in SDS)	n = 12	n = 9	n = 17	n = 10	n = 15	n = 14			
Physical complaints	–1.11	–1.41	–1.50	–1.38	–1.67	–0.74*b	.74	.30	.05
Motor functioning	–0.10	–0.45	–0.14	0.43	–0.37	0.29*b	.74	.17	.24
Autonomy	–0.54	–0.69	–0.80	0.22	–0.41	0.13	.59	.14	.16
Cognitive functioning	0.28	0.20	0.24	0.65	–0.11	0.44*b	.67	.19	.60
Social functioning	–2.37	–1.25	–1.68	–0.69	–2.64	–0.56*a	.22	.00	.61
Positive emotions	–0.51	–0.41	–0.78	–0.22	–0.75	0.10*c	.87	.11	.95
Negative emotions	0.05	0.00	–0.21	0.00	–0.17	0.03	.14	.66	.80
ISSQOL-CF (scale 0-100)	n = 12	n = 9	n = 17	n = 10	n = 15	n = 14			
Vitality	77	74	76	82	70	85*a	.59	.13	.04
DUCATQOL (in SDS)	n = 15	n = 13	n = 18	n = 15	n = 18	n = 15			
Home	–0.15	–0.40	0.19	0.01	0.19	0.24	.12	.67	.81
Physical	–0.12	–0.29	0.36	0.07	0.19	0.10	.26	.58	.66
Emotional	0.10	–0.03	0.61	0.42	0.34	0.31	.11	.69	.89
Social	–0.35	–0.10	0.51	0.17	0.09	0.67	.06	.60	.19
Total QOL	–0.16	–0.20	0.55	0.24	0.26	0.42	.05	.82	.47
Height appreciation: "about how tall I am I feel" (item from the physical scale)	–0.39	–0.57	–0.24	–0.03	–0.12	–0.67	.48	.61	.50
Self-Perception Profile (in SDS)	n = 14	n = 12	n = 18	n = 15	n = 18	n = 15			
Scholastic competence	0.66	0.26	0.57	0.51	0.41	0.84	.22	.95	.05
Social acceptance	–0.17	0.19	0.39	0.36	0.25	0.85	.21	.27	.27
Athletic competence	–0.05	0.20	0.27	0.22	0.31	0.43	.11	.68	.84
Physical appearance	–0.06	–0.16	–0.22	0.17	–0.09	0.14	.65	.52	.92
Behavioral conduct	0.41	0.55	–0.02	0.64	0.09	1.00	.67	.10	.27
General self-worth	0.18	0.32	0.43	0.22	0.01	0.36	.68	.76	.26

Higher scores represent better HRQOL or self-esteem.
*Between groups: Mann-Whitney *U* test: [a]$P \leq .01$, [b]$P \leq .05$, [c]$P \leq .10$.
†Results of the RM-ANOVAs, *P* values of ≤ .10 are underlined.

standardized with the mean and SD of a healthy norm group, to correct for age-related changes. Because standardization of the TACQOL to the norm group may be influenced by using the previous version of this instrument, raw scores were used in all analyses.

The results of the treatment and control groups were expressed as the mean scores and the SD at all points of measurement. Differences between groups at each time with respect to HRQOL and self-esteem were tested by Mann-Whitney *U* test for independent samples. The measurements over time were analyzed by using mixed-model ANOVA for repeated measurements (RM-ANOVA) with the patient as the random factor, and time and treatment and their interaction as fixed factors.[24]

Linear regression analyses were computed for every scale to reveal possible relationships between the dependent variable changes in HRQOL or self-esteem and the independent variables: growth (objective and subjective), growth expectations, satisfaction with height, and group. In this analysis, the difference between T2 and T3 was used for 2 reasons; at T1, some children had missing data and most growth was expected after T2 because of increasing GH doses. To control for potential differences between the groups at that time, T2 scores were also used as a covariate. Agreement between children and parent reports on the TACQOL was tested and quantified with paired *t* tests and intraclass correlations.[25]

Overall, results of statistic analyses were reported as significant with a *P* value of ≤ .05 or as trends with a *P* value between .05 and .10. Because of the small sample size, we expected to have little power for clinically important differences. Therefore, Bonferroni correction for multiple testing was not performed.

The open-ended questions from the TES were subjected to qualitative analyses according to Grounded Theory principles.[26] The answers were categorized by content, and the distribution

of the data over the categories in the 2 groups was studied. Although the frequency of certain answers can verify the importance of a statement, results can be used to generate hypotheses but not to test them.

RESULTS

Children With ISS Compared With a Reference Group

Analyses with the raw data (not shown) were similar to the results with the data standardized according to age and sex, indicating a negligible effect of age and sex.

The standardized scores of the children's HRQOL (TACQOL, ISSQOL, and DUCATQOL) and self-esteem (Self-Perception Profile) questionnaires are given in Table II and the parents' and pediatricians' measurements are given in Table III. Most SDS at T1 were around zero. The only scales showing scores at approximately –2 SDS were the HRQOL social functioning scales (TACQOL-CF and PF). Therefore, there was little support for the hypothesis that children with ISS have lower HRQOL and self-esteem than a normal reference group.

Control Group Versus Treatment Group

Low HRQOL or self-esteem at T1 was expected in the control group because of children's possible disappointment at the start as a result of not being selected for treatment. This effect was found in the HRQOL positive emotions (significant) and cognitive functioning (trend) scales as reported by the parents only, and it disappeared at T2 (see Table III).

It was expected that the treatment group would gain more HRQOL and self-esteem than the control group. According to child reports (Table II), there were few significant differences between groups according to the Mann-Whitney *U* test and all were in a direction opposite to the one expected. Most differences were found at T3 in the TACQOL-CF; the children from the treatment group had significantly worse HRQOL than the children in the control group in some scales (Table II). No differences between groups were reported by the parents except for the ones at T1 mentioned above (Table III). The pediatrician reported at T3 more distress in the control group than in the treatment group (Table III).

The RM-ANOVAs revealed some interaction effects, indicating that the scores changed differently between groups during the project. According to the children, the treatment group decreased and the control group increased in some scales (see Table II). According to the parents, the TACQOL-PF positive emotions scale changed differently in both groups, probably because of the low scores in the control group at T1. Height expressed in centimeters improved more in the treatment group than in the control group, whereas the height SDS improved significantly in the treatment group only. The satisfaction with height—covered by an item from the DUCATQOL physical scale "about how tall I am I feel…"—was not significantly different between groups.

A group effect in the TACQOL-CF social functioning and Self-Perception Profile's behavioral conduct indicates a systematic difference between groups according to the children, with lower scale scores for the treatment group. The group effect in the judgement of the pediatrician on the seriousness of, and distress by, the current medical situation indicates that there was a difference between groups from the start.

Pros and Cons for Participation: Qualitative Data

The treatment group differed from the control group with regard to the motivation for participation (Table IV). Both groups provided answers indicating that they participated because this was not a burden and they stated that there were no serious drawbacks.

Growth Expectations, Growth, and Satisfaction With Height Versus Changes in HRQOL and Self-Esteem

According to the linear regression analyses, the changes in HRQOL and self-esteem between T2 and T3 were generally predicted by the scores at T2. Significant β-weights ($P \leq .05$) were found for all scales in a range between –0.41 and –0.83. A significant β-weight means that one SD change of the T2 score of a scale relates to β units of change in HRQOL or self-esteem, given that other independent variables are held invariable. This indicates that the lower the T2 scores, the greater the improvement in HRQOL or self-esteem. T2 scores did not differ between groups (see also Table II).

More satisfaction with the current height at T3 related significantly ($P \leq .05$) to improvement in TACQOL-CF cognitive functioning (β = 0.37) and social functioning (β = 0.44); DUCATQOL home (β = 0.47), physical (β = 0.73), emotional (β = 0.88), and total quality of life (β = 0.82); and Self-Perception Profile general self-esteem (β = 0.37). More growth as perceived by the child related significantly to TACQOL-CF positive emotions (β = 0.57), Self-Perception Profile athletic competence (β = 0.54), physical appearance (β = 0.55) and general self-esteem (β = 0.47). More growth in height SDS related significantly to DUCATQOL physical (β = 0.68). This means that satisfaction with height, which did not differ significantly between groups, had a stronger relationship with changes in HRQOL than both growth variables. Growth expectations did not contribute to the HRQOL changes between T2 and T3.

Agreement Between Informants

According to paired *t* tests between the TACQOL-CF and PF (not shown), the children reported significantly lower HRQOL than their parents on physical complaints at T2, higher HRQOL on cognitive and social func-

Table III. Parents' and pediatricians' perception: Health-related quality of life and height at all measurements

	T1		T2		T3		Longitudinal changes†		
	Treatment M	Control M	Treatment M	Control M	Treatment M	Control M	*P* time	*P* group	*P* time × group
TACQOL-CF (in SDS)	n = 15	n = 13	n = 18	n = 15	n = 17	n = 15			
Physical complaints	–0.78	–0.98	–1.25	–1.17	–1.50	–1.37	.22	.98	.96
Motor functioning	–0.26	–0.22	–0.29	–0.25	–0.15	0.05	.60	.73	.95
Autonomy	–0.76	–1.03	–1.30	–1.50	–0.21	0.01	.07	.92	.83
Cognitive functioning	0.34	–0.77*c	–0.79	–0.10	–0.79	–0.53	.29	.94	.47
Social functioning	–2.34	–2.69	–2.96	–2.48	–2.16	–2.25	.21	.95	.54
Positive emotions	–0.05	–2.10*a	–0.86	–0.15	–0.21	–0.07	.29	.45	.03
Negative emotions	–0.48	–0.68	–0.93	–0.38	–0.78	–0.39	.79	.43	.61
ISSQOL-PF (scale 0-100)	n = 15	n = 13	n = 18	n = 15	n = 17	n = 15			
Vitality	75	76	75	77	76	78	.94	.65	.93
Judgment of the pediatrician (scale 0-100)	n = 15	n = 13	n = 18	n = 15	n = 18	n = 14			
Seriousness of current medical situation	81	77	75	68	83	81	.05	.08	.73
Distress from current medical situation	56	49	63	57	79	58*a	.02	.04	.27
Distress from participating in research program	63	55	64	66	79	63*a	.05	.17	.27
Objective measurements	n = 15	n = 12	n = 18	n = 15	n = 18	n = 14			
Height (cm)	115	114	123	120	132	124*a	.00	.24	.00
SDS for height at given age	–2.95	–2.70	–2.53	–2.55	–1.85	–2.50*b	.00	.32	.00

Higher scores represent better HRQOL or self-esteem.
*Between groups: Mann-Whitney *U* test: [a]$P \leq .01$; [b]$P \leq .05$, [c]$P \leq .10$.
† Results of the RM-ANOVAs, *P* values of < .10 are underlined.

Table IV. Pros and cons for participation: An overview of the qualitative data

Treatment group	Control group
Parents' motivation for participation	
Child is too short and needs to grow	Child is too short and needs to grow (disappeared as motivation)
Child had problems with being short	Hoped that child could have treatment after all (disappeared as motivation)
Wanted to use every opportunity to let child grow	To have their child closely monitored by professionals
Optimistic about growth results	For the benefit of the research project and other children in the future
Went on because of good growth results	
Children's motivation for participation	
Wanted to grow, partly to resolve	Did not know why they were participating
Psychosocial problems (eg, being teased less)	Their parents decided to go on with the project
Parents about possible drawbacks	
No drawbacks: half of the group stated participation is no burden	No drawbacks: half of the group stated participation is no burden
Drawbacks: daily injections; going to the hospital	Drawbacks: having blood samples taken; absence from school
Drawback: uncertainty about possible side effects of GH and about final height	Drawback at start: fear that participation puts more stress on being short
Children about possible drawbacks	
No drawbacks: half of the group stated participation is no burden	No drawbacks: half of the group stated participation is no burden
Drawback: daily injections	Drawback: having blood samples taken

tioning at T2 and T3, and higher HRQOL on negative emotions (= less negative emotions reported) at T3. The intraclass correlations between TACQOL-CF and PF were very low (–.29 to .54) and mostly not significant, except for negative emotions (T1 = .52; T2 = .46), positive emotions (T2 = .49; T3 = .54), and physical complaints (T2 = .38). In the previous section, it was shown that the pattern of longitudinal changes differed between child, parent, and pediatrician. It can be concluded that the agreement between informants is low.

DISCUSSION

One of the arguments in support of GH therapy in ISS is that increasing height would cause more age-appropriate reactions to children, improving their HRQOL or self-esteem. In contrast to these common assumptions but in concordance with previous reports in referred[6,7,13,27] and nonreferred children,[5] we found that children with ISS did not have a lower HRQOL and self-esteem than the norm population, except for the HRQOL domain of social functioning as reported by children and parents. Furthermore, no improvements occurred and no change was noted in the parents' opinion about social competence. This is in contrast to earlier findings about changes in parental perception of social competence and behavior in an uncontrolled study.[28] Although in other studies a relationship was found between GH treatment and energy level,[2,14,16] the HRQOL vitality scores did not improve in our treatment group. Improvement was expected if children with ISS had symptoms of GH deficiency (eg, lack of vitality).[15] Thus, the results of the current study provide no support for improvement of HRQOL, self-esteem, or vitality, except in the eyes of the pediatrician. The latter illustrates the low agreement between informants, further stressed by the low correlations between parents' and children's reports. Yet, the attitude of parents and pediatricians is important to determine how a child copes with his or her short stature.[13]

In recent studies, some specific short stature instruments were presented[29]: measuring vitality and self-esteem,[13] but also stigmatization, juvenilization, and future anxieties.[16] In future research, it would be of interest to include such measures besides the generic instruments. Nevertheless, it is unlikely that with specific instruments, large improvements could have been found, because the short stature-specific themes are reflected more or less in the generic instruments used (eg, in the TACQOL social functioning scale or the Self-Perception Profiles social acceptance and physical appearance scales).

One of the factors that could disturb a straightforward relationship between growth and HRQOL or self-esteem is the effect of participation in the study itself. A limitation of the study was that the first point of measurement was planned after the randomization process so the results at T1 were already influenced by the selection itself. Parents of children in the control group indicated temporarily less positive emotions. In addition, results indicate that the pediatrician saw a difference between groups from T1 onward. Furthermore, participants in the 2 groups gave different answers to the retrospective open-ended question about why they started to participate in the study. It is not likely that these differences between groups originated from before the randomization, although the retrospective question pointed at that period. In the absence of a real baseline measure, we suppose that the differences between groups are the results of psychologic changes because of the randomization.

The relationship between growth and HRQOL or self-esteem could furthermore be disturbed by the expectations of the participants. Growth expectations of the children in the treatment group could be unrealistically high because the effect of GH on growth in ISS is variable. On the other hand, children in the control group might grow more than they expected at the start. Although in the current study, height SDS improved significantly in the treatment group only, height expressed in centimeters improved in both groups, which could be a surprise to children in the control group. According to Calman,[30] the smaller the gap between expectations and achievements, the better the HRQOL would be. Lower expectations in the control group could have made the small growth achievements less frustrating. However, growth expectations and achieved growth were either not or only a little related to changes in HRQOL or self-esteem. Nevertheless, it is possible that other expectations and achievements than those about growth affect HRQOL. For instance, becoming more independent or participating in the project to help other children could be an achievement as well. Yet, children from the treatment group who expected to achieve psychosocial benefits from their growth might be disappointed. Furthermore, uncertainty in the treatment group about final height, even if they grew well at that time, could postpone the feeling that growth was really achieved.

It was formerly reported that short children had lower satisfaction with their height, although their self-esteem concerning body image seemed to be good.[5] We found that measured height did not relate to HRQOL or self-esteem. Instead, perceived height and, even more, the child's satisfaction with the current height related positively to improvements in HRQOL and self-esteem. Perceived height appears more strongly associated with psychologic adaptation than measured height, which supports our results.[31]

Concerning the burden that GH treatment can impose, parents and children from both groups overall provided an-

swers indicating that participation was not felt as a burden. However, although the pediatrician stressed that GH is considered a safe product, some parents in the treatment group were afraid of unknown side effects. The fear for side effects of medication is widespread and therefore difficult to eradicate.[32]

Short stature may affect HRQOL more in adolescence than in childhood, although the effects of short stature also appear modest in that age range.[5,33] Our data cannot be generalized to nonreferred children with short stature, because they generally are not short,[1,8,14] whereas their parents are less worried about shortness than the parents of referred children.[8,14,34] Therefore, the parents' valuation of the child's HRQOL may be lower in referred children than in nonreferred children (referral bias).[1,5] Nevertheless, apart from social functioning, the parents of our referred children did not report lower HRQOL than parents from the norm group. Future studies will have to elucidate whether these results hold true for adolescence and young adulthood. The assumption that GH treatment improves HRQOL in children with ISS could not be confirmed.

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