Electronic patient and parent reported outcomes in pediatric clinical practice
Haverman, L.

Citation for published version (APA):
Haverman, L. (2013). Electronic patient and parent reported outcomes in pediatric clinical practice

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Download date: 10 Jan 2019
Chapter 2

Predictors of Health Related Quality of Life in Children and Adolescents with Juvenile Idiopathic Arthritis: Results from a Web-Based Survey

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Arthritis Care and Research
2012 May; 64(5):694-703
Abstract

Objectives
Children with juvenile idiopathic arthritis (JIA) experience functional impairment due to joint manifestations of the disease. The aim of our present study was to assess health related quality of life (HRQOL) and its predictors in a group of children and adolescents with JIA.

Methods
The study sample includes all JIA patients (ages 6-18 years) who consulted a pediatric rheumatologist in Amsterdam, the Netherlands, between February 2009 and March 2010. HRQOL was measured using the Paediatric Quality of Life Inventory 4.0 (ages 6-18 years). Functional ability was measured using the Child Health Assessment Questionnaire, and medical and socio-demographic parameters were assessed. The study sample was compared to a Dutch youth norm population including children with other chronic health conditions. The proportion of children with JIA with an impaired HRQOL (< 1 SD) was evaluated and multivariate regression analyses were performed to predict HRQOL outcome.

Results
Of the eligible patients, 64.1% (n = 152) participated. Both children (ages 6-12 years) and adolescents (ages 13-18 years) with JIA reported a significantly lower HRQOL in almost all domains compared to either healthy controls or children with other chronic health conditions. Approximately half of the children with JIA showed an impaired HRQOL. The main predictors of HRQOL were functional ability, pain, subjective burden of medication use, and school absence.

Conclusion
The HRQOL is severely affected in children and adolescents with JIA. These findings underline the necessity to systematically monitor HRQOL in daily clinical practice.
Introduction

Juvenile idiopathic arthritis (JIA) is arthritis of unknown etiology that starts before the age of 16 years. It is one of the most common rheumatic diseases in childhood and a major cause of childhood disability. Worldwide, 0.07-4.01 per 1000 children are affected. Children with JIA experience functional impairment due to joint manifestations of the disease, morning stiffness, and fatigue. There is no definite cure for JIA; treatment is aimed at controlling pain and achieving inactive disease or remission by means of medication, which might have side effects as well.

Physical measures alone are not sufficient to assess the impact of JIA on a child’s life. The evaluation of health related quality of life (HRQOL) is essential for a full assessment of the influence of the disease on a child’s life. Quality of life is defined by the World Health Organization as “individuals’ perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”. HRQOL is a concept that incorporates measures of physical symptoms, functional status, and disease impact on psychological and social functioning.

Some studies suggest that JIA does not negatively affect HRQOL or psychosocial functioning, whereas other studies report that children with JIA have a lower HRQOL compared to healthy children and compared to children with other chronic health conditions. Although a large number of studies have assessed HRQOL in children with JIA, only few studies focused on predictors of HRQOL in children with JIA. Risk factors identified for impaired HRQOL are polyarticular arthritis or extended oligoarthritis, short disease duration, pain, disabilities, and increased disease severity.

HRQOL studies in JIA patients are scarce in Europe and include heterogeneous groups of patients based on different age cohorts and with different national health care systems. Many studies use proxy reporting, whereas other studies have shown that self-reporting appears to be more reliable for evaluating HRQOL. Different HRQOL questionnaires, both generic and disease-specific, have been used for children with JIA. Because of the aforementioned aspects, it is difficult to compare the various studies. Our present study therefore aimed to examine the HRQOL of all children and adolescents with JIA attending one of the pediatric rheumatology centers in Amsterdam, the Netherlands, with the use of self-report (ages 8-18 years) or proxy report (ages 6-7 years). We investigated the HRQOL of children with JIA of a broad range of ages using generic HRQOL questionnaires. We compared the HRQOL of children with JIA to a healthy Dutch youth norm population and to children with other chronic health conditions. In addition, we assessed the proportion of children with JIA and an impaired HRQOL and the predictors of HRQOL.
Patients and Methods

Patients
In a prospective study, we collected data from all children who consulted a pediatric rheumatologist between February 2009 and March 2010 at one of the 4 referral centers in Amsterdam: the Emma Children’s Hospital/Academic Medical Center, VU Medical Centre, Reade (location Jan van Breemenstraat) and Sint Lucas Andreas Hospital. All children (ages 6-18 years) with JIA were eligible. Data were collected as part of the multi-center Kwaliteit van Leven in Kaart (KLIK; Quality of Life in Clinical Practice). The KLIK study assesses the effect of discussing HRQOL during a consultation using Patient Reported Outcomes (PROs) 28-30. Prior to a planned outpatient consultation, a letter was sent to the parents and patients, which set out the purpose and the procedure of the KLIK study. All patients gave informed consent according to regulations and the study was approved by the medical ethics committees of the participating centers.

A username and password were sent by e-mail to the participating patients, enabling them to log in to the study website (www.hetkliktnu). The patient (ages 8-18 years) or parent (for children ages child 6 or 7 years) could fill in the questionnaires after the computer system had automatically selected the appropriate questionnaires (depending on the child’s age). Eligible JIA patients attending the outpatient department during the study period who did not complete the questionnaires were defined as nonparticipants.

Measures
Socio-demographics
Socio-demographics on participating children and parents were collected using the online baseline questionnaires completed by the mother or father. The following information concerning the child was obtained: age, age at onset of disease, school absence (missed days at school in the last 3 months), sex, participation in sports, and subjective burden of medication use. Data were obtained from the parents on their age, sex, country of birth, education (where low indicates no education, primary school or primary vocational education; middle indicates secondary school or secondary vocational education; and high indicates higher vocational education or university) and employment status. Information on child's age, sex, and parental country of birth in the non-participants group was retrieved from medical files.

Medical data and assessment of JIA severity
The participants’ medical data were assessed by the pediatrician during the consultation. The non-participants’ medical data were collected retrospectively, based on the reports in the medical files. All patients were classified according to
the International League of Associations for Rheumatology criteria. During the consultation, the physician assessed the disease activity on the 100-mm Visual Analogue Scale (VAS; where 0 = no disease activity and 100 = very severe activity) and the number of active joints. These were classified as follows: no active joints, monarthritis (1 joint), oligoarthritis (2 to 4 joints), polyarthritis (5 to 10 joints), and severe polyarthritis (≥11 active joints). The patient’s medication at the time of the consultation was recorded. Current or previous presence of uveitis was noted. The time between disease onset and diagnosis was calculated, as well as disease duration (time from disease onset to the date of the consultation). Finally, as other studies have shown that being overweight has a negative impact on HRQOL, length and weight were also noted so as to calculate the Body Mass Index (BMI).

**Functional ability and discomfort**

**Childhood Health Assessment Questionnaire (CHAQ)**
The Dutch version of the CHAQ was used to measure functional ability. The disability index is a summarized score ranging from 0 to 3, with higher scores indicating higher disability. The CHAQ can be used as a self-report, as well as a parent proxy report. Both versions, the proxy report (ages 6 or 7 years) and the self-report (ages 8-18 years), were used in this study.

**Discomfort**
Discomfort was assessed by the completion of a 100-mm VAS for the evaluation of pain (where 0 = no pain and 100 = very severe pain) and a VAS for the evaluation of overall well-being (where 0 = very well and 100 = very poor) by the parent or patient, depending on the age of the child.

**HRQOL**
In order to compare the HRQOL scores of children with JIA to those with other chronic health conditions, we used the generic version of the Paediatric Quality of Life Inventory 4.0 (PedsQL). The PedsQL (past week version) appeared to be most appropriate because of its broad age range (6-18 years), its inclusion of self-reports as well as proxy reports, its short completion time (approximately 5-10 minutes), and good feasibility, validity, and reliability. The proxy report (ages 6 or 7 years) and self-report version (ages 8-18 years) were used. The 23 PedsQL items are divided into 4 subscales (including 5-point Likert scales): physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), and school functioning (5 items). Previous research provided data on a Dutch healthy norm population (n = 401) and on children with other chronic health conditions. Children with chronic health conditions were identified if the parents reported at the socio-demographic
questionnaire that their child suffered from a chronic health condition. This group (n = 62) included: asthma (36.4%), congenital defect (13.6%), skin disease (6.1%), and migraine (6.1%). The Dutch PedsQL version differentiates between children with and without a chronic condition. The socio-demographics about the parents were as follows; women (80.6%), parental country of birth (the Netherlands, 85.9%), high education (48.4%), employment (72.9%).

In rheumatology, the PedsQL generic scale has shown excellent reliability, validity, and responsiveness. Because the reliability appeared to be less in younger children with rheumatic diseases, we used the PedsQL in children from the age of 6 years.

Statistical Analyses

The SPSS software, version 16.0 was used to manage and analyze the data. First, differences between participants and non-participants were analyzed. Age and age at onset were analyzed using independent t-tests. Age group, sex, JIA subtype, parental country of birth, number of active joints, and medication were analyzed using a chi-square tests. Differences in physician disease activity rating (VAS score), disease duration, and time between disease onset and diagnosis were examined using Mann-Whitney tests.

Second, differences between the JIA group, the Dutch norm group, and the children with other chronic health conditions were analyzed. The PedsQL scores were computed according to the manual. Independent sample t-tests were conducted to analyze differences between the JIA group (ages 6-18 years) and the norm group, as well as the group with other chronic health conditions (PedsQL). To report the strength of this difference, effect sizes were calculated by dividing the difference in mean scores between the JIA group and the norm group/chronic health condition group by the pooled SD of both groups. Effect sizes were considered small up to 0.2, moderate at approximately 0.5, and large at approximately 0.8. The 95% confidence interval of the effect sizes were calculated.

The proportion of children with an impaired HRQOL was based on a HRQOL score ≥1 SD below the mean of the Dutch norm population as defined by Varni et al. In the Dutch norm population, around 16% of children had impaired HRQOL (based on a normal distribution). The percentages of children with JIA scoring ≥1 SD below the mean of the norm population were compared to the norm using chi-square tests.

Linear multiple regression analyses were performed to predict HRQOL as expressed by the scores on the PedsQL. First, univariate analyses were performed on all the selected predictors for every HRQOL domain separately. Variables with P < 0.05 in at least 1 of the PedsQL domains were included simultaneously in the final regression model. Disease duration, parental country of birth and participation in sports were therefore removed from the multivariate regression. Owing to multicolinearity (high
correlation between predictors, correlation >0.80), general well-being (VAS score) and number of active joints were excluded. Age, physician disease activity score (VAS score), medication use, subjective burden of medication use, BMI, CHAQ total score, patient reported pain (VAS score), parental education, and school absence were included. Standardized regression coefficients (β) are reported, which express the strength of the association between the predictor variables and the outcomes. Standardized regression coefficients of 0.1 are considered small, of 0.3 are considered medium, and of 0.5 are considered large for continuous predictors. For binary-coded predictor variables, regression coefficients of 0.2 are considered small, of 0.5 are considered medium, and of 0.8 are considered large 38. For each regression, the explained variance (R²) was determined, and it was tested using the F test. The effect sizes of explained variance of 0.02 are considered small, of 0.13 are considered medium, and of 0.26 are considered large 37. T-values and their significance level were calculated to test the hypothesis whether the contribution (the regression coefficient [β]) of an entered variable significantly differed from zero.

Results

Socio-demographic and medical information

The results are shown in Table 1. Between February 2009 and March 2010, 237 children with JIA and their parents were approached to participate in the KLIK study. A total of 152 (64.1%) participants completed the online HRQOL questionnaire. A total of 67% of the participating children were female participants, and the mean age of all the children was 13.03 years.

A total of 135 parents completed the socio-demographic questionnaire; 80.9% of the parents were mothers, the mean ± SD age was 42.86 ± 5.0 years and 74.3 % were employed. In 80% of these parents the parental country of birth was the Netherlands. The distribution of education was as follows: 15.1% of the parents were low educated, 47.4% were middle educated, and 26.3% were high educated.

Scores for functional ability and discomfort

The CHAQ scores were available for 151 patients. The mean ± SD total score was 0.82 ± 0.7. The mean ± SD patient reported VAS pain score was 30.51 ± 29.5, and the mean ± SD VAS score of patient reported general well-being was 30.77 ± 27.1.

Results for HRQOL

The results are shown in Table 2. The HRQOL of children ages 6 and 7 years, based on proxy reporting, was significantly lower compared to the Dutch healthy norm population.
(P <0.05) in all the domains except emotional functioning. Large effect sizes were found for the total score, physical health and school functioning. Children (ages 8-12 years) reported significantly lower HRQOL scores in all domains compared to the Dutch norm.

### Table 1. Socio-demographics and disease characteristics of participants and non-participants

<table>
<thead>
<tr>
<th>SOCIO-DEMOGRAPHICS</th>
<th>Participants</th>
<th>Non-participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>152</td>
<td>85</td>
</tr>
<tr>
<td>Age of onset JIA</td>
<td>151</td>
<td>82</td>
</tr>
<tr>
<td>Missed days at school</td>
<td>142</td>
<td>76</td>
</tr>
<tr>
<td>Body Mass Index (BMI)**</td>
<td>137</td>
<td>21.2</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>102</td>
<td>51</td>
</tr>
<tr>
<td>Playing sports</td>
<td>80</td>
<td>52.6</td>
</tr>
<tr>
<td>Subjective burden of medication use</td>
<td>77</td>
<td>50.7</td>
</tr>
<tr>
<td>Parental country of birth (Netherlands)*</td>
<td>120</td>
<td>57</td>
</tr>
<tr>
<td><strong>JIA subtype</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oligo-articular JIA, persistent</td>
<td>30</td>
<td>14</td>
</tr>
<tr>
<td>Oligo-articular JIA, extended</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td>Poly-articular JIA, RF negative</td>
<td>66</td>
<td>37</td>
</tr>
<tr>
<td>Poly-articular JIA, RF positive</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Systemic JIA</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Enthesitis related Arthritis</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Undifferentiated JIA</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Chronic arthritis with other autoimmune inflammatory disease</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Months between symptom onset and diagnose</td>
<td>151</td>
<td>80</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>181</td>
<td>82</td>
</tr>
<tr>
<td>Physician disease activity (VAS score range 0-100)</td>
<td>181</td>
<td>85</td>
</tr>
<tr>
<td>Number of joints with arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No arthritis</td>
<td>63</td>
<td>40</td>
</tr>
<tr>
<td>monarthritis (1 joint)</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>oligoarthritis (2-4 joints)</td>
<td>43</td>
<td>15</td>
</tr>
<tr>
<td>polyarthritis (&gt; 4 joints)</td>
<td>26</td>
<td>15</td>
</tr>
<tr>
<td>Uveitis presenting during disease course</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Medication at time point of evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No medication</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>NSAID</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>DMARDS (including methotrexate, sulfasalazine)</td>
<td>120</td>
<td>59</td>
</tr>
<tr>
<td>Biologicals (Anti-TNF) with or without DMARDS</td>
<td>22</td>
<td>8</td>
</tr>
</tbody>
</table>

*P<.05, **P<.01, ***P<.001, n = 5 parents had missing data, n =1 had missing date of onset
HRQOL in children with JIA

Chapter 2

Figure 1 shows the percentages of children and adolescents with an impaired HRQOL on all PedsQL scales. The proportion of JIA patients with an impaired HRQOL was significantly larger than the proportion in the Dutch norm population in almost all domains. Almost half of the children with JIA (47-57%) had an impaired HRQOL, which is a significant difference in comparison with the approximately 16% in the Dutch norm population.

(P <0.05). Large effect sizes were found for the total score and physical health. Adolescents (ages 13-18 years), in line with the group ages 6 and 7 years, reported significantly lower HRQOL scores on all scales compared to the Dutch healthy norm population, except for emotional functioning. Large effect sizes were found for the total score and physical health.

Compared to children with other chronic health conditions, children with JIA (ages 6 and 7 years) showed no differences on HRQOL scores. Children ages 8-12 years with JIA scored significantly lower in all domains except social functioning. Adolescents with JIA also consistently reported lower HRQOL scores compared to the chronic health condition group; only the score for physical health was significantly lower. A large effect size was found in the group ages 6 and 7 years on psychosocial health.

Proportion of JIA patients with an impaired HRQOL

Figure 1 shows the percentages of children and adolescents with an impaired HRQOL on all PedsQL scales. The proportion of JIA patients with an impaired HRQOL was significantly larger than the proportion in the Dutch norm population in almost all domains. Almost half of the children with JIA (47-57%) had an impaired HRQOL, which is a significant difference in comparison with the approximately 16% in the Dutch norm population.
Chapter 2

Predictors of HRQOL in children and adolescents with JIA

The results of the univariate analysis are shown in Table 3, and the multivariate analysis in Table 4. The explained variance of the scales ranged from 26-81%. Older children reported fewer problems in HRQOL domains compared to younger children. The pediatricians reported disease activity was not significantly related to HRQOL. The subjective burden of medication use and pain was significantly associated with the total functioning, psychosocial functioning, and emotional functioning of children with JIA. Children with higher scores on the CHAQ reported a worse HRQOL score at physical, psychosocial, and social functioning. Children with more days missed at school reported lower HRQOL for total, psychosocial, and school functioning.

Table 2. HRQOL (PedsQL) of children with JIA aged 6 – 18 years compared to Dutch norm data and children with other chronic health conditions.

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Children with JIA</th>
<th>Norm population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
</tr>
<tr>
<td>Total score</td>
<td>14</td>
<td>70.26*</td>
</tr>
<tr>
<td>Psychosocial health</td>
<td>14</td>
<td>72.98*</td>
</tr>
<tr>
<td>Physical health</td>
<td>14</td>
<td>65.18*</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>14</td>
<td>69.29</td>
</tr>
<tr>
<td>Social functioning</td>
<td>14</td>
<td>76.79*</td>
</tr>
<tr>
<td>School functioning</td>
<td>14</td>
<td>72.86*</td>
</tr>
<tr>
<td>Group 8-12 (self-report)</td>
<td>63</td>
<td>71.67****</td>
</tr>
<tr>
<td>Total score</td>
<td>63</td>
<td>71.9***</td>
</tr>
<tr>
<td>Psychosocial health</td>
<td>63</td>
<td>71.23****</td>
</tr>
<tr>
<td>Physical health</td>
<td>63</td>
<td>69.84**</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>63</td>
<td>76.98***</td>
</tr>
<tr>
<td>Social functioning</td>
<td>63</td>
<td>68.89****</td>
</tr>
<tr>
<td>School functioning</td>
<td>75</td>
<td>71.91***</td>
</tr>
<tr>
<td>Psychosocial health</td>
<td>75</td>
<td>74.38**</td>
</tr>
<tr>
<td>Physical health</td>
<td>75</td>
<td>67.29****</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>75</td>
<td>72.60*</td>
</tr>
<tr>
<td>Social functioning</td>
<td>75</td>
<td>83.27***</td>
</tr>
<tr>
<td>School functioning</td>
<td>75</td>
<td>67.27**</td>
</tr>
</tbody>
</table>

1) *p<.05, **p<.01, ***p<.001 versus Dutch norm population, "p<.05, ^^p<.01, ^^^p<.001 versus children with a chronic health condition, Higher scores represent a better HRQOL, p values at two sample t-test: JIA versus norm and JIA versus chronic health condition
2) Effect sizes up to 0.2 were considered to be small, effect sizes of about 0.5 moderate and effect sizes of about 0.8 large

Predictors of HRQOL in children and adolescents with JIA

The results of the univariate analysis are shown in Table 3, and the multivariate analysis in Table 4. The explained variance of the scales ranged from 26-81%. Older children reported fewer problems in HRQOL domains compared to younger children. The pediatricians reported disease activity was not significantly related to HRQOL. The subjective burden of medication use and pain was significantly associated with the total functioning, psychosocial functioning, and emotional functioning of children with JIA. Children with higher scores on the CHAQ reported a worse HRQOL score at physical, psychosocial, and social functioning. Children with more days missed at school reported lower HRQOL for total, psychosocial, and school functioning.
HRQOL in children with JIA

Discussion

Our study shows significant impairment of HRQOL in patients with JIA in nearly all domains, almost independent of pediatrician reported disease activity status or disease duration. Four factors appear to be strongly related to impaired HRQOL in all patients: functional ability (CHAQ score), patient reported pain, school absence and the subjective burden of medication use.

Both the child age group (6-7 years) and the adolescent age group (13-18 years) reported lower HRQOL compared to their healthy peers; HRQOL scores were equal compared to peers with other chronic health conditions. The 8-12 years age group reported lower HRQOL scores compared to their healthy peers, as well as to the children with other chronic health conditions. In all age groups the largest effects were found for physical and psychosocial functioning. These findings are consistent with previous JIA studies. Emotional functioning, however, seems to be less affected than other domains in all age groups.
Chapter 2

We tried to get more insight into HRQOL outcomes by using predictive statistical models, but with the use of linear multivariate regression analyses causality cannot be proven. In other studies, physical disability also appears to be strongly related to HRQOL.\textsuperscript{14,16,22,39} Besides, physical activity is generally impaired in adolescents with

\begin{table}
\centering
\caption{Univariate regression analysis of HRQOL \textit{PedsQl} scores of children with JIA and medical predictors}
\begin{tabular}{|l|c|c|c|c|c|c|}
\hline
 & Total score & Psychosocial health & Physical health & Emotional functioning & Social functioning & School functioning \\
\hline Age & -.02 & .03 & -0.08 & .05 & .18* & -.013 \\
Disease duration & .06 & .05 & .05 & .04 & .10 & .01 \\
Physician disease activity (VAS score) & -.44** & -.34** & -.47** & -.21** & -.36** & -.30** \\
Number of active joints & -.41** & -.30** & -.46** & -.20* & -.22** & -.31** \\
Use of medication & -.30** & -.26** & -.29** & -.15 & -.24** & -.28** \\
Subjective burden of medication use & .15 & .15 & .13 & .08 & .09 & .18* \\
Body mass index & -.25** & -.17* & -.30** & -.15 & -.07 & -.19* \\
CHAQ total score & -.77** & -.57** & -.86** & -.47** & -.56** & -.41** \\
Patient reported pain (VAS score) & -.71** & -.52** & -.80** & -.49** & -.46** & -.35** \\
Patient reported well-being (VAS score) & -.71** & -.54** & -.77** & -.51** & -.43** & -.38** \\
Parental country of birth & -.08 & -.10 & -.05 & -.03 & -.12 & -.11 \\
Parental education & .12 & .05 & .19* & .02 & .06 & .05 \\
School absence & -.48** & -.40** & -.48** & -.27** & -.30** & -.42** \\
Sports & .03 & .04 & .02 & .04 & .10 & -.04 \\
\hline
\end{tabular}
\end{table}

\begin{table}
\centering
\caption{Standardized Regression Coefficients $\beta$ from Forced entry Regression Analysis predicting HRQOL outcomes}
\begin{tabular}{|l|c|c|c|c|c|c|}
\hline
 & Total score & Psychosocial health & Physical health & Emotional functioning & Social functioning & School functioning \\
\hline Age & .10 & .19 & -.04 & .26* & .36** & -.14 \\
Disease activity & .05 & -.08 & -.01 & .13 & .04 & -.02 \\
Use of medication & -.10 & -.12 & -.04 & -.06 & -.05 & -.17 \\
Burden of medicines & -.17** & -.21* & -.09 & -.21* & -.12 & .19 \\
Body mass index & -.13 & -.15 & -.07 & -.21 & -.17 & .01 \\
CHAQ total score & -.38*** & -.21 & -.49*** & -.13 & -.27* & -.13 \\
CHAQ pain score & -.29** & -.19 & -.35*** & -.32* & -.13 & .01 \\
Parental education & -.00 & -.04 & -.05 & -.05 & .00 & -.02 \\
Missing days at school & -.19* & -.22* & -.11 & -.06 & -.14 & -.33** \\
$R^2$ & .67 & .41 & .81 & .33 & .35 & .26 \\
F & 19.05*** & 6.19*** & 41.32*** & 4.56*** & 5.00*** & 3.39** \\
\hline
\end{tabular}
\end{table}

*p<0.05; **p<0.01; ***p<0.001

We tried to get more insight into HRQOL outcomes by using predictive statistical models, but with the use of linear multivariate regression analyses causality cannot be proven. In other studies, physical disability also appears to be strongly related to HRQOL.\textsuperscript{14,16,22,39} Besides, physical activity is generally impaired in adolescents with
HRQOL in children with JIA 40. Individualized training programs may significantly improve physical ability of the adolescent 41 and therefore positively influence a child’s HRQOL.

As well as physical disability, pain is also a very important predictor for HRQOL as compared to other studies 12,14,16,22. The relief of pain and pain management are therefore important factors to deal with in the care of children with JIA 42-45. The physician reported VAS score of disease activity appear to be less directly related to HRQOL, whereas functional ability as measured by the CHAQ and VAS pain, all reported by the patient, are obviously strongly related 46.

In our study, another important predictor of impaired HRQOL appeared to be school absence. Children who reported more school absence in the 3 months prior to the consultation showed lower HRQOL and more impaired school functioning than those children with less school absence. Therefore, parents and teachers should be informed about the consequences of school absence to the HRQOL for a child with JIA, not only in regard to school functioning but also for the other domains of HRQOL.

The reported subjective burden of medication use is also important in explaining HRQOL. Although receiving medication is not a predictor of impaired HRQOL, when children report the experience of a burden from their medication use, they are at risk for impaired HRQOL. It is important to educate patients and their parents about the (side) effects of medication. This issue should be addressed during consultation, and in complex cases support should be provided, e.g., with a psychoeducational program 47,48.

When the insights into the medical and nonmedical predictors of HRQOL are increased, health care workers will be enabled to optimize their treatment strategy to improve the effect of treatment on HRQOL 22. The influence of disability and pain on HRQOL has been described in other studies 14 and was confirmed in our findings. From our study, we can add 2 nonmedical predictors to the explanation of HRQOL in children with JIA: school absence and subjective burden of medication use.

Our study shows that approximately half of the children with JIA have an impaired HRQOL as compared to 16% of the general population. This more clinical way of looking at the data is new in the JIA population and provides more insight into the number of children with JIA with a low HRQOL. Based on the results of our study, most patients with JIA are at risk of an impaired HRQOL. Systematic monitoring of HRQOL in children with JIA is therefore warranted 4,22. By using PROs such as HRQOL questionnaires in daily clinical practice care, pediatricians, psychologists, and nurses can adequately identify the specific problems in HRQOL domains of children with JIA. Consequently, more tailored advice and referrals can be given to these children. Children with JIA can be provided with HRQOL questionnaires before a consultation. Systematically reporting PROs to the pediatric rheumatologist during the consultation can facilitate communication about HRQOL. The PedsQL is a suitable instrument for systematic HRQOL assessment in daily clinical practice, as this is a questionnaire that
is simple, easy to administer, and requires only 5-10 minutes to complete.\textsuperscript{28,29} The PROs can easily be expanded with the information about functional ability, pain, the subjective burden of medication, and information on school absence.

Our study has some limitations. First, differences in age, parental country of birth and patient’s BMI were found between participants and non-participants. This is not surprising as older children and adolescents are, in general, less willing to participate in clinical studies, and parents decide whether the younger children should participate. The percentage of parents born in the Netherlands was also significantly higher among the participants. Nevertheless, 20\% of the participating parents were born outside the Netherlands, which reflects the population of the Amsterdam region. Both parental country of birth and BMI were not significant factors in contributing to HRQOL among the participating children with JIA. We therefore assumed that the differences in these factors between participants and non-participants did not influence our findings.

In our study, data on HRQOL were compared with a Dutch norm population containing a sample of healthy children and children with a chronic health condition.\textsuperscript{36} These Dutch norm data for the norm population were collected in previous research in children and their parents from Amsterdam and surrounding regions at 4 elementary schools (3 suburban and 1 urban), 4 high schools (1 rural, 1 suburban and 2 urban), and 1 school for vocational education (urban) and are considered to be representative for the Netherlands.\textsuperscript{36}

Due to the lack of data, we could not fully compare the socio-economic status of the participants and non-participants. We only could compare parental country of birth. For the participants, the parental country of birth was most often the Netherlands. In the comparison between the Dutch norm data and our sample, a difference in education was found. An influence of these aspects of socio-economic status on the HRQOL of the children in our sample cannot be ruled out.

Regarding the comparison of HRQOL of our sample with children with a chronic health condition from the Dutch norm population, some aspects need to be taken into account. Children with a chronic health condition were identified in the norm population based on proxy report. It is plausible that the more severely ill children were not included in the norm population, since the for the norm population were collected from regular schools. In addition, the sample sizes of children with chronic health condition are relatively small. The differences in HRQOL between children with JIA and other chronic health conditions will be investigated further.

In the univariate analyses, the VAS general well-being and the number of active joints were moderately to highly correlated to HRQOL, but we had to reject these correlations for inclusion in the regression model because of high multicollinearity. Based on previous studies, VAS general well-being and the number of active joints are important factors for a child’s HRQOL.
Unfortunately, we were unable to report on the influence of fatigue and sleep problems on HRQOL. For practical reasons, we did not add questionnaires for the evaluation of fatigue and sleep problems to our web-based survey. Recent studies have demonstrated that children with JIA report more fatigue and sleep problems compared to healthy children and that these factors appear to highly correlate with HRQOL 16,39,46.

A strong point of our study is that we focused not only on outcomes of HRQOL, but also on the determinants. These determinants can be taken into account during consultations by the health care workers. If indicated, both children and parents can be educated and supported during the developmental trajectory. We used a website for data collection. Having the participants use the internet to complete the PedsQL questionnaire is valid, reliable, less time consuming, and more efficient compared to a paper and pencil version. Lastly, we used self-reports from the age of 8 years; at this age it is reasonable to assume that children are capable of reporting their own HRQOL 49. Moreover, self-reporting appears to be more reliable as compared to proxy report 20,27 for evaluating HRQOL.

The best way to evaluate HRQOL is to use a standardized generic instrument with a disease specific supplement 50. Depending on the availability of validated questionnaires, disease specific rheumatology questionnaires can be added. It would be interesting, if possible, to add the PedsQL 3.0 rheumatology module 13 to the PedsQL 4.0 generic core scales to evaluate HRQOL.

In the near future, HRQOL studies in children with JIA should be extended so as to investigate more predictive and resilient factors that have been identified in pediatric psychology research, such as self-management, family and social circumstances. In this study we already found a substantial percentage of explained variance in HRQOL, but there appears to be other important factors that are predictors of HRQOL. By identifying all predictors of HRQOL, the quality of care for children and adolescents with JIA can increase further.

In conclusion, from the data on 152 children with JIA, age ≥ 6 years, and from consulting with pediatric rheumatologists in Amsterdam, we concluded that the HRQOL of children with JIA is considerably lower than that of the Dutch norm population, as well as compared to children with another chronic health condition. The 4 important predictors of these problems are impaired physical ability, patient reported pain, school absence, and subjective burden of medication use. To improve patient care in children with JIA, we believe that it is important to systematically monitor HRQOL by the use of PROs 28. Based on our findings, we suggest discussing subjective burden of medication use and school absence during consultations. More risk and resilient factors influencing HRQOL in patients with JIA need to be investigated in future studies.
Chapter 2

Reference List


Chapter 2


