Electronic patient and parent reported outcomes in pediatric clinical practice
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Introduction

In this thesis, the three dimensions of the use of Patient Reported Outcomes (PROs) in pediatrics are presented; Patient Reported Outcomes, Parent Reported Outcomes and the use of PROs in daily pediatric clinical practice. The chapters in this thesis together constitute the ‘circle of knowledge’ (figure 1). To identify problems it is necessary to research PROs as an outcome (chapter 2, 3, 4 and 5). To get insight in the functioning of patients or parents it is necessary to develop suitable (valid and reliable) questionnaires (Patient Reported Outcomes Measurements; PROMs) (chapter 6). Thereafter, it is important to develop interventions for the determined problems (chapter 7 and 8). The effectiveness of these interventions needs to be investigated (chapter 9). When the intervention has proven to be effective, it can be implemented (chapter 10). This implementation needs to be evaluated, and in this ongoing process it is important to continually evaluate the intervention, to identify the main obstacles in the process, to improve the implementation and if necessary, to examine issues and questions that arise during the process. In this thesis the following aims were studied:

Patient Reported Outcomes

Aims:
- To assess the HRQOL and the predictors in a group of children and adolescents with JIA.
- To assess the HRQOL and the psychosocial developmental trajectory of young female beneficiaries with JIA.

Parent Reported Outcomes

Aims:
- To assess the HRQOL, parental perceived child vulnerability and the associated variables of parents of a child with JIA.
- To determine the levels of anxiety and depression and the associated variables in parents of a child with a chronic illness.
- To develop and validate the Distress Thermometer for Parents (DT-P) and to determine a cut-off score for clinical parental distress.

Development, effectiveness and implementation of PROs in pediatric clinical practice

Aims:
- To describe the development of the QLIC-ON and KLIK ePROfile and intervention.
- To investigate the effectiveness of the KLIK ePROfile.
- To describe the implementation of the KLIK ePROfile in pediatric clinical practice.
In this concluding chapter the main findings are summarized. This chapter highlights the key messages and considers the limitations and challenges of the studies. Finally, because the use of PROs is an increasingly important aspect of patient care, the future perspectives of the use of PROs in pediatrics are discussed.

**Patient Reported Outcomes**

We conducted two studies to evaluate the HRQOL of children with JIA and the developmental trajectory and HRQOL of young female adults grown up with JIA. The main results are presented in table 1.

**Main findings**

The first study (chapter 2, part of the KLIK study) shows significant impairment of HRQOL in 152 patients with JIA (6-18 years old) in almost all HRQOL domains. This impairment is 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. The largest effects are found for physical and psychosocial functioning. Emotional functioning, however, seems to be less affected than other domains. Our study shows that approximately half of the children with JIA have an impaired HRQOL 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 in the number of children with JIA with a low HRQOL. Based on the results of our study, most patients with JIA are at risk for an impaired HRQOL. As Seid ¹ stated in

### Table 1. Patient Reported Outcomes

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| 2 | To assess HRQOL and its predictors in a group of children and adolescents with JIA. | - n = 152 (64.1%) children with JIA (6-18 years old), mean age = 13.03 (SD 3.4)  
- n = 401 Dutch healthy norm population  
- n = 62 Children with other chronic health conditions | **Predicting variables**  
- Sociodemographics  
- Illness characteristics  
- Pain  
- School absence  
- Functional ability: * Childhood Health Assessment Questionnaire (CHAQ) | 1) Both children and adolescents with JIA reported a significantly lower HRQOL in almost all domains compared to healthy controls and children with other chronic health conditions.  
2) Approximately half of the children with JIA showed an impaired HRQOL (< 1SD than mean norm).  
3) The main predictors of HRQOL were functional ability, pain, subjective burden of medication use, and school absence. |
| 3 | To assess the HRQOL and the psychosocial developmental trajectory of young female beneficiaries with JIA. | - n = 43 young females with JIA, mean age = 25.8 (SD 2.3)  
- n = 269 Peer group of CoLQ and RAND, mean age = 24.3 (SD 3.8) | **Outcomes**  
- Course of Life Questionnaire (CoLQ), scales:  
* Autonomy development (6 items, autonomy at home and outside the home)  
* Psychosexual development (4 items, love and sexual relations)  
* Social development (12 items, contacts with peers)  
- HRQOL: RAND-36 | 1) The beneficiaries reported worse HRQOL than the peer group.  
2) The beneficiaries achieved fewer milestones or the milestones at a later age than the peer group in the autonomy, social and psychosexual domain. |
the editorial with this paper “It is one thing to know that children with JIA have lower HRQOL compared to healthy peers, yet quite another to understand that fully half of children in treatment experience impaired HRQOL. Such data should be a wake-up call to clinicians that this is a serious problem.” In addition, he also emphasizes the need for the treatment of the whole child within the context of medical care for JIA 1.

To get more insight in how children with JIA develop into young adulthood, we used the data of the EMWAjong study 2, as described in chapter 3. In the Netherlands, if young adults are (partially) unable to work because of a chronic disease or disability (at least 25% occupationally disabled before the 17th birthday or during study), they may be eligible for benefits provided by the state social services for young disabled persons: WAJONG Act (Work and Labor Support for Young Disabled Persons). This study reports significant impairment of HRQOL in almost all domains in young females with JIA and claiming state benefit financial support; WAJONG. Obviously disability can have lasting and large effects on subjective well-being 3. This study also shows that the psychosocial developmental trajectory of young females with JIA is delayed. These young adults achieve fewer psychosocial milestones, or achieve the milestones at an older age than the peer group. During primary school, children with JIA seem to be able to keep up with peers, as is shown by the items about the primary school, but at middle or high school it seems to be more difficult to keep up with healthy peers.

Our results of both studies underline that children, adolescents and young adults with JIA face many additional challenges in achieving normative developmental milestones and acquiring adaptive functioning in society. Therefore, children and adolescents with JIA need a systematic monitoring of HRQOL and psychosocial functioning 4,5.

Limitations
These two studies have some limitations to take into account. 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 6-8. In our study regarding the HRQOL of children with JIA, we were unfortunately unable to report on the influence of fatigue and sleep problems on HRQOL. We wanted to feed back the PROs to the pediatrician, which required the amount of information to be manageable; therefore, we did not add questionnaires for the evaluation of fatigue and sleep problems into our web-based survey.

Regarding the comparison of HRQOL of our sample of children with a chronic health condition from the Dutch norm population, some aspects need to be taken into account as well. 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 sample for the norm population
was collected from regular schools. The differences in HRQOL between children with JIA and children with other chronic health conditions need to be investigated further.

The limitations of the study on young female beneficiaries should also be addressed. This study only concerns women, probably because of the higher prevalence of JIA in girls. It is unknown which part of all young women with JIA in the Netherlands apply for disability benefits. Therefore, we do not know whether the results are an underestimation or an overestimation of the problems of this group.

Secondly, objective information about the disease status of this group of young females with JIA was not available. Since this study concerns only young adults who are not able to earn a full salary as a result of their disease, we assume that their limitations are considerable.

In addition, as the treatment of children with JIA has improved over recent decades, it is to be expected that the number of young adults with JIA with a better HRQOL will increase and experience a less overall burden of the disease over time. The young women in our study grew up in the period before the JIA treatment strategy of early intensification and availability of highly effective treatment, including biologics. However, the elucidated problems are substantial and give a point of departure for future research.

Future perspectives

Regarding PROs as outcome measurement in studies the following future perspectives are of utmost importance.

The selection of the Patient Reported Outcome Measurements (PROMs)

To gain reliable PROs, it is important to select the appropriate questionnaires. One of the requirements is the availability of a representative norm group. In pediatrics, these specific data are scarce and hard to collect. Research in the field of pediatric psychology and PROs should therefore be focused on the collection of reliable norm data in different age populations.

One of our new projects is the collection and validation of norm data for the Dutch PedsQL Young Adult Generic and Fatigue module and the Course of Life Questionnaire (CoLQ). When these questionnaires are available, it is possible to expand our research on HRQOL in children with a chronic illness to adolescents and young adults who are chronically ill.

Longitudinal data

It is also very important to identify the children and adolescents who are most likely to develop difficulties in their lives (for example related to HRQOL and workforce participation). Therefore, it is important to collect longitudinal data. Longitudinal
data provide more insight into the causality of outcomes over time. The KLIK website can help to collect a lot of data from children and adolescents with different chronic illnesses. On the website, before completing the first KLIK questionnaire, parents and children (12 years and older) are asked for their permission to use their data for scientific research. The database can easily be imported into Excel and SPSS to facilitate statistical analysis. In a few years, we will have collected valuable longitudinal data on HRQOL, psychosocial and physical functioning and other outcomes of children with different chronic illnesses and their parents, and KLIK therefore offers a unique opportunity to longitudinally study PROs.

Patient Reported Outcomes Measurements Information System (PROMIS)
So far, we only used static questionnaires, but in the near future we plan to use dynamic questionnaires in pediatric psychology research, such as computerized adapted tests. In a multicenter collaboration, we are working on the translation and validation of the pediatric Patient-Reported Outcomes Measurements Information System (PROMIS) item banks. PROMIS aims to develop self-reported item banks using Computerized Adaptive Tests (CAT) and Item Response Theory (IRT) that are applicable across a wide variety of chronic disorders. By using PROMIS item banks, patients or parents only need to answer 4 to 8 items per item bank. As a result, the burden for patients and parents is less, while the reliability of the provided information is similar (or even better) compared to the information gained from the regularly used questionnaires. Our goal is to integrate PROMIS within the KLIK system, when appropriate norm data are collected in a healthy norm and different pediatric patient groups.

The use of PROs in pediatric clinical trials
In adult medicine, it is very common to use PROs as primary or secondary outcome measure in clinical trials, but in pediatrics, this is rarely the case. Since 1991, PROs are incidentally used as outcome in pediatric clinical trials. Although the use of PROs increases, a recently conducted systematic review shows that currently PROs are only included in 1.1% of the pediatric medical trials. PROs are regularly used in pediatric psychology outcome research and in educational and psychological interventions, but hardly in medical trials. This underscores that pediatric psychologists, in collaboration with pediatricians, need to focus on this issue and have to convince researchers that PROs need to be added as outcomes in pediatric clinical trials. The KLIK website is a convenient and fast way to collect the PROs during future clinical trials.
Parent Reported Outcomes

This part of the thesis focuses on the psychosocial functioning of parents with a chronically ill child. Chapter 4 focuses on parents of a child with JIA, as part of the KLIK study, and chapter 5 and 6 focus on a heterogeneous group of parents of a child with a chronic illness and is based on another study (the DT-P study). In the DT-P study, 711 parents of a chronically ill child participated.

Main findings

Chapter 4 shows that the HRQOL of parents of children with JIA is comparable to the HRQOL of parents of healthy children; parents of children with JIA score lower on ‘fine motor functioning’ and higher on ‘social functioning’. Parents of children with JIA with arthritis report a lower HRQOL compared to parents of children with JIA without arthritis, especially for daily activities, cognitive functioning, and depressive emotions. Parents of children with JIA perceive their child as more vulnerable compared to parents of a healthy child and compared to parents of a chronically ill child. Of the parents of a child with JIA, more than 30% scored in the clinical range (high scores of parental perception of child vulnerability) compared to 7% in the group of parents of a chronically ill child. Parental perception of child vulnerability was especially associated with more functional disability and shorter disease duration.

The results presented in chapter 5 show that parents of a chronically ill child report significantly higher levels of anxiety and depression than parents in the reference group. Almost one third of the mothers of a chronically ill child report clinically significant anxiety and almost one fourth of the mothers report clinically significant depression. Fathers of a chronically ill child do not differ from fathers in the reference group with respect to the proportion of fathers in the clinical anxiety and depression range. Based on the mean scores, fathers of a chronically ill child report significantly more feelings of depression than fathers in the reference group, no difference is found for the mean scores on anxiety. Practical problems in daily life and parenting stress emerge as the strongest associated factors to parental anxiety and depression. Illness-related characteristics of the child such as admission to the hospital, illness severity, duration of the child’s illness and child taking medicines are not related to parental anxiety and depression.

So, identifying those parents who are experiencing psychological distress or who are at risk for distress is important, but can be difficult to accomplish and is time consuming. A short non-invasive screening-tool that detects the level of parental distress, indicates a starting point for targeted interventions and can monitor the functioning of parents over time, would be useful to identify those parents in need of additional support. However, currently no appropriate short questionnaire is available. Therefore, we adapted a self-report screening-tool for adult patients with...
cancer, the Distress Thermometer (DT)\textsuperscript{18}, for use in parents: the Distress Thermometer for Parents (DT-P). The DT-P consists of a Thermometer-score and a Problem List. The development and validation of DT-P in parents of a chronically ill child is described in chapter 6. The DT-P appears to be a reliable and valid instrument for measuring levels of distress in parents of a chronically ill child. The internal consistency of the separate assessment of problem domains using the Problem List for emotional, physical, cognitive and total problem domains is good. The practical, social and parenting problem domains are moderately reliable. The DT-P (Thermometer-score and Problem List) is moderately to strongly associated with both the HADS and the PSI, indicating good convergent validity. The Thermometer-score (one-item question) shows to adequately measure the overall level of distress of parents of a chronically ill child.

Table 2. Parent Reported Outcomes

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| 4       | To assess the HRQOL and parental perception of child vulnerability of parents of children with JIA. | - n = 168 parents, mean age = 42.0 (SD 5.4)  
- n = 425 TAAQOL norm group, mean age = 43.7 (SD 5.5)  
- n = 450 CVS norm group of parents of a healthy child, mean age = 44.3 (SD 5.8)  
- n = 69 CVS norm group of parents of a chronically ill child, mean age = 44.4 (SD 5.9) | Associated variables  
- Sociodemographics  
- Illness characteristics of the child  
- Pain  
- Functional ability:  
  * Childhood Health Assessment Questionnaire (CHAQ)  
Outcomes  
- HRQOL: TNO-AZL questionnaire (TAAQOL)  
- Child Vulnerability Scale (CVS) | 1) The HRQOL of parents of children with JIA was comparable to the HRQOL of parents of healthy children on 10 of the twelve subscales.  
2) Parents of children with JIA with arthritis showed lower HRQOL scores compared to parents of children with JIA without arthritis on three scales.  
3) Parents of children with JIA perceive their child as more vulnerable compared to parents of a healthy child and parents of a chronically ill child (on 5 of the 8 items).  
4) More than 30% of the parents of a child with JIA scored in the clinical range.  
5) The CHAQ total score (functional ability) and disease duration were significantly associated with parental perception of child vulnerability. |
Table 2. Parent Reported Outcomes (cont.)

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| 5       | To determine the levels of anxiety and depression in parents of children with a chronic illness and the characteristics which are associated with parental anxiety and depression. | - \(n = 692\) parents of a chronically ill child, mean age = 40.3 (SD 6.9)  
- \(n = 736\) HADS norm group, mean age = 41.6 (SD 8.5) | Associated variables  
- Sociodemographics  
- Illness characteristics of the child  
- Parental Stress Index (PSI)  
- Problems:  
  * The practical and social problem domains of the Distress Thermometer for Parents (DT-P)  
Outcomes  
- Hospital Anxiety and Depression Scale (HADS) | 1) Father’s anxiety scores were comparable to the norm, but they showed more feelings of depression.  
2) Mothers had significantly higher scores on both anxiety and depression.  
3) 23% respectively 32% of the mothers scored in the clinical range of anxiety or depression.  
4) Disease related characteristics of the child did not predict anxiety and depression.  
5) Practical problems in daily life and parenting stress showed the strongest association with anxiety and depression. |
| 6       | To develop and validate a Distress Thermometer for Parents (DT-P) and to determine a cutoff-score for clinical parental distress. | \(n = 706\) parents of a chronically ill child, mean age = 40.3 (SD 6.9) | Screening tool  
- Distress Thermometer for Parents (DT-P) consists of a Thermometer and a Problem List with 6 domains: practical family/social, emotional, physical, cognitive, and parenting  
Questionnaires to validate the DT-P  
- Hospital Anxiety and Depression Scale (HADS)  
- Parenting Stress Index (PSI). | 1) The mean Thermometer-score (range 0-10) of the parents was 3.7 (SD 3.0).  
2) The Thermometer-score and the scores in the practical, emotional, physical and cognitive problem domains were strongly related to anxiety and depression.  
3) The Thermometer-score and all problem domain scores were moderately to strongly related to the parenting stress.  
4) A Thermometer score cutoff of 4 correctly identified 86% of ‘clinical-HADS-cases’ (sensitivity) and 67% of ‘non-clinical-HADS-cases’ (specificity). |
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Our study also aimed to calculate a cut-off score for clinical parental distress. We find that, for parents of a chronically ill child, a cut-off score of 4 (range 0-10) has optimal sensitivity and specificity relative to the HADS. According to this cut-off score, 47% of the parents report clinically elevated overall distress.

Limitations

In the study on parents of a child with JIA (chapter 4) there are a number of caveats that need mentioning. We measured functional ability with the CHAQ. For children 0-7 years old the CHAQ is completed by parents. Although the CHAQ is a more objective measure than the CVS, they are both completed by parents and therefore can influence the association between both questionnaires.

Our Dutch norm population of the CVS included around 60 parents who reported on their child with a chronic health condition. Regarding the comparison of our sample of a parent of a child with JIA and the parents of a child with a chronic health condition from the Dutch norm population on the CVS, the same aspects as mentioned as one of the limitations in chapter 2 need to be taken into account. Children with a chronic health condition were identified in the norm population based on proxy report. And therefore, it is plausible that the more severely ill children were not included in the norm population.

The literature on parents of children with JIA is inconsistent; some studies report significant psychosocial impact on parents, while others find no differences in parents of a child with JIA compared to normative data. Most studies are retrospective reports, consist of a relatively small sample of children or parents and most studies are published more than a decade ago. Therefore the data may not be representative for the current group of children with JIA and their parents, since the treatment of children with JIA has significantly improved over recent years. Due to these treatment changes, it is to be expected that more children and adolescents with JIA will have a better quality of life and less overall burden of the disease over time. As a consequence, parents may also experience less psychosocial problems.

Our study contributes to the existing literature on the functioning of parents of a child with JIA, by including a relatively large study sample and by highlighting two important factors in the parental functioning and care for a chronically ill child.

Regarding the DT-P study, some limitations should be addressed as well. A first limitation concerns the representativeness. Almost all participating parents were born in the Netherlands, most had a high educational level and ethnic minorities were underrepresented. Because of the open recruitment, the participants volunteered and therefore we could not influence or monitor the distribution over the illness groups. In addition, we did not have any information about non-respondents and as a consequence it was not possible to examine selection-bias. This might raise questions
about the generalizability of the results. However, because of the large and diverse sample, we can state that parents of chronically ill children are at risk for anxiety and depression.

The second limitation of the DT-P study is the study design (cross-sectional), which made it impossible to examine the course of distress or anxiety and depression over time and to evaluate test-retest reliability of the DT-P. In addition, no information was available about the causality of the relationships of practical problems in daily life and parenting stress with parental anxiety and depression.

Future perspectives
To improve the care for chronically ill children, more attention should focus on the needs of the parents. While care for the child is the first priority, parent’s burden should be recognized, as well as their stress levels and reactions to the uncontrollable aspects of illness.

Screening parents at risk
The results of this study indicate that health care providers should be aware that parents of chronically ill children are at risk for high levels of distress. Parents with high levels of distress should be identified by members of the multidisciplinary team. For the health care professional, it is often difficult to determine which parents need and want a referral for psychosocial support. Using screening tools can be helpful. Kazak et al. 20 and Patel et al. 21 suggested the use of both the Psychosocial Assessment Tool (PAT) and a DT in clinical practice of pediatric oncology. The PAT is a two-page family questionnaire to systematically assess risk and protective factors in families with a child with newly diagnosed cancer. The PAT inquires, for example, the psychosocial problems in families after the diagnosis of cancer in their child, problems in beliefs regarding the illness, availability of social support, symptoms of traumatic stress, other psychosocial strains and severe concerns within the family.

After identifying which parents are at risk, referrals to a social worker could be made, for example to provide assistance with practical issues like housing or finances.

Interventions for parents of chronically ill children
As practical problems in daily life and parenting stress show the strongest association with parental anxiety and depression, this could be a starting point for individual or group interventions, e.g. problem solving therapy. Although more research is needed to develop the appropriate treatments for parents, a recently published review showed that problem solving therapy can improve parent’s distress and their ability to solve problems. In addition, our study shows that receiving social support from surroundings could be a protective factor for depressive symptoms. Therefore, this
could be used as an element in parent support groups for parents with a chronically ill child.

The psychosocial department of the Emma Children’s Hospital is now working on the development of an online intervention for parents with a chronically ill child. Problem solving therapy and the stimulation of social support can be an important base of the intervention. Additionally, it is important to empower these parents in caring for their child. Empowerment interventions are effective for the child’s health and parental well-being. Parents gain more feeling of control over their life, and the interventions lead to increased self-efficacy and self-awareness. The advantages of an online intervention are the time-saving aspect. Parents do not have to come to the hospital and in the future, it can be integrated in the KLIK website.

DT-P in the KLIK website
We developed the DT-P and examined its diagnostic utility, in a large sample. Our study shows that the DT-P is a valuable addition to the existing questionnaires for parents and facilitates providing support for those parents who most need and want it. Therefore, the DT-P is a desirable addition to the questionnaires on the KLIK website. With the use of the DT-P, parents’ functioning can be followed over time. The answers to the questionnaires, which is the parent’s PROfile, can be provided to and discussed by the social worker of the multidisciplinary team. If parents report to have problems or a high level of distress a referral can be made. If a social worker is not part of the multidisciplinary team, the pediatrician or nurse can discuss the parents’ KLIK PROfile.

The use of PROs in pediatric clinical practice
In the past ten years, there has been a growing interest in the use of Patient Reported Outcomes (PROs) in clinical practice. Research in adult patients shows that the integration of PROs in clinical practice generally improves patient-clinician communication; PROs help in identifying and discussing HRQOL issues, and add to improvement of a patient’s health outcomes and satisfaction with care. Studies on the use of (HRQOL) PROs in pediatric clinical practice were scarce compared to adult practice, while there is a particular need to address HRQOL in pediatric clinical practice. In the context of a child’s development, the repeated measurement of HRQOL in different developmental stages can be valuable.

In 2005, the psychosocial department of the Emma Children’s Hospital started with a study on the use of PROs in pediatrics: The Quality of Life in Childhood Oncology (QLIC-ON) study. This study, which was performed in collaboration between TNO,
Leiden University Medical Centre and the Emma Children’s Hospital, was presented in the thesis of Vivian Engelen and was the second study on the use of PROs in clinical pediatric practice after the study of de Wit et al. Engelen et al. showed that the feedback of HRQOL via PROs during the consultation with the pediatric oncologist resulted in increased discussion on emotional and psychosocial functioning during consultation, and improved identification of emotional problems in pediatric oncology patients. In addition, the intervention did not lengthen the duration of the consultation. As a result of this QLIC-ON study, it was possible to expand the research on the use of PROs in pediatrics from clinical oncology practice into pediatric clinical rheumatology practice. We started of the KLIK study, presented in the last chapters of this thesis.

**Main findings**

Several steps have been made to optimize the use of PROs in pediatric clinical practice: (1) the development of an appropriate PROfile for the use of PROs in pediatrics, (2) the selection of suitable questionnaires, (3) the development of a training for pediatricians in the use of PROs and (4) the development of a website to collect the PROs. After the development of the website, we conducted a study to examine the effectiveness. When the KLIK PROfile showed to be effective, we decided to implement the KLIK PROfile in pediatric clinical pediatric practice in our hospital. The separate elements of this process are described in the last chapters and summarized below.

**Development of the PROfile**

The first steps in this process were part of the QLIC-ON study and are described in chapter 7. The aim of the chapter 7 is to provide a thorough description of the development and implementation of the QLIC-ON PROfile based on the five conclusions of Greenhalgh et al. which include; (1) the applied instrument needs to prioritize the views of the individual in order to adequately reflect the individual’s HRQOL; (2) health care providers other than physicians may also find HRQOL information useful; (3) feedback of HRQOL information should be longitudinally measured and presented over a period of time; (4) a clinically important difference or change in HRQOL data does not always resemble the physicians’ perceptions of this difference or change; and finally, (5) commitment and education of the PRO user are needed to address the multiple barriers to the use of PRO in clinical practice. In chapter 7, it is concluded that each of the five recommendations of Greenhalgh et al. were followed up as optimal as possible.

During the QLIC-ON study, HRQOL questionnaires were completed at the clinic immediately before the actual doctor’s visit, with patients using stand-alone or touch screen computers. A printed version of the PRO was handed to the pediatric oncologist.
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to be discussed during the consultation. This method was very time consuming and often caused logistical problems because of lack of privacy and room at the clinic. It was therefore concluded that the use of a web-based program could overcome these problems and could contribute to an improvement in the use of PROs in clinical practice.

Website development and the effectiveness of the KLIK intervention

To study the use of PROs in clinical practice using a website, we conducted a new multicenter study: the KLIK study (in Dutch: Kwaliteit van Leven In Kaart, in English: Quality of Life in Clinical Practice). We developed a website (http://www.hetklikht.nu) and children between 0 and 18 years old with Juvenile Idiopathic Arthritis (JIA) were included. Children and/or their parents completed the HRQOL questionnaires on the website at home. The answers on the questionnaires were schematically converted into a so-called KLIK electronic PROfile (ePROfile; figure 1 and 2). Pediatricians could retrieve these KLIK ePROfiles directly from the website during the consultation.

The web-based ePROfile appears to be an efficient application to systematically pay direct attention to HRQOL issues in daily pediatric clinical practice. This development is described in chapter 8.

To study the effectiveness of the KLIK ePROfile, we used a sequential cohort design. Patients took part in either the control or intervention group, depending on the date of consultation. All Pediatric Rheumatologists (PRs) first participated in the control group and thereafter in the intervention group. Shortly after the consultation, the parents and the PR completed an online questionnaire about the HRQOL topics discussed, referrals, and their satisfaction with the consultation, again using the website. In addition, the ePROfile was evaluated by the parents and PRs in the intervention period.

Our study shows that providing information to PRs on a patient’s HRQOL, disease-specific symptoms and functional ability with an ePROfile leads to significantly more discussion of emotional and social functioning during consultation and improves the PR’s satisfaction with the provided care. The use of the ePROfile during consultation seems to result in more psychosocial referrals, although this was not significant. Overall parents, children and PRs evaluate the use of the ePROfile positively.

Strength of our ePROfile for children with JIA is that it includes all relevant domains for the provision of clinical care for these children. It is well-documented that children with JIA are at risk for a low HRQOL and that pain, physical functioning, school absence and the subjective burden of medication use are the main predictors of their HRQOL. The ePROfile incorporated all these aspects as well as information on specific symptoms of JIA and general well-being.
Implementation of the KLIK ePROfile in daily pediatric clinical practice

Our hospital appeared to be ready to incorporate systematic attention for HRQOL in clinical practice as a result of the positive findings in both adult 33-37 and pediatric care 39-41,51. Therefore, we decided to implement the use of the KLIK ePROfile in daily clinical practice for children with various chronic illnesses. The implementation of the use of PROs in daily clinical practice creates new challenges and opportunities for care, as is extensively described in the International Society for Quality of Life Research (ISOQOL) guidelines 52,53. These guidelines offer considerations for using PROs in clinical practice, options for designing the PROs, and strengths, weaknesses and resource requirements associated with each option. According to the ISOQOL guidelines, implementing PROs involves a number of methodological and practical decisions. These include: (1) identifying the goals for collecting PROs in clinical practice; (2) selecting the patients, setting of care and timing of assessment; (3) determining which questionnaires to use; (4) choosing a mode for administering and scoring the questionnaires; (5) designing processes for reporting results; (6) identifying aids to facilitate score interpretation; (7) developing strategies for responding to issues identified by the questionnaires; and finally: (8) evaluating the impact of using PROs in clinical practice 53. Chapter 10 describes the implementation of the KLIK ePROfile in pediatric clinical practice following the methodological recommendations and decisions using the guidelines provided by the ISOQOL 52,53.

Limitations

Regarding the KLIK study (chapter 9), some limitations need to be taken in account. To avoid contamination we did not randomize our study participants. A sequential cohort design was considered most suitable for the KLIK-study 39. An additional limitation of the KLIK study was the possible confounding influence of the provision of the questionnaires to the control group. Therefore, the control group could also be considered as an attention control group. In future research, it would be interesting to add a control group which receives only standard care, without the use of questionnaires 37,54.

Furthermore, we did not determine the association between alarming HRQOL scores and communication. In the future, it is interesting to investigate whether pediatricians pay more attention to the KLIK ePROfile when patients have low HRQOL scores, for example by audio taping the consultations.

Finally, it should be considered that we did not include the patient’s HRQOL as an outcome measure to study the effectiveness. In our opinion, the duration of our study was too short to establish any differences in HRQOL. However, other studies using PROs in clinical practice did not find the direct effect on HRQOL scores with the use of PROs during consultations. And maybe, it is unrealistic to expect a direct
Table 3. Using PROs in clinical practice

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Aim</th>
<th>Sample/Content</th>
<th>Measures/Content</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>To provide a thorough description of the development and implementation of a PRO on HRQOL-the QLIC-ON PROfile-in clinical pediatric oncology practice.</td>
<td>The development of the QLIC-ON PROfile is explained by elucidating important choices: the HRQOL instrument, the professional that uses the QLIC-ON PROfile, the optimal form of HRQOL feedback. The description of the implementation of the QLIC-ON PROfile focuses on the education and commitment of the professional that uses the QLIC-ON PROfile.</td>
<td>Important considerations regarding the development and implementation of PRO interventions are reported. These considerations have also resulted in educational material.</td>
<td>1) This paper can be used as a practical guide for researchers and other professionals, who are interested in setting up PRO interventions in any clinical setting.</td>
</tr>
<tr>
<td>8</td>
<td>To describe the development and introduction of a new web-based application for the use of PROs in daily paediatric clinical practice.</td>
<td>Currently, the use of PROs in daily clinical practice is very time consuming and often has logistical problems. The use of a web-based program can overcome these problems and contributes to an improved use of PROs in clinical practice. We therefore developed an easy accessible website (KLJK) for outpatient treatment.</td>
<td>This article describes our first experiences with the KLJK application and makes recommendations for future practice.</td>
<td>1) Development of realizing a web-based application that could systematically direct attention to HRQOL issues in daily pediatric clinical practice. The web-based PROfile appears to be an efficient application to achieve this goal.</td>
</tr>
<tr>
<td>9</td>
<td>To investigate the effectiveness of ePROs in clinical pediatric rheumatology care.</td>
<td>Effectiveness of the KLIK ePROfile - Communication about HRQOL - Referrals - Satisfaction - Evaluation of the ePROfile</td>
<td>Use of the ePROfile increased discussion of psychosocial topics, as well as the PR's satisfaction with provided care during consultation. 2) The use of ePROfiles did not affect referrals to a psychologist or parental satisfaction. 3) Parents and PRs evaluated the use of the ePROfile as positive in 80% - 100% of the consultations.</td>
<td>1) Use of the ePROfile increased discussion of psychosocial topics, as well as the PR’s satisfaction with provided care during consultation. 2) The use of ePROfiles did not affect referrals to a psychologist or parental satisfaction. 3) Parents and PRs evaluated the use of the ePROfile as positive in 80% - 100% of the consultations.</td>
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<tr>
<td>9</td>
<td>To investigate the effectiveness of ePROs in clinical pediatric rheumatology care.</td>
<td>- n = 176 (65%) children with JIA participated (0-18 years), mean age = 11.6 (SD 4.5) - n = 67 in the control period, n = 109 in the intervention</td>
<td>Effectiveness of the KLIK ePROfile - Communication about HRQOL - Referrals - Satisfaction - Evaluation of the ePROfile</td>
<td>Use of the ePROfile increased discussion of psychosocial topics, as well as the PR’s satisfaction with provided care during consultation. 2) The use of ePROfiles did not affect referrals to a psychologist or parental satisfaction. 3) Parents and PRs evaluated the use of the ePROfile as positive in 80% - 100% of the consultations.</td>
</tr>
</tbody>
</table>
Table 3. Using PROs in clinical practice (cont.)

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Aim</th>
<th>Sample/Content</th>
<th>Measures/Content</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>To describe the KLIK implementation following the methodological recommendations composed by the International Society for Quality of Life (ISOQOL).</td>
<td>Implementation is described following the recommendations provided by the ISOQOL: (1) identifying the goals for collecting PROs in clinical practice; (2) selecting the patients, setting of care and timing of assessment; (3) determining which questionnaires to use; (4) choosing a mode for administering and scoring; (5) designing processes for reporting results; (6) identifying aids to facilitate score interpretation; (7) developing strategies for responding to issues identified; (8) evaluating the impact of using PROs in clinical practice and our experience with the KLIK ePROfile in pediatric rheumatology clinical practice.</td>
<td>- Since the start of the implementation of KLIK in June 2011, 12 patient groups have started using KLIK - More than 100 professionals followed a training course - Over 800 patients have registered</td>
<td>1) The implementation of KLIK in daily clinical pediatric practice appears to be feasible. Many pediatricians have shown their interest in using KLIK and we are therefore expanding the use of KLIK in order to make KLIK applicable in different patient groups and hospitals.</td>
</tr>
</tbody>
</table>

main effect on HRQOL scores due to discussing PROs during consultation. Santana and Feeny published a framework (figure 2) with the different expected effects of the use of PROs in clinical practice. In this framework, they highlighted the direct effects of discussing PROs on different levels of communication and the effect of communication on the patient management and clinician's satisfaction. This is in line with our findings. Therefore, the current evidence of the positive effects of PROs as shown in the studies of Maartje de Wit, Vivian Engelen (QLIC-ON), this study (KLIK) and adult studies justify the implementation of ePROs.

Future perspectives

Maartje de Wit and Vivian Engelen, who conducted the two former studies on the use of PROs in pediatrics, made some recommendations for future research and the implementation of PROs in their theses. Maartje de Wit conducted her study in adolescents with diabetes. In her thesis, the recommendations were as follows: use the internet for collecting PROs, involve the parents, use PROs for younger children - not only adolescents, and use computer adaptive testing (CAT). Vivian Engelen conducted her study in the Emma Children's Hospital in children with cancer after the end of successful treatment. She also suggested to include parents in the future
use of PROs and to use the internet for collecting and using PROs. In addition, she proposed to add screening tools to the existing PROs. With the use of the KLIK website and the development of the DT-P, we meet most of the afore mentioned recommendations. However, the implementation of PROs is a dynamic and challenging process, in which several factors play a role at both the level of the professional, the health care team, the hospital, and the patient and therefore still several issues need to be considered.

Expanding the implementation of KLIK to other groups
We started with the KLIK implementation in our hospital in June 2011, now in December 2012, 12 pediatric patient groups have started with the use of KLIK in daily clinical practice (table 4). More groups are scheduled to start using KLIK in the following months. So far, more than 100 professionals followed the training course and over 800 patients are registered on the KLIK website. Besides the implementation in our hospital, we also started to implement KLIK in other hospitals and clinics, as a result of collaborative projects. This includes other centers in pediatric oncology and pediatric rheumatology.

In the upcoming years, we will continue to implement KLIK in more pediatric patient groups. Pediatricians working with the KLIK ePROfile recognize the importance of the KLIK ePROfile and tell their colleagues, which encourages others professionals to use KLIK in the near future. Our goal is to implement KLIK for as many patient
groups as possible. Moreover, we would like many different hospitals and disciplines to be able to use KLIK.

Besides including more patient groups, we also want to start using KLIK for children in transition to adult care. Transition of adolescents from pediatric to adult care can be challenging. Transition is defined as a multi-faceted, active process that attends to the medical, psychosocial, educational and vocational needs of adolescents as they move from a child-focused to an adult-focused health-care system. KLIK can be used as a tool to fill the gap between the pediatric and adult health care for adolescents. We are therefore working on the validation and collection of norm data for the Dutch PedsQL Young Adult Generic and Fatigue module and the Course of Life Questionnaire (CoLQ), in order to make it possible to add these questionnaires to the KLIK website.

In addition, in collaboration with the Erasmus university, we are working on a digital version of the ‘Growing up ready’ checklist (in Dutch: Groeiwijzer) for children with different chronic illnesses. The Growing up ready checklist aims at helping families identify what areas their child needs to work on and can be a starting point

Table 4. Progress of the KLIK implementation

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Start KLIK implementation</th>
<th>Response rate so far</th>
<th>Number of patients registered on the KLIK website</th>
<th>Number of centers participating</th>
<th>Trained professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatology/Immunology</td>
<td>June 2011</td>
<td>266/421=63%</td>
<td>266</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Nephrology</td>
<td>July 2012</td>
<td>67/84=79%</td>
<td>67</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Coagulation diseases</td>
<td>October 2011</td>
<td>102/152=67%</td>
<td>102</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>HIV</td>
<td>November 2011</td>
<td>53/67=79%</td>
<td>53</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>February 2012</td>
<td>42/47=89%</td>
<td>42</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>Aftercare IC *</td>
<td>April 2012</td>
<td>19/20=95%</td>
<td>19</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>April 2012</td>
<td>146/214=68%</td>
<td>146</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Oncology *</td>
<td>June 2012</td>
<td>75/80=93%</td>
<td>75</td>
<td>3</td>
<td>24</td>
</tr>
<tr>
<td>Home Parenteral Nutrition</td>
<td>June 2012</td>
<td>14/21=66%</td>
<td>14</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Sferocytosis</td>
<td>September 2012</td>
<td>18/48=38%</td>
<td>18</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>October 2012</td>
<td>53/250=21%</td>
<td>53</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Cleft-lip</td>
<td>December 2012</td>
<td>48/408=12%</td>
<td>48</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>planned start: January 2013</td>
<td>n/a</td>
<td>n/a</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Neonatology</td>
<td>planned start: February 2013</td>
<td>n/a</td>
<td>n/a</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>903</strong></td>
<td></td>
<td><strong>106</strong></td>
<td></td>
</tr>
</tbody>
</table>
for discussion with professionals. The Growing up ready checklist is a valuable tool for monitoring the transition period in adolescents 56,58.

The information available from the KLIK portal will be helpful for the adult health care provider in interpreting the health status, HRQOL and psychosocial functioning of the patient retrospectively and to continue the use of the PROs in their own practice. I believe the environment of the KLIK website can easily be adapted to adult practice.

Expanding the implementation of KLIK to other users
Currently, only children and their parents have the possibility to complete questionnaires on the KLIK website. However, in the near future it will be possible for pediatricians, teachers and siblings of the patient to provide information via KLIK (figure 3). An overview of who are able to complete questionnaires on the KLIK website and which members of the team can use that information is provided in figure 3. In PROs research, official terms for the different users are now defined (figure 3) as follows: PROs (Patient Reported Outcomes - A measurement based on a report that comes directly from the patient, ObsRO - (Observer-Reported Outcomes - An assessment that is determined by an observer who does not have a background of professional training that is relevant to the measurement being made, i.e. a non-clinician observer such as a caregiver) and ClinROs (Clinician-Reported Outcomes - An assessment that is determined by an observer with some recognized professional training that is relevant to the measurement being made) 59. In the KLIK system we have all options, the PROs, ObsRO and ClinROs, but the Parent Reported Outcomes (a measurement based on the report that comes directly from a parent about themselves) are missing in this list. We therefore propose now to add ParRO as an official term.

In our experience, it depends on the logistical organization in the specific department, which person completes or discusses the PROs. For example, in some patient groups a nurse practitioner is part of the multi-disciplinary team and discusses the PROs, whereas in other groups the pediatrician discusses the PROs. In my opinion, it is not important who discusses the PROs, but whether or not the PROs are discussed. If not, the patient and/or parent get the feeling that all their efforts in completing the questionnaires have been in vain, and their needs are left unmet. When implementing the PROs in clinical practice, the multidisciplinary team has the obligation to have a look at and to discuss the PROfile. A team should decide beforehand by whom and when the PROfile is discussed.

KLIK training for the users
Recent research on pediatrician’s knowledge, willingness, and barriers of measuring patient-reported outcomes in clinical practice 60 showed that pediatricians have limited knowledge about PROs. Pediatricians who are research-oriented, have greater
knowledge in PROs/HRQOL measures, and report less barriers and greater interests in using PROs/HRQOL measures than those who are practice-oriented. Pediatricians report important barriers of using PROs/HRQOL measures in pediatric clinical practice.

Previous research showed that physicians are willing to discuss psychosocial problems with their patients, yet they often report that they consider themselves inadequately trained to discuss such issues. Thus, a training program that focuses on discussing and interpreting psychosocial aspects of chronic illness can be very valuable. Because every department can decide when the PROs will be used and who will use it, it is important to train all members of the multidisciplinary team. Our one-hour KLIK training aims to teach the KLIK users how to use the KLIK website and to adequately respond to the patient’s HRQOL outcomes. The training course is given by a member of the KLIK team. The training consists of a short theoretical part and an extensive practical part. For the practical part, we use DVD material containing three short patient cases (duration: ± 5 minutes), representing real consultations and actual KLIK ePROfiles. Before the demonstration of each case, the KLIK ePROfile is discussed (‘How would you interpret and discuss this PROfile?’) and the pediatricians/practitioners receive different assignments concerning each case. If children report to have problems, pediatricians/practitioners have different options to choose from, for example to give advice or to make a referral to the psychosocial department. After the demonstration of the cases, the skills of the pediatrician depicted on the DVD are evaluated and the pediatricians/practitioners receive a list of key reminders to assist in the use of the KLIK ePROfile. After the training session, the pediatricians/practitioners receive a syllabus, presenting the decision tree, an example of the KLIK PROfile, a paper with a summary of the acquired information (reminders) and theoretical background articles.

In addition, patients and parents should be reminded that they can play an active role in discussing their completed PROfile.

Incorporating the KLIK ePROfile in the electronic chart
Discussing the KLIK ePROfile is tied to a consultation with the pediatrician or multidisciplinary team. Currently, the KLIK ePROfile is not integrated into the hospital’s electronic patient chart. Pediatricians or the members of the multidisciplinary team retrieve the KLIK ePROfile from the KLIK website; this KLIK website is not linked to the existing electronic patient systems. We chose for a web-based application to be able to use the KLIK ePROfile in different hospitals, but in the future it would be desirable to have the KLIK ePROfile directly available in the electronic patient systems. Depending on the development of these new systems, it is necessary to adapt KLIK in the future.
Chapter 11

eKLIK PROfile on other electronic devices

For the small number of patients without direct access to the internet at home or for those who did not complete the questionnaires at home, it is possible to complete the questionnaires at the outpatient clinic direct before the consultation with the pediatrician. These patients are assisted by a member of the KLIK team and can complete the questionnaires on a regular PC in the outpatient clinic or on a laptop or iPad in the waiting room. A KLIK app would be a valuable addition to the existing methods on how the PROs are collected, especially for adolescents, because the majority of adolescents in the Netherlands have a smartphone and therefore can easily get access to internet on their phones.

Evaluation of the implementation

To get insight in the implementation process, it is important to study this process. In our hospital, we are currently using a quasi-experimental design to conduct implementation research within pediatric oncology practice: the IMPROVE (Implementation of Patient Reported Outcomes Via Electronics in pediatric oncology) study. Different pediatric oncology centers recently started to implement KLIK as part of their standard care for inpatient patients by means of a plan-do-study-act cycle. An extra challenge is the implementation of the KLIK PROfile during active treatment. During this study, KLIK is constantly evaluated and adapted if necessary.
To evaluate this new implementation method, we monitor the process in terms of registration, uptake-rate, characteristics of the users, facilitating and obstructing factors and satisfaction with the implementation of oncologists, parents and children. The implementation takes place in three different pediatric oncology settings. The logistics of each individual center has to be taken into account to achieve the optimal effect of discussing PROs. As a result, we can make meaningful changes in the process to make KLIK-oncology as feasible as possible and patients/parents/pediatrics may directly benefit from these changes.

For the evaluation of KLIK in daily clinical practice, evaluation questionnaires are available on the website. After a patient has used the KLIK website for one year, the patient and parents are asked to complete the questionnaires about the (use of the) KLIK website and the ePROfile. Pediatricians/practitioners are asked to evaluate KLIK after using KLIK for one year during a focus group meeting. Some multidisciplinary teams evaluate KLIK with pre- and post-test measurements because they want to evaluate the implementation from the beginning.

The selection of PROMs for use in clinical practice
There are several considerations regarding which questionnaires to use; generic or disease-specific questionnaires, profile or preference-based measures, single or multi-item scales and static or dynamic questionnaires. The basis of the KLIK ePROfile is a generic HRQOL questionnaire. We included the TAPQOL (TNO-AZL Preschool children Quality of Life) and the PedsQL Generic Core Scale (Pediatric Quality of Life Inventory). The TAPQOL is used for parents of children ages 0 to 5 years (proxy-report). The PedsQL self-report form is used for children ages 8 to 18 years; parents of children ages 6 to 7 complete the PedsQL proxy-report. We chose these questionnaires because they have been proven to be valid, sensitive to changes over time, easy to administer, and well capable of being transformed into an ePROfile. Besides the generic HRQOL questionnaires, there are many other, disease-specific, validated HRQOL questionnaires available on the KLIK website (table 5). We included disease-specific HRQOL questionnaires for specific patient groups, because this enables comparison with healthy norm scores as well as with population-specific scores.

The main focus of the use of the KLIK ePROfile was a psychosocial monitoring tool. The purpose of monitoring is to help pediatricians, patients and parents to discuss HRQOL issues systematically and to identify problems; the KLIK ePROfile is a communication aid. Thus, during the studies and implementation, no cut-off scores were used, and the scale mean scores of the healthy norm population were only handed over to the pediatrician to give them a sense of how the child scored compared to healthy peers. In addition, psychosocial screening tools are used for
diagnostic purposes and should only be estimated by a trained clinician, for example the psychologist of the specific multidisciplinary team. At the KLIK website, all users have different rights to see the different questionnaires.

At this point, we have added questionnaires to the KLIK website measuring concepts other than HRQOL, such as coping, illness perception, vulnerability and functional status.

Feedback of the PROs
Based on the opinion of different pediatricians 61, the questionnaires used at the KLIK website are presented to the pediatrician on item level and in a graph. There

<table>
<thead>
<tr>
<th>Table 5. Questionnaires in KLIK available at January 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHILD</strong></td>
</tr>
<tr>
<td>HRQOL Generic</td>
</tr>
<tr>
<td>Pediatric Quality of Life Inventory (PedsQL) 66,67</td>
</tr>
<tr>
<td>PedsQL Fatigue module 68,69</td>
</tr>
<tr>
<td>HRQOL Disease-specific</td>
</tr>
<tr>
<td>PedsQL Transplant module: nephrology 70</td>
</tr>
<tr>
<td>PedsQL Cancer module: oncology 71</td>
</tr>
<tr>
<td>Childhood Health Assessment Questionnaire (CHAQ): rheumatology 72,73</td>
</tr>
<tr>
<td>Dutch Defecation Questionnaire (DDL): gastroenterology 74</td>
</tr>
<tr>
<td>Questionnaire Juvenile Idiopathic Arthritis *</td>
</tr>
<tr>
<td>Medication and appearance after kidney transplant *</td>
</tr>
<tr>
<td>Medication and transition questions HIV *</td>
</tr>
<tr>
<td>Psychosocial screening tools</td>
</tr>
<tr>
<td>Strengths and Difficulties Questionnaires (SDQ) 75,76</td>
</tr>
<tr>
<td>Children’s Revised Impact of Event Scale (CRIES) 77</td>
</tr>
<tr>
<td>Child Behavior Checklist (CBCL) 78</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Course of Life questionnaire (LVJV/CoL) 12</td>
</tr>
<tr>
<td>Questions about school *</td>
</tr>
<tr>
<td>Evaluation of the KLIK ePROfile *</td>
</tr>
<tr>
<td><strong>PARENTS</strong></td>
</tr>
<tr>
<td>HRQOL Generic about child</td>
</tr>
<tr>
<td>TNO-AZL Preschool children Quality of Life (TAPQOL) 64</td>
</tr>
<tr>
<td>Pediatric Quality of Life Inventory (PedsQL) 66,67</td>
</tr>
<tr>
<td>PedsQL Fatigue module</td>
</tr>
<tr>
<td>HRQOL Disease-specific about child</td>
</tr>
<tr>
<td>PedsQL Transplant module: nephrology 70</td>
</tr>
<tr>
<td>PedsQL Cancer module: oncology 71</td>
</tr>
<tr>
<td>Childhood Health Assessment Questionnaire (CHAQ): rheumatology 72</td>
</tr>
<tr>
<td>Psychosocial screening tools about child</td>
</tr>
</tbody>
</table>
are several ways to provide this feedback of PROs. For example, PROs shown in a histogram, PROs with the use of signs when the scores are alarming or by providing the sum scores on a questionnaire. In all cases, it is important to use questionnaires with good psychometric properties. Once a questionnaire is selected to collect PROs, it is important to know whether the questionnaires are valid to measure changes over time or to provide scores on the level of an individual patient.  

At the moment, more than 40 questionnaires are available into the KLIK website. Most of the questionnaires are well validated and reliable. However, it is challenging to find the appropriate questionnaires. Therefore, it is necessary that questionnaires for (young) patients and parents are being evaluated in an ongoing process. Currently, we are using the KLIK website in different illness groups and as a consequence it will be possible in the near future to compare a PRO with the scores of chronically ill peers or even with peers with the same illness.

In addition, it is important to consider that the questionnaires used in pediatrics have different versions for each age group, including other norm scores. With the KLIK website, we now differentiate between the different questionnaires by providing the

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**Strengths and Difficulties Questionnaires (SDQ)** 75,76

**Behavior Rating Inventory of Executive Function (BRIEF)** 79

**Questionnaire for Behavioral Problems in Children (VvGK)** 80

**Children’s Revised Impact of Event Scale (CRIES)** 77

**HRQOL Generic about parent**

**TNO-AZL Questionnaire for Adult Health-Related Quality of Life (TAAQOL)** 81

**Psychosocial screening tools about parent**

**Distress Thermometer for Parents (DT-P)** 82

**Hospital Anxiety and Depression Scale (HADS)** 83,84

**Parental Stress Index (NOSIK/PSI)** 85,86

**Psychological Assessment Tool (PAT)** 87

**Pediatric Inventory for Parents (PIP)** 88

**The self-rating scale for post traumatic stress disorder** 89

**Child Vulnerability Scale (CVS)** 90,91

**Social Support Scale (ISB)** 92,93

**Illness Cognition Questionnaire for chronic diseases (ZCL/ICQ)** 93

**Other**

**Evaluation of the KLIK ePROfile** *

**Socio-demographic questionnaire** *

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**PEDIATRICIAN**

**VAS pain and VAS well-being** 72

**Evaluation of the KLIK ePROfile** *

* self-composed questionnaire
norm scores from the different age groups when a patient gets older and completed two versions of one questionnaire (figure 4a). In the developmental perspective of a child, it would be more informative to provide the feedback as one line with on both sides the norm line with the SD for all ages, such as the growth curves used by pediatricians (figure 4b).

Finally, as previously described, we are working on the translation of the PROMIS questionnaires. In the near future, we will add the PROMIS questionnaires to the KLIK website. However, not all questions on the PROMIS questionnaires will be answered by a child, because these are computer adaptive tests and therefore the feedback of these questionnaires will be very different from the existing KLIK PROfile. The most easy and informative way to feed back these questionnaires to a pediatrician needs to be investigated.

Considerations regarding the use of PROs

The measurement of PROs in clinical practice is an important aspect and a great addition to medical care. The administration of PROs serves several purposes. For example, to improve the HRQOL of an individual patient by using PROs in clinical practice, which is the main goal of the KLIK website. Besides that goal, PROs are increasingly used as a quality indicator and/or as an evaluation tool for departments, treatments (clinical trials), health institutions or for the evaluation of an individual practitioner. For example, in the United Kingdom, they recently started using PROs to evaluate the quality of National Health Service care. With using PROs for different purposes, it is necessary to take into account that the burden for patients will increase if we will not collaborate in collecting the PROs. In the ideal situation, patients would complete a package of questionnaires at one point, and this information would be used in clinical practice, in clinical trials and to evaluate a department or health institution.
Incorporating mental e-health with the KLIK website

In the Emma Children’s Hospital, the psychosocial department is well represented and for the medical staff it is easy to make a referral to a social worker or psychologist. Unfortunately, this is not the case in all children’s hospitals in the Netherlands. Therefore, providing links to general online mental health care programs and interventions, but which are not specifically developed for parents of a chronically ill child, would be a great addition to the KLIK website.

In addition, it would be interesting to have tailored interventions available, for children with a chronic illness and their parents, when a child or parent reports to have problems. These interventions could range from accessible psycho-education to an online intervention group based on problem-solving therapies, even individual cognitive behavioral therapy. There are several options for providing these interventions online, for example, with the use of a game (serious gaming) for the children or with a link to the cyber clinics (www.cyberpoli.nl), a website about post-traumatic medical stress (www.nahetziekenhuis.nl) or to the website of Emma@Work (www.emma-at-work.nl). If parents or children need more than psycho-education or support, the online ‘Op Koers’ program, developed in the Emma Children’s Hospital, would be a good intervention to offer. In conclusion, with the use of online interventions available at the KLIK website, it is possible to provide tailored care for those parents and children who most need and want it.

Independent use of KLIK in pediatric clinical practice

The most important challenge we face in the near future is the implementation of the KLIK ePROfile without the support of the KLIK team. During the start of the implementation, the KLIK team supports the multidisciplinary teams. However, in the long run, every department has to use the KLIK website without this support. KLIK has to become a routine in the outpatient clinics.

To achieve independent use of the KLIK website, several factors play a role, at the level of the professional, the health care team, the hospital, and the patient.

At the level of the professional, time and resource constraints are frequently mentioned obstacles for implementing PROs. It is therefore essential that pediatricians realize that the use of the KLIK ePROfile does not lengthen the consultation.

At the level of the team, motivation is an important factor. If the medical staff is not enthusiastic about the use of ePROs in clinical practice, implementation is being obstructed. All members of the team should fully support the use of KLIK.

At the level of the hospital, the following barriers are present: doubts about the fit within the clinical workflow and reimbursement obstacles. Regarding the workflow, it is very important to guide the implementation process and to add the KLIK ePROfile.
to the electronic patient chart in the future. This will contribute to fitting the KLIK ePROfile in the workflow.

At the level of the patient, language and literacy could be a barrier. To enable the use of KLIK for parents and children for whom Dutch is not their native language, the entire KLIK website is available in English. The ‘main’ questionnaire (PedsQL) is available in eight different languages. In the near future, illiterate patients will be able to play an audio version of the text on the website. Last but not least, patient barriers can be overcome by giving direct feedback to patients after they have completed the questionnaires, for them to understand the goal and motivate them to complete the questionnaires again before their next visit.

Finally, capable web designers are essential, as they are responsible for ongoing adaptation of the KLIK website. In addition, to simplify the KLIK website, the web designers are working on the development of a KLIK app for smart phones and tablets.

**Conclusions**

In this thesis the results of the three dimensions of using Patient Reported Outcomes (PROs) in pediatrics are presented; PROs, ParROs and PROs in pediatric clinical practice. The chapters in this thesis together constitute the model of knowledge (figure 1). Researching PROs as an outcome gave us insight in the lowered HRQOL of children, adolescents and young females with JIA. To gain more insight in the outcomes of parents (ParROs) of a chronically ill child, we conducted two studies and we found that these parents report a high level of anxiety and depression. A short screening-tool was not available; so we developed the valid and reliable DT-P.

To pay systematically attention to children and adolescents with a chronically illness, we developed a KLIK ePROfile to use in pediatric clinical practice and studied the effectiveness of this intervention. The intervention showed to be effective on the discussion of psychosocial and emotional topics. In addition, pediatricians reported to be more satisfied about the provided care with the use of the ePROfile. For those reasons, we started to implement the KLIK ePROfile in pediatric clinical practice.

It is a challenge to achieve the optimal use of the KLIK ePROfile in pediatric clinical practice. The first steps of implementing this in clinical practice are made, but we still have many future goals. As far as we know, KLIK is the only web-based application for the use of ePROs that is implemented in daily pediatric clinical practice in the world. To keep providing chronically ill children with tailored care, we will continue to improve the KLIK system and evaluate the use of KLIK.

Based on our experience, we can state that the implementation of the KLIK ePROfile in daily clinical pediatric practice is feasible, workable and that the users are enthusiastic and optimistic about the use of KLIK. More and more pediatricians
want to work with the KLIK system and we are expanding the use of KLIK for different patient groups and hospitals in the Netherlands and abroad. KLIK is available for other hospitals upon payment of a required yearly fee.

With the use of the feasible and effective KLIK website, we can systematically pay attention to PROs and ParROs in pediatric clinical practice, and hope that many children and parents will profit from this application in the future. This is because all chronically ill children and their parents have the right to get systematic attention to their HRQOL, psychosocial functioning, and the implications of their disease on their daily lives and development.

Key messages

Patient Reported Outcomes
1. HRQOL of Dutch children with JIA is low.
2. 50% of the children with JIA have an impaired HRQOL.
3. Important predictors of impaired HRQOL are physical ability, pain, school absence and subjective burden of medication use.
4. Young female beneficiaries with JIA have a delayed psychosocial developmental trajectory and an impaired HRQOL.

Parent Reported Outcomes
1. HRQOL of parents of children with JIA is comparable to parents of a healthy child.
2. Parents of a child with JIA perceive their children as very vulnerable.
3. Almost one third of mothers of a chronically ill child reports clinically significant anxiety, and almost one fourth of the mothers reports clinically significant depression.
4. Practical problems in daily life and parenting stress have the strongest association with parental anxiety and depression.
5. The Distress Thermometer for Parents (DT-P) is a valid screening-tool which is usable in pediatric settings.

The use of PROs in daily clinical practice
1. The web-based application KLIK to systemically monitor HRQOL problems in pediatric clinical practice is effective in increasing discussion about psychosocial topics and satisfaction with the provided care by the PR.
2. Patient Reported Outcomes (PROs) and Parent Reported Outcomes (ParRos) are essential outcomes in pediatric practice.
Reference List


