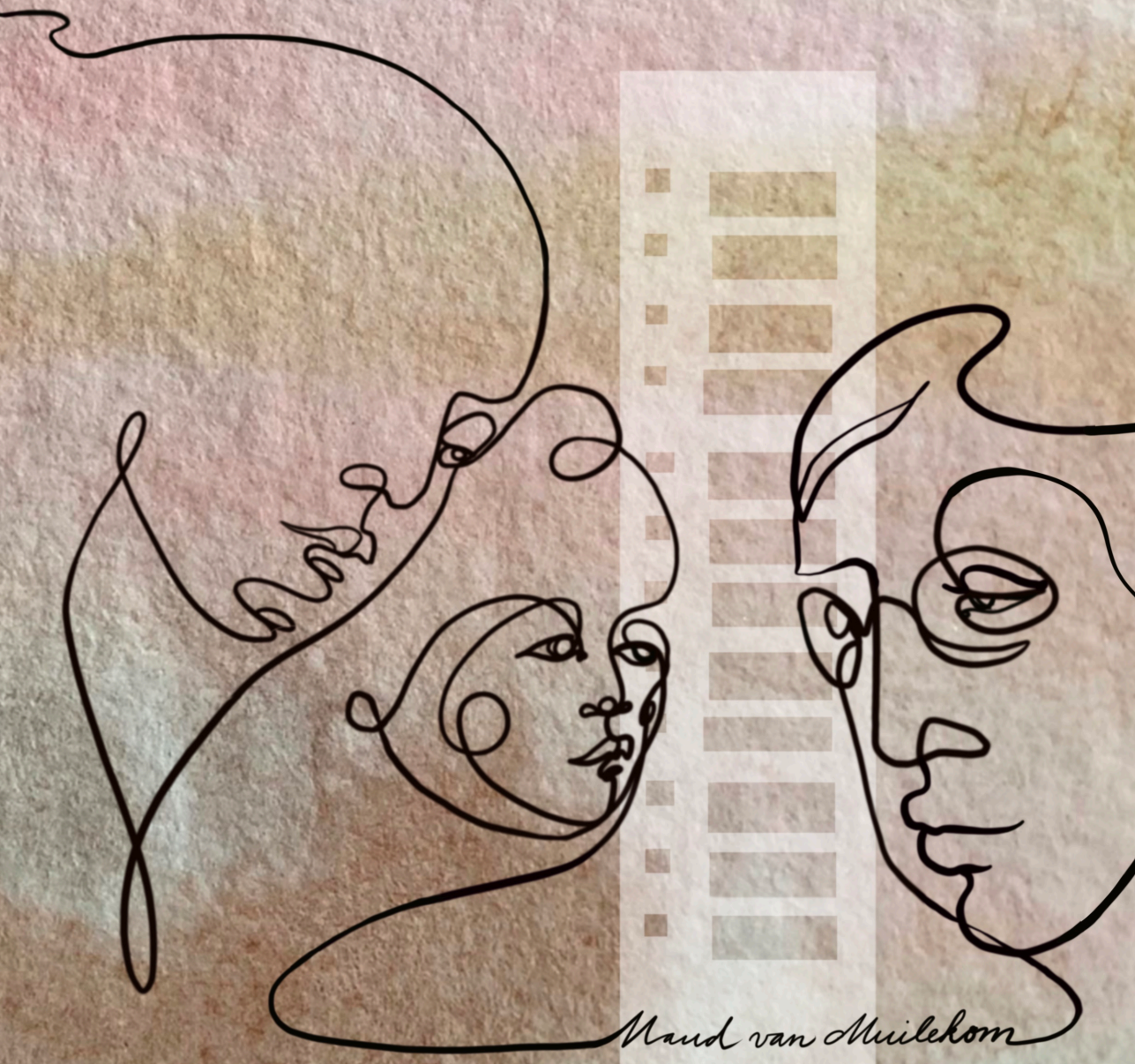
Patient Reported Outcome Measures in clinical practice:

from implementation to optimization



Maud van Muilekom

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CHAPTER 1

General introduction

Chronic conditions and their impact

Approximately one in four children, adolescents and young adults in the age of 0-25 years old in the Netherlands grow up with a chronic condition (diagnosed based on medical scientific knowledge, not (yet) curable, and present for at least three months) [1, 2]. Due to medical developments that improved detection and treatment techniques, more children survive previously terminal medical childhood conditions. As a consequence, the prevalence of chronic conditions in children increased and it is expected it will only continue to increase in the coming decades [2, 3].

Growing up and living with a chronic condition has a huge impact on patients. They have frequent appointments in the hospital, have to undergo medical procedures, need to use medication and adhere to dietary restrictions, and as a consequence have more school/work absence and reduced participation in activities. As a result, it was often shown that pediatric and young adult patients report higher levels of anxiety and depressive symptoms, experience elevated levels of (internalizing and externalizing) behavior problems and report a lower Health-Related Quality of Life (HRQOL) compared to their healthy peers [4-8]. Cognitive and physical effects due to certain treatments (e.g., neurocognitive deficits due to radiation therapy or impaired physical growth due to steroid use) have also been reported [9, 10]. Additionally, having a child with a chronic condition also has an effect on parents; they report higher levels of distress, anxiety and depressive symptoms and a worse HRQOL than parents of healthy children [11-15]. Chronic conditions thus have substantive effects on patients and their families.

Patient Reported Outcome Measures

A way to gain insight into the impact of chronic conditions on patient outcomes, is by focusing on Patient Reported Outcomes (PROs). PROs are aspects of a patient's health status or well-being directly reported by the patient (e.g., mobility, anxiety, pain), without interference of another person [16]. PROs are influenced by multiple factors, such as medical determinants (e.g., biological variables), environmental factors (e.g., social support), individual characteristics (e.g., coping), and treatment. Several theoretical frameworks are therefore available that have classified these health outcomes or PROs and influencing factors. Examples are the conceptual model of patient outcomes by Wilson and Cleary [17], the International Classification of Functioning, Disability and Health (ICF) model [18], and a combination of the previous two in the integrated model of Valderas and Alonso [19]. Additionally, the conceptual framework of the Patient Reported Outcomes Measurement Information System (PROMIS) is useful to categorize PROs, which is increasingly used [20]. In this framework, PROs are divided over three main categories; physical (e.g., fatigue, pain), mental (e.g., anxiety, cognitive functioning) and social health (e.g., social functioning), with HRQOL or Global Health as overarching term. In this thesis we will use this framework for categorizing PROs.

To measure these PROs, standardized questionnaires, also called Patient Reported Outcome Measures (PROMs) can be used. PROMs can either be generic (measuring broad, general health concepts relevant for a wide range of conditions or the general population, e.g., anxiety) or condition-specific (measuring elements of health relevant to a specific

condition, e.g., cognitive deficits due to specific treatment) [21] and are available for several users. Patients aged 8 years and older can complete PROMs themselves (self-report). When the patient is younger than 8 years old or when he/she cannot complete PROMs due to e.g. cognitive impairment, parents/caregivers can complete PROMs about the patient (proxy-report). And finally, parents can complete PROMs about their own well-being and functioning, which are called Parent Reported Outcome Measures or ParROMs.

PROMs can be used for several purposes. Originally, they were developed for use in scientific research, where PROMs were used as outcome measures in clinical trials to assess treatment effectiveness [22] or to evaluate the burden of chronic conditions in descriptive clinical studies [23]. PROMs can also be used for (internal and external) quality registration of care, where PROM outcomes are used on aggregated level to gain insight into quality of care. The outcomes can subsequently be compared between for example clinicians or healthcare institutions, based on which quality improvements can be made [24]. The third and final purpose of PROM use is on the individual patient level in clinical practice, where PROMs support communication between patients and clinicians, facilitate shared-decision making and promote patient-centered care [25-27]. The focus in this thesis is on the use of PROMs in clinical practice.

PROMs in clinical practice

The use of PROMs on the individual patient level in clinical practice encompasses several aspects (Figure 1). Patients complete PROMs regarding physical, mental and social health before each consultation with the clinician as standard part of care. These PROMs can be completed with paper-pencil, but preferably online at home. Responses are visualized in a dashboard, and shown to the clinician before or during the consultation. The clinician is ideally trained in how to interpret and use the PROM data in clinical practice [28], and subsequently discusses the PROM outcomes with patients during consultation. In this way, they can monitor functioning over time, screen for and identify problems and subsequently provide tailored advice and interventions, or refer to the appropriate help on time.

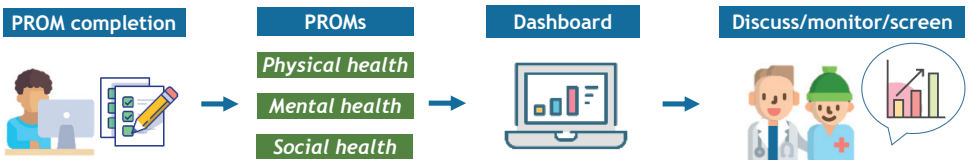

Figure 1. Pathway PROMs in clinical practice

Effects of PROMs in clinical practice

Over the years many studies have been performed that studied the effect of the use of PROMs in clinical practice. These studies showed that using PROMs in adult clinical practice increased the discussion of patient outcomes, enhanced patient-clinician communication, resulted in higher patient satisfaction, and improved patient outcomes such as HRQOL,

mental functioning, and even survival [29-36]. For pediatric patients, using PROMs in clinical practice resulted in improved psychosocial outcomes and HRQOL, increased discussion and better detection of problems, higher satisfaction with care, increased treatment engagement and enhanced patient-clinician communication [37-43].

Results of these separate studies have been combined in several systematic reviews [44-55], which provide an overview of the overall impact of PROMs in clinical practice on the following three endpoint categories: 1) Outcomes of care, 2) Processes of care, and 3) Experiences with care (Table 1).

Table 1. Endpoint categories and examples of outcomes looked at in the systematic reviews on PROM effects

Endpoint category	Examples of outcomes
Outcomes of care	Health-Related Quality of Life Mental functioning Social functioning Physical functioning Survival
Processes of care	Patient-clinician communication Diagnosing/screening Health services use Referral Pharmacological treatment Consultation duration Clinician's detection of problems
Experiences with care	Patients' satisfaction with care Clinicians' satisfaction with care

Overall, the reviews show a positive effect on processes of care (increased discussion and detection/diagnosis of patient issues), but less consistently on outcomes of and experiences with care. Only the more recent reviews, including the review of Gibbons et al. 2021 [53] and reviews focusing on oncological conditions [49, 51, 52], showed, with moderate certainty, a promising effect of PROMs on outcomes of care, such as HRQOL, (pain) symptoms, and survival. Finally, PROM effect studies in pediatric clinical practice have been summarized in two systematic reviews that were performed in the same year. Bele et al. 2020 [54] showed significant positive effects of using PROMs on processes of care (increased detection and identification of HRQOL problems) and on outcomes of care (higher HRQOL), and positive trends towards experiences with care (both patient and clinician satisfaction). Cheng et al. 2020 [55] concluded that there is a trending positive effect of PROMs in pediatric clinical practice. They found some significant moderate effects on outcomes of care (better mental and social health), and positive results on patient/parent communication with clinicians, but found less strong effects of PROMs on other processes of care and on experiences with care. Both reviews thus showed similar results. The difference between the reviews lies in the inclusion criteria used, which were stricter in the review of Bele et al., resulting in less included studies.

Barriers for using and implementing PROMs in clinical practice

With the growing number of PROM effect studies and the increased use of PROMs in clinical practice, several barriers for using and implementing PROMs in clinical practice have been identified on multiple levels [56, 57] (Table 2). Examples are barriers on the level of the system, such as increased workload when the PROM data collection and analysis/scoring are not automated in the consultation process [58-60] or when there is no integration of the PROM data collection system with the electronic health record (EHR) and clinicians have to login into additional systems [51, 57, 59, 61]. Another barrier on the level of the system regards the PROM dashboard, where suboptimal and complex visualization of PROM outcomes limits effective PROM use. This influences interpretation of outcomes by clinicians and patients and the subsequent discussion they have, the decisions they make, and actions they take [58, 59]. Barriers on the level of the PROMs used are that currently used PROMs are often considered burdensome for patients due to questionnaire length, irrelevancy and repetitiveness of questions, and complexity of the questions [51, 59, 60, 62, 63]. Many different PROMs are available that measure the same PRO, and when patients have multiple conditions and thus have to complete different PROMs, scores often cannot be compared due to different scoring methods [64]. Moreover, reviewing the large amount of PROM data before a consultation can be very burdensome for clinicians [51]. Another barrier is the lack of knowledge on how to utilize PROMs in clinical practice, resulting in suboptimal use and interpretation of PROMs. Provision of training to clinicians and patients in how to use PROMs effectively might help, but this is not always sufficiently provided [56, 57, 62, 63]. And finally, there is lack of focus on patients with lower health or technology literacy, cognitive challenges, or low proficiency in the language the PROM is available in. For them it is difficult to complete and interpret PROMs, and they often thus cannot benefit from the advantages of using PROMs [59, 60, 65]. All the previously mentioned barriers can be addressed and overcome. Barriers hard to influence are on the global, national or organizational level. On the highest level, the public and governmental opinion can be a barrier. However, in the last years, the use of PROMs is increasingly acknowledged as important and in line with the worldwide shift towards value-based healthcare [66]. On the level of the hospital or organization, it is important that the board of directors support and facilitate the use of PROMs as the implementation is otherwise hampered by lack of resources [56].

Table 2. Barrier levels and identified barriers in literature for using and implementing PROMs in clinical practice

Barrier level	Barriers identified in literature
Clinicians	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training
Patients	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training - Lack of focus on patients with lower health literacy or language proficiency
PROM system	- Non-automated PROM data collection system - No integration of PROM data collection system in EHR - Suboptimal and complex PROM visualization in dashboard
PROMs	- Burdensome PROMs - PROM scores not comparable due to different scoring methods

Initiatives supporting implementation of PROMs in clinical practice

The implementation of PROMs in clinical practice is thus an ongoing challenge. Worldwide, this resulted in several initiatives that support the implementation process of PROMs for clinicians or organizations. These initiatives describe steps that need to be taken to implement PROMs in clinical practice in a consistent way. This is necessary as there is a wide variation in how PROMs are implemented in clinical practice, which impacts their effect on patient outcomes [67]. An example of such an initiative is the User's Guide with eight methodological recommendations and practical decisions on implementing PROMs in clinical practice, developed by the International Society for Quality of Life Research (ISOQOL) [68, 69]. Another example is the more recently published PROM-toolbox (including the PROM cycle), which is meant as a framework to inform involved parties and create awareness about the selection and implementation of PROMs in healthcare, developed by the Dutch National Healthcare Institute and the Dutch Federation of University Medical Centers [70]. The PROM cycle includes eight steps divided over four phases. For each step, supporting tools are offered, such as checklists or guides, where the ISOQOL user's guide is mentioned as a useful tool at step 1, 3 and 7. Both initiatives can thus be used conjunctively, but the PROM cycle takes into account a broader range of PROM implementation aspects.

The KLIK PROM portal

KLIK is an evidence-based PROM portal (www.hetklikt.nu) that facilitates the use of PROMs and patient-clinician communication in clinical practice for already over 10 years (Figure 2). The KLIK PROM portal was developed in a pediatric oncology research setting (QLIC-ON study) in 2005 [71]. Children or parents completed a generic HRQOL PROM on a stand-alone laptop at the outpatient clinic in the hospital. Answers were printed (PROfile), consisting of literal representations of individual items and graphs, and provided to the pediatric oncologist and subsequently discussed. This study showed an increased discussion of psychosocial functioning and better identification of HRQOL problems, while duration of the consultation was not lengthened [37]. However, this use of PROMs was not feasible for larger-scale implementation due to the stand-alone laptop and the printed PROfile. In 2008, the KLIK study therefore started in a pediatric rheumatology setting, in which the first version of the online KLIK PROM portal was developed to overcome the logistical barriers of the QLIC-ON study [72]. From then on, patients and parents could complete PROMs at home and results were automatically converted into an electronic KLIK dashboard (the KLIK ePROfile), which was directly available for the clinician during consultation. The study showed increased communication of psychosocial topics and resulted in a higher satisfaction of the clinician with the care provided [43]. Based on these positive outcomes, the implementation of KLIK in daily clinical practice for pediatric patient groups started in 2011, in line with the recommendations described in the ISOQOL user's guide [68, 69, 73]. As part of the implementation process, clinicians are trained in the use of KLIK, to prepare them in how to work with KLIK and how to discuss the KLIK ePROfile [28]. In 2012, the Improve study started, in which it was shown that KLIK implementation in a pediatric oncology setting was feasible, but also challenging as the

KLIK ePROfiles were often not discussed by clinicians [74].

Between 2012 and 2017, implementation of the KLIK PROM portal in clinical practice continued. In 2013, ParROMs were added to the KLIK PROM portal to measure parents' own well-being and from 2016, KLIK could also be used by pediatric patients transitioning to adult care and by adult patients. More and more PROMs were built into the KLIK PROM portal and the KLIK ePROfile also evolved into a broader spectrum of visualization options; literal representation of individual items, summary scores, and graphic representations (4 options; longitudinal trend line, reference line, clinical cut-offs and pictures) [75]. At the beginning of 2017, this all led to a successful implementation of KLIK in many patient groups (>7000 patients) in 17 hospitals in the Netherlands.

However, during these years of implementation, several barriers for further implementation of the KLIK PROM portal were identified (Table 3). Until now, the most important stakeholders, the clinicians and patients/parents, were not systematically involved and asked for their opinion about the implementation of the KLIK PROM portal. Additionally, barriers on the level of the PROM system were acknowledged, e.g., no integration of the KLIK PROM portal with the EHR, suboptimal use of KLIK on a mobile phone or tablet, and a need to improve the PROM visualization in the KLIK ePROfile (dashboard). On the level of PROMs used, it was recognized that these were often considered burdensome for patients. Furthermore, on the level of patients and parents, tools that support them in discussing PROs during consultation were lacking. Finally, an overview and integration of available psychosocial interventions for patients and parents in the KLIK PROM portal was missing.

Therefore, a project funded by the Dutch National Healthcare institute (Zorginstituut Nederland) started at the end of 2017 to overcome these barriers, which was the starting point of the current thesis.

Table 3. Barrier level and identified barriers in literature and during the KLIK implementation process for using and implementing PROMs in clinical practice

Barrier level	Barriers identified in literature	Barriers identified during KLIK implementation process
Clinicians	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training	- Not systematically involved in implementation of PROMs - No information on available psychosocial interventions
Patients/ parents	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training - Lack of focus on patients with lower health literacy or language proficiency	- Not systematically involved in implementation of PROMs - Supportive tools/training for discussing PROs missing - No information on available psychosocial interventions
PROM system	- Non-automated PROM data collection system - No integration of PROM data collection system in EHR - Suboptimal and complex PROM visualization in dashboard	- No integration with EHR - Suboptimal PROM visualization in dashboard - Suboptimal use on mobile phone/tablet
PROMs	- Burdensome PROMs - PROM scores not comparable due to different scoring methods	- Burdensome PROMs

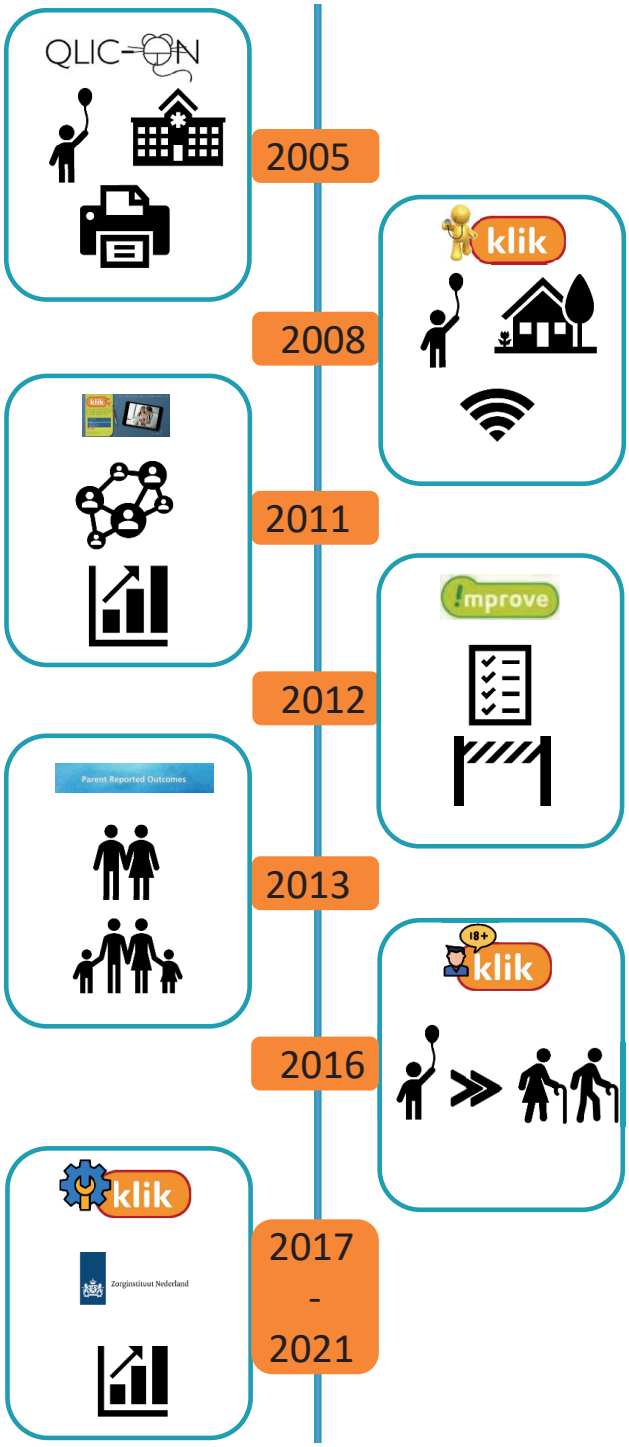

Figure 2. Visual timeline development KLIK PROM portal

Aim and outline of this thesis

The aim of this thesis is to overcome several identified barriers, on the level of the patients/parents, clinicians, the PROM system, and PROMs. The ultimate goal is to optimize the use of PROMs in clinical practice.

This thesis consists of two parts. The first part addresses the stakeholders' perspective on using PROMs in clinical practice. The second part focusses on optimization of PROM use in clinical practice, by dashboard improvement, PROM improvement and empowering patients and parents.

Part 1: Stakeholders' perspective on PROM use in clinical practice

The most important stakeholders in the development and implementation process of PROMs are the users: the clinicians, patients and parents. When their wishes and needs are not taken into account, implementation of PROMs will not be successful. It is thus necessary to gain insight into their experiences to be able to optimize and further implement PROMs in clinical practice. Therefore, in **Chapter 2**, the perspective of clinicians on the implementation of PROMs is investigated. In **Chapter 3**, patients' and parents' perspective on the implementation of PROMs in clinical practice is described.

Part 2: Optimization of PROM use in clinical practice

Dashboard improvement

Clear visualization of PROM outcomes in a dashboard is essential to correctly interpret PROM outcomes and subsequently detect problems and provide the appropriate help to patients. In the KLIK dashboard line graphs are often used, as these were shown to be best interpreted and preferred visualization formats [76]. To aid interpretation, adding normative information to the graphs, for example by showing a reference line of the Dutch general population, or of other patients with chronic conditions was shown to be helpful [77, 78]. However, in the KLIK PROM portal improvements were necessary regarding these reference lines. In **Chapter 4,** we therefore collect normative data for an often used HRQOL PROM of the Dutch general population and a pediatric population.

PROM improvement

PROMs are often experienced as burdensome due to questionnaire length and irrelevancy, and repetitiveness of questions. This can be overcome by using PROMIS computerized adaptive tests (CAT). With CAT, items are selected based on responses to previously completed items by a patient, resulting in a selection of more relevant questions and a reduction of questionnaire length [79]. To be able to use these PROMIS CATs, they were previously translated from English into Dutch-Flemish by the Dutch-Flemish PROMIS national center [80] and validated in a Dutch clinical sample [81].

However, to be able to use the PROMIS measures for all patient groups both in research and clinical practice, they have to be validated in the Dutch general population as well. Therefore, as part of a broad spectrum of PROMIS measures validation studies in our research group, **Chapter 5** describes the validation process of the PROMIS pediatric Anger scale in the Dutch general population. To show how PROMIS CATs can be applied

in research, without burdening patients with long PROMs, **Chapter 6** describes the application of PROMIS CATs in a COVID-19 study. In this study normative data of the PROMIS measures validation studies is used as reference data to assess the impact of the COVID-19 lockdown on mental and social health of children and adolescents in the Dutch general population.

Finally, to be able to use the PROMIS CATs in clinical practice, the outcomes have to be visualized in a clear way for both clinicians and patients. As with CAT not all items are administered, domain scores are calculated differently, and an evidence-based visualization was missing, new visualization options had to be developed. In **Chapter 7,** we therefore focus on the development of visualization options for PROMIS CATs on individual item and domain score level.

Patient/parent empowerment

Finally, on the level of patients and parents, it was recognized that they need help or training to initiate discussion about certain PROs and PROM outcomes themselves, especially children. Therefore, **Chapter 8** investigates which PROs are difficult yet important to discuss for pediatric patients and parents, and which barriers and facilitators they experience for discussing these PROs. The outcomes will subsequently inform the development of tools to support and empower patients and parents in discussing difficult PROs with the clinician during consultations.

This thesis ends with **Chapter 9**; the general discussion. In this chapter, a reflection on the main findings, clinical implications, methodological considerations and the current implementation of the optimized KLIK PROM portal is provided. Additionally, further steps and remaining barriers are discussed and directions for future PROM implementation and research are provided.

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PART 1

Stakeholders' perspective on PROM use in clinical practice

CHAPTER 2

Clinicians' perspective on the implemented KLIK PROM portal in clinical practice

Lorynn Teela, Maud M. van Muilekom, Lieke H. Kooij, Anouk W. Gathier, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman, Hedy A. van Oers

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Abstract

Purpose

Since 2011, the evidence-based KLIK Patient Reported Outcome Measure (PROM) portal has been implemented in clinical practice in > 20 Dutch hospitals. Patients and/or parents complete PROMs on Health Related Quality of Life, symptoms and psychosocial functioning before their outpatient consultation. Answers are converted into an ePROfile and discussed by clinicians during consultation to monitor well-being over time and detect problems early. This study aims to get insight into the KLIK implementation from the clinician's perspective.

Methods

As part of the KLIK implementation process, annual meetings were held with multidisciplinary teams to evaluate the use of KLIK. An online questionnaire was sent regarding (1) overall satisfaction, (2) feeling competent to discuss PROMs, (3) use of KLIK during the consultation, (4) influence of KLIK on the consultation, (5) usability of the KLIK PROM portal, (6) satisfaction with PROMs and feedback, and (7) support of the KLIK expert team. Open questions about (dis)advantages were included. Descriptive analyses were used.

Results

One hundred and forty-eight clinicians (response-rate 61%) from 14 hospitals in the Netherlands participated. Results show that: (1) clinicians report an overall satisfaction of median = 69/100 (visual analogue scale), (2) 85.8% feel competent discussing the ePROfile, (3) 70.3% (almost) always discuss the ePROfile, (4) 70.3% think that KLIK improves consultation, (5) 71.6% think KLIK is easy to use, (6) 80.4% are satisfied with the feedback of the overall KLIK ePROfile, 7) 71.6% experience sufficient support of the KLIK team.

Conclusion

Participating clinicians are generally satisfied with KLIK. Improvements to the KLIK PROM portal are now realized based on the mentioned disadvantages (e.g., shorten PROM completion by use of PROMIS and integrating KLIK with Electronic Health Records).

Keywords

Patient Reported Outcomes, Patient Reported Outcome Measures, healthcare professionals, providers, implementation.

Introduction

In the past decades, there has been increased attention for the use of Patient Reported Outcome Measures (PROMs) in daily clinical practice enabling patient-centered care [1]. Discussing PROMs in the consultation room empowers patients, enhances patient-clinician communication and promotes shared decision making [2-5]. Monitoring patients by using PROMs increases awareness for patients' concerns, facilitates recognition of physical or psychological problems, improves patient satisfaction with health care and is associated with improved treatment outcomes, including survival [3, 4, 6-8].

After two efficacy studies [9, 10], the KLIK PROM portal (www.hetklikt.nu) is being implemented in daily clinical practice since 2011. These studies showed that the feedback and discussion of PROMs in the consultation room resulted in more attention for, and improved identification of, psychosocial and emotional problems and increased satisfaction of pediatricians with the provided care [9, 10]. Within the KLIK PROM portal, pediatric patients (≥ 8 years) and/or their parents and adult patients are asked to complete PROMs regarding Health Related Quality of Life (HRQOL), symptoms and/or psychosocial functioning online at home prior to the outpatient consultation. The answers are converted into an electronic PROfile (KLIK ePROfile, Figure 1) that contains a broad range of feedback options tailored to each specific PROM [11]. The clinician discusses the KLIK ePROfile during the outpatient consultation with patients and/or parents in order to monitor well-being over time, detect problems at an early stage and provide tailored advice and interventions. Currently, more than 17,000 patients from 70 different patient groups (e.g., rheumatology, diabetes, oncology) have registered themselves on the KLIK website and around 1,000 clinicians (e.g., physicians, nurses, psychologists, social workers, physiotherapists, dieticians, and speech therapists) have been trained (around 800 active users) in the use of KLIK in daily clinical practice in > 20 different hospitals in the Netherlands [12] and 3 hospitals in the United Kingdom (www.klik-uk.org).

Nevertheless, implementing a PROM portal in clinical practice is a challenging process in which the interests of different stakeholders are involved [12, 13]. For a successful implementation, different determinants can be distinguished on the level of intervention characteristics, the clinician, the patient (and parent), and the socio-political context. In the past years, the intervention characteristics of the KLIK PROM portal have been evaluated repeatedly and adapted so that identified barriers for implementation for this determinant have been addressed [12, 13]. For example, PROMs are now available in multiple languages and KLIK has become an adaptable system to meet many individual wishes of the multidisciplinary teams [11]. However, little is known about barriers at the level of both clinicians and patients/parents. More insight is needed to fully understand the experienced barriers and to be able to optimize the KLIK PROM portal with regard to the wishes and needs of the user. Therefore, the aim of this study is to get more systematic insight into the experiences with KLIK from a clinician's perspective.

1a

Child

○ 03-11-2016 ⊘ 03-06-2017 ○ 23-12-2017 ⊘ 26-04-2018

Physical	03-06-2017	26-04-2018
It is hard for me to walk more than one block	Sometimes	Never
It is hard for me to run	Often	Almost always
It is hard for me to do sports activity or exercise	Often	Often
It is hard for me to lift something heavy	Sometimes	Almost always
It is hard for me to take a bath or shower by myself	Never	Never
It is hard for me to do chores around the house	Almost always	Often
I hurt or ache	Almost never	Sometimes
I have low energy	Often	Sometimes
Emotional	**03-06-2017**	**26-04-2018**
I feel afraid or scared	Never	Never
I feel sad or blue	Never	Almost never
I feel angry	Almost never	Sometimes
I have trouble sleeping	Never	Sometimes
I worry about what will happen to me	Never	Never
Social	**03-06-2017**	**26-04-2018**
I have trouble getting along with other kids	Never	Never
Other kids do not want to be my friend	Never	Never
Other kids tease me	Never	Almost never
I cannot do things that other kids my age can do	Sometimes	Often
It is hard to keep up when I play with other kids	Never	Never
School	**03-06-2017**	**26-04-2018**
It is hard to pay attention in class	Never	Never
I forget things	Almost never	Sometimes
I have trouble keeping up with my schoolwork	Sometimes	Never
I miss school because of not feeling well	Sometimes	Sometimes
I miss school to go to the doctor or hospital	Sometimes	Sometimes

1b

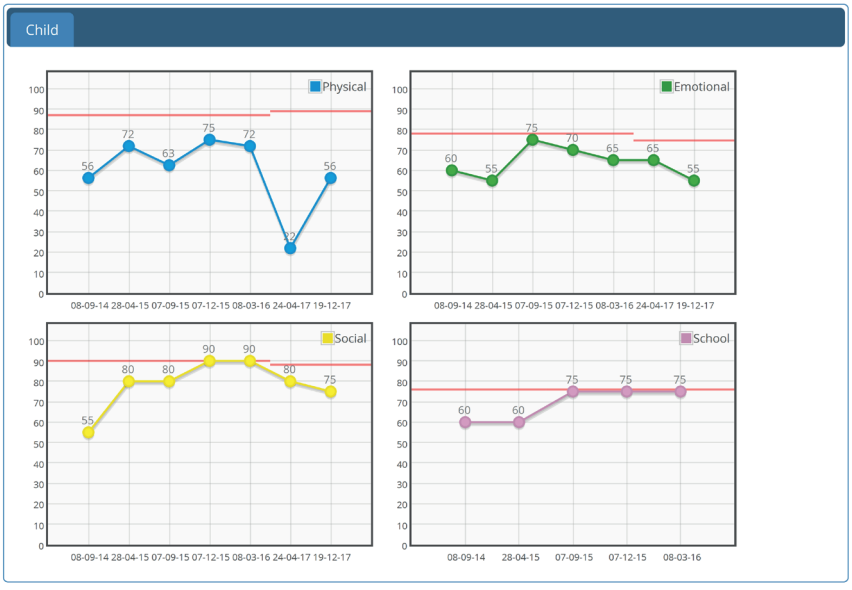

Figure 1. a KLIK ePROfile – literal feedback of the individual items on the Pediatric Quality of Life Inventory (PedsQL) **b** KLIK ePROfile – graphical feedback of the PedsQL, including norm lines

Methods

KLIK implementation process

KLIK can be implemented for every multidisciplinary team (e.g., diabetes, dermatology) in health care [12]. The implementation process starts at request of a multidisciplinary team and is guided by the KLIK expert team (consisting of researchers with expertise in the field of PROMs and HRQOL research) of the Emma Children's Hospital Amsterdam UMC through the following phases (Figure 2):

1. The KLIK expert team has an exploratory meeting with the clinicians of the multidisciplinary team to get an impression of the patient group and the Patient Reported Outcomes (PROs) they would like to discuss in the consultation room.
2. The KLIK expert team gives advice about reliable, sensitive and valid PROMs to measure the desired PROs. Whenever possible, PROMs with high reliability for specific populations and settings are selected to be able to use them on an individual level. However, sometimes the psychometric properties are not sufficient or unknown for the specific population, but no alternatives are available (e.g. in pediatrics, or in rare diseases).
3. The KLIK website is set up according to the wishes and workflow of the multidisciplinary team (e.g., frequency of completing PROMs, which reminder e-mails should be sent etc.). At this moment, over 300 PROMs have been built into the KLIK PROM portal. PROMs are offered to patients depending on age and patient group. Each member of the multidisciplinary team sees feedback of their preferred outcome measure set in a personal KLIK ePROfile.
4. Prior to the start of the implementation, all clinicians are trained in the use of KLIK in the consultation room. The 1.5 h training consists of a theoretical and a practical part. In the theoretical part, attention is paid to the definition of PROs and PROMs, the importance of discussing PROMs in the consultation room, and the use of the KLIK PROM portal including the different feedback options. In the practical part clinicians are trained in discussing the KLIK ePROfile with patients [14].
5. Throughout the implementation process, the KLIK expert team acts as a helpdesk for both clinicians and patients. For example, the KLIK expert team supports the integration of KLIK into the existing workflow of a multidisciplinary team and helps patients and/or parents to log into the KLIK website and complete PROMs.
6. As standard part of the KLIK implementation process, the KLIK expert team offers annual one-hour evaluation meetings to multidisciplinary teams to evaluate the use of KLIK in daily clinical practice and to identify and overcome barriers in the implementation process.

1. Exploratory meeting with the multidisciplinary team

- To get an impression of the patient group in which KLIK will be implemented
- To discuss which PROs the team would like to measure and discuss with their patients during the consultation

2. Advice KLIK team

- The KLIK team gives advice about reliable, sensitive and valid PROMs to measure the desired PROs
  - The KLIK team recommends the use of generic PROMs whenever possible
  - The KLIK team searches the literature for valid, reliable and sensitive PROMs
  - If no suitable PROMs are available, the KLIK team supports the validation and translation of PROMs°

3. Setting up the KLIK PROM portal

- The KLIK PROM portal is set up according to the wishes of the multidisciplinary team:
  - Frequency of completing PROMs
  - Reminder e-mails
  - Preferred feedback of the PROMs·
- The KLIK team helps incorporating the use of KLIK into the existing workflow

4. Training clinicians

- All clinicians are trained in the use of KLIK in the consultation room, prior to the start□
- The training (1.5 hour) consists of two parts:
  - Theoretical part
    - Background of using PROMs in clinical practice
    - Use of the KLIK PROM portal for both clinicians and patients
    - Feedback options in the KLIK ePROfile
  - Practical part
    - Video material is used to show examples of clinicians discussing the KLIK ePROfile with patients
    - Support tools (decision tree & summary of the KLIK ePROfile) are provided to clinicians

5. The implementation process

- Invitation letters are sent to (new) patients by the secretariat of the multidisciplinary team or KLIK team*
- Patients themselves create a KLIK account on the website and complete PROMs online at home. If patients do not have internet access at home, it is possible to complete PROMs at the outpatient clinic (98% of the Dutch households have access to internet⁻)
- Clinicians discuss the KLIK ePROfile with patients during the consultation
- For a follow-up visit, the consultation date is added to the KLIK account by the patient, secretariat or KLIK team*
- Automatic e-mails are sent to patients when the PROMs are available
- If necessary, automatic e-mail reminders are sent to patients one day prior to the consultation

- The KLIK team acts as a helpdesk during the implementation process
  - The KLIK team answers questions from both clinicians and patients
  - The KLIK team trains new clinicians in the use of KLIK
- The KLIK team helps incorporating the use of KLIK in the existing workflow
- The KLIK team facilitates the KLIK implementation process in the Amsterdam UMC

6. Evaluation

• One-hour annual evaluation meetings are held with the multidisciplinary team
  ◦ Experiences with the use of the KLIK PROM portal
  ◦ Workflow regarding the use of the KLIK PROM portal
• If possible, adjustments are made to the specific settings of the KLIK PRO M portal

Figure. 2. Overview of the KLIK implementation process for one multidisciplinary team
Note. °[15, 16], •[11], ¤[14], *The KLIK implementation process is different for every multidisciplinary team depending on their wishes and workflow, ¨[17]

Design and procedure

From February 2018 until August 2019, online evaluation questionnaires were sent out one week prior to each evaluation meeting. Reminder e-mails were sent to clinicians who had not completed the questionnaire one day before the meeting. The answers of the clinicians on the questionnaire on a team level provided a starting point for the evaluation meeting. Clinicians who had not completed the questionnaire prior to this meeting were asked to do so afterwards. This study has been approved by the Medical Ethics Committee of the Amsterdam University Medical Centers (Amsterdam UMC).

Participants

Two hundred and forty-three team members (independent of their presence during the evaluation meeting) of 36 multidisciplinary teams in 14 hospitals that use KLIK were approached to participate in this study prior to a KLIK evaluation meeting. Multidisciplinary teams who use the KLIK PROM portal only for scientific purposes (6 multidisciplinary teams), where the implementation process started less than a year ago (N=14) or teams that did not respond (N=14) were not eligible. Supplement 1 provides an overview of the inclusion process.

Measure

An evaluation questionnaire (Supplement 2) was developed to obtain the opinion of clinicians about the use of KLIK in daily clinical practice. The evaluation questionnaire was composed by four researchers of the KLIK expert team and reviewed by three nurses and one pediatrician. The questionnaire consisted of 20 closed questions (response options: three- and five-point Likert Scales, Visual Analogue Scales (VAS) and check boxes) and four mandatory open questions ((a) advantages and (b) disadvantages of KLIK, (c) incentives for patients and (d) frequently heard reactions of patients about KLIK) regarding (1) overall satisfaction, (2) feeling competent to discuss PROMs, (3) use of KLIK during the consultation, (4) influence of KLIK on the consultation, (5) usability of the KLIK PROM portal, (6) satisfaction with PROMs and feedback, and (7) support of the KLIK expert team. There was room to add a comment or explanation with each question. Since every multidisciplinary team uses a different subset of PROMs and feedback options, not all questions in the domain 'satisfaction with PROMs and feedback' could by answered be all clinicians.

Analysis

The Statistical Package for Social Sciences (SPSS) version 25.0 was used for descriptive statistics (percentages) to provide insight into the opinion of clinicians regarding KLIK and to study barriers and facilitators for the implementation process. Open questions of the evaluation questionnaire were analyzed qualitatively, by clustering the answers of all clinicians into main themes. This was done by two researchers (LT & HAvO) following the method for thematic analysis in Psychology [18]. Themes are ranked based on the number of times they have been mentioned by the clinicians (most often to fewest times).

Results

Participants

The online evaluation questionnaire was completed by 148 clinicians (61%), who were part of 36 different multidisciplinary teams from the following 14 different hospitals (Supplement 1): Emma Children's Hospital (N = 57 participating clinicians), Amsterdam UMC locations VU Medical Center (N = 24) and Academic Medical Center (N = 4), Kidz & Ko – diabetes collaboration centers (N = 18), Reade (N = 8), University Medical Center Groningen (N = 7), Spaarne Hospital (N = 6), VieCuri Medical Center (N = 6), Zuyderland Medical Center (N = 5), Maasstad Hospital (N = 5), Kempenhaeghe epilepsy center (N = 3), Sophia Children's Hospital (N = 2), Radboud University Medical Center (N = 2), and Wilhelmina Children's Hospital (N = 1). Discipline and disease group of participating clinicians are shown in Table 1. On average, participating clinicians used KLIK for 3.3 years (range 0.2-8.8 years). Most participating clinicians were employed as medical doctor (N = 57), psychologist (N = 39) or nurse (N = 36), and multidisciplinary teams were divided into pediatrics (32 teams) and adult health care (4 teams).

Overall satisfaction

Clinicians (N = 147) reported an overall satisfaction with the KLIK PROM portal of *median* = 69, range 13-100, on a VAS ranging from 0 (not satisfied) to 100 (very satisfied). One clinician could not fill in the VAS due to technical problems.

Feeling competent to discuss PROMs

Almost all clinicians (89.9%) indicated that the KLIK training had prepared them sufficiently to use KLIK in daily clinical practice (8.1% neutral, 2% disagree). In addition, 85.8% of the clinicians felt competent to discuss the KLIK ePROfile with patients and/or parents in the consultation room (7.4% neutral, 6.8% disagree).

Use of KLIK during the consultation

Table 2 gives an overview of the use of KLIK reported by the clinicians. Most clinicians (70.3%) indicated they discuss the KLIK ePROfile (almost) always with patients and/or parents, 18.2% reported to discuss the KLIK ePROfile sometimes and 11.5% indicated to (almost) never discuss the KLIK ePROfile. Reasons for not discussing the KLIK ePROfile with patients and/or parents, as indicated by clinicians in the comments section, were

lack of time, PROMs not completed, forgot to discuss, technical problems, no priority, no problems reported in the KLIK ePROfile, the KLIK ePROfile was discussed by another team member or KLIK was no longer part of standard care. Clinicians indicated they discuss the KLIK ePROfile at the start (42.6%), middle (37.8%) or end (19.6%) of the consultation. Clinicians estimated that they spend on average 15% of the consultation (broad range of consultation time; 10–50 min) on discussing the KLIK ePROfile and 85.8% of the clinicians were satisfied with this percentage.

The majority of the clinicians (70.3%) invited all patients to participate in the KLIK PROM portal. Patients were not invited for the following reasons: absence of a chronic health condition, presence of a language barrier, a mental disability, illiteracy or not falling into a specific age range. In addition, clinicians mentioned they sometimes forgot to invite patients or they did not see it as their responsibility. 43.2% of the clinicians estimated that 75-100% of their patients and/or parents completed the PROMs. According to clinicians, reasons for not completing PROMs by patients were no Internet access, language barrier, forgetting and loss of motivation.

Table 1. Characteristics of participants

	Participants (N = 148)
	N (% response-rate within discipline or group)
Discipline	
Medical doctor	57 (63.3)
Psychologist	39 (52.0)
Nurse	36 (66.7)
Dietitian	5 (71.4)
Physiotherapist	4 (100.0)
Social worker	3 (50.0)
Occupational therapist	2 (66.7)
Speech therapist	2 (100.0)
Disease group	
Diabetes (6 hospitals)	42 (63.6)
Juvenile Idiopathic Arthritis (2 hospitals)	12 (80.0)
Medical psychology (2 hospitals)	10 (52.6)
Sickle cell disease	9 (100.0)
Gender dysphoria	8 (27.6)
Coagulation diseases (4 hospitals)	7 (77.8)
Diagnostic Center Nutritional problems	6 (100.0)
Gastrointestinal diseases	6 (75.0)
Marfan syndrome	5 (100.0)
Neonatology follow-up	5 (71.4)
Spina Bifida	5 (55.6)
Cystic Fibrosis	4 (100.0)
Nephrology (2 hospitals)	4 (50.0)
Epidermolysis Bullosa	4 (44.4)
Surgery follow-up	4 (36.4)
Epilepsy	3 (75.0)
Human Immunodeficiency Virus	3 (50.0)
Congenital hand and arm disorders	2 (100.0)
Home Parenteral Nutrition	2 (66.7)
Metabolic diseases (2 hospitals)	2 (66.7)
Dermatology	2 (40.0)
Neurofibromatosis type 1	1 (100.0)
Muscle diseases	1 (50.0)
Endocrinology	1 (33.3)

Table 2. Scores on the domain 'use of KLIK during the consultation' (N = 148)

Clinicians			**(Almost) always (%)**	**Sometimes (%)**	**(Almost) never (%)**
			104 (70.3)	27 (18.2)	17 (11.5)
			Start (%)	**Middle (%)**	**End (%)**
I discuss the KLIK ePROfile at the … of the consultation			63 (42.6)	56 (37.8)	29 (19.6)
			Median (range)		
On average, I spend …% of the consultation on discussion of the KLIK ePROfile (N=147)			15 (0-100)		
			Yes (%)	**No, I need more time (%)**	**No, I need less time (%)**
I am satisfied with the time I spent discussing the KLIK ePROfile			127 (85.8)	20 (13.5)	1 (0.7)
About patients			**Agree (%)**	**Neutral (%)**	**Disagree (%)**
All patients are invited to participate in the KLIK PROM portal			104 (70.3)	13 (8.8)	31 (20.9)
	100 (%)	**75 (%)**	**50 (%)**	**25 (%)**	**0 (%)**
I estimate that …% of patients/parents complete the PROMs	2 (1.4)	62 (41.8)	50 (33.8)	33 (22.3)	1 (0.7)

Influence of KLIK on the consultation

According to 70.3% of the clinicians, their consultation improved by the use of the KLIK PROM portal (24.3% neutral, 5.4% disagree) and 60.1% of the clinicians detected problems in functioning of patients and/or parents sooner (33.8% neutral, 6.1% disagree). Reasons for not detecting problems sooner with the use of KLIK were that another team member discussed the KLIK ePROfile with patients and/or parents or that the clinician was already aware of the functioning of the patients. Half of the clinicians (48.6%) indicated that they thought patients and/or parents were satisfied with the use of KLIK, 45.3% of the clinicians indicated that they did not know and 6.1% of the clinicians indicated that they thought patients and/or parents were not satisfied. Reasons why patients were not satisfied according to clinicians were: *many questions* (time intensive, having to complete PROMs too often, repetition in questions), *practical problems* (no Internet, login problems) and/or *no motivation* (annoying, no added value).

Regarding the open questions (Table 3), main advantages of KLIK for clinicians were: *insight in patient's functioning, improved communication, detecting problems, insightful feedback, patients being better prepared, easy to use, time saving, and clinician was better prepared.* Main disadvantages of KLIK for clinicians were: *low response-rate, takes time for clinician, irrelevant content of PROMs, complex procedure, technical aspects, no integration with Electronic Health Record (EHR)*, and *takes time for patients*. Table 3 shows the most important advantages and disadvantages of KLIK, expressed by clinicians.

According to clinicians, incentives for patients to use the KLIK PROM portal were: *insight in functioning* (reflection, awareness), *preparation for consultation* (time to think, conversation topics), *improved communication* (starting point for conversation, structure, comprehensive),

feeling heard (being taken seriously, acknowledgement), *to be offered interventions in time* (signaling, intervene), and *empowerment* (involvement, request for help). Ten clinicians (6.8%) indicated that they do not know what the benefits for patients are.

Table 3. Advantages and disadvantages of KLIK and the use of PROMs, according to clinicians (N = 148)

Advantages of KLIK/PROM use	Examples
Insight in patient's functioning	'You quickly can get an impression of the things that are (not) going well' 'Monitoring the patient over time' 'Quick overview of how the patient is doing'
Improved communication	'The KLIK ePROfile structures the consultation' 'It provides a starting point for the conversation on difficult topics' 'Makes it possible to go in depth more quickly'
Detecting problems	'Problems are recognized earlier' 'It provides information about the disease/person that I would not have discovered otherwise' 'Standardized screening'
Insightful feedback	'Graphs provide insight' 'Convenient that scores are calculated directly and automatically' 'Better overview of the results through traffic light colors and graphs'
Patients being better prepared	'Provides patients the opportunity to think in advance about questions and concerns. They are not confronted with these during the consultation' 'Patients and parents talk to each other about items that matter' 'Patients think in advance about their own functioning and request for help'
Easy to use	'User-friendly' 'Accessible' 'Completing PROMs at home is easier for patients/parents'
Time saving	'The consultation is quicker' 'Saves time' 'As a clinician, it takes me less time than PROMs on paper'
Clinician was better prepared	'Better and more targeted preparation of the consultation' 'Prior to the consultation, I have important information from patient and parents' 'Before the consultation, I already have an impression of the complaints'
Disadvantages of KLIK/PROM use	**Examples**
Low response-rate	'Patients often do not complete PROMs' 'Patients with problems, for whom KLIK adds value, rarely complete the questionnaires' 'Reminders are necessary for patients to complete PROMs'
Takes time for clinician	'Extra time is needed to prepare the consultation' 'It takes time to discuss, since KLIK is not integrated into the EHR' 'Motivating patients to complete PROMs takes time'
Irrelevant content of PROMs	'Not all questions are relevant for every patient' 'Patients misunderstand questions' 'Many questions'
Complex procedure	'Patients lose username and password' 'PROMs are not easy to complete for parents with a cognitive disability or foreigners' 'Not all patients have access to Internet'
Technical aspects	'It takes effort to log in' 'I do not receive an automatic message when patients have completed PROMs' 'I have to print the KLIK ePROfile, because we do not have computers in the consultation room'
No integration with EHR	'The data from KLIK does not end up directly in the EHR' 'No integration with Epic©' 'Need to open a separate window, besides EHR'
Takes time for patients	'Requires time investment of patients' 'Patients indicate that they sometimes spend a long time completing PROMs' 'Extra burden for busy parents'

Table 4. Scores on the domain 'satisfaction with PROMs and feedback'

	N	Agree (%)	Neutral (%)	Disagree (%)			
I am satisfied with the PROMs offered	134	87 (64.9)	36 (26.9)	11 (8.2)			
I am satisfied with the feedback of:							
Overall KLIK ePROfile	148	119 (80.4)	26 (17.6)	3 (2.0)			
Literal answers	148	112 (75.7)	33 (22.3)	3 (2.0)			
Traffic light colors	137	115 (83.9)	19 (13.9)	3 (2.2)			
Graphs (scores over time and comparison with peers)	137	105 (76.6)	25 (18.3)	7 (5.1)			
		Literal answers (%) (N=148)	**Traffic light colors (%) (N=137)**	**Graphs (%) (N=137)**			
I look at the following parts of the feedback in the KLIK ePROfile (multiple answers possible)		124 (83.8)	116 (84.7)	97 (65.5)			
		Literal answers			**Graphs**		
		Green answers (%)	**Orange answers (%)**	**Red answers (%)**	**Comparison with peers (graph) (%)**	**Scores over time (graph) (%)**	**Other (%)**
I discuss the following parts of the KLIK ePROfile (multiple answers possible)	137	47 (34.3)	80 (58.4)	116 (84.7)	46 (33.6)	65 (47.4)	24 (16.2)*
		Median (range)					
I think the following parts of the feedback of the KLIK ePROfile are important:							
Literal answers	147	71 (35-100)					
Traffic light colors	136	72 (11-100)					
Graphs	136	70 (12-100)					

* Other parts of the KLIK ePROfile that clinicians discuss with patients: open questions and changes in literal answers over time. A part of the clinicians does not discuss the KLIK ePROfile with patients.

Usability of the KLIK PROM portal

According to 71.6% of the clinicians, the KLIK portal is easy to use (19.6% neutral, 8.8% disagree) and 83.8% of the clinicians indicated that the KLIK portal has an attractive lay-out (15.5% neutral, 0.7% disagree).

Satisfaction with PROMs and feedback

In general, 64.9% of the clinicians were satisfied with the selected PROMs (Table 4). Reasons why clinicians were not satisfied with the PROMs were too many PROMs, PROMs are not suitable for every patient and not all PROMs are available in multiple languages. Regarding the feedback of answers of the PROMs, 80.4% of the clinicians were satisfied with the feedback in the overall KLIK ePROfile. In the KLIK ePROfile the individual items in traffic light colors (Figure 1a) were viewed most frequently by the clinicians (84.7%). Of these traffic light colors, clinicians discussed the red answers most often with patients/parents (84.7%), followed by orange (58.4%) and green answers (34.3%). The graphs (scores over time resp. comparison with peers) are discussed by 47.4% resp. 33.6% of the clinicians. Clinicians thought that the traffic light colors of the KLIK ePROfile are most important (*median* = 72), followed by literal answers (*median* = 71) and graphs (*median* = 70) (Figure 1b), reported on a VAS, ranging from 0 (not important) to 100 (very important).

Support KLIK expert team

82.5% of the clinicians indicated to know where to ask their questions regarding the use of the KLIK PROM portal (10.1% neutral, 7.4% disagree) and 71.6% indicated that there is enough support from the KLIK expert team (25.7% neutral, 2.7% disagree).

Discussion

This study provided insight into the experiences of clinicians with the use of the KLIK PROM portal in daily clinical care, at a group level. Overall, clinicians were satisfied with discussing PROMs in the consultation room via the KLK PROM portal. Clinicians indicated that discussing PROMs helps them to gain more insight into patient functioning, to improve the communication with patients, to detect psychosocial or physical problems, and to empower patients. These benefits are in line with previous effectiveness studies [3, 4, 6]. In addition, clinicians valued specific characteristics of the KLIK ePROfile, such as ease of use and the well-developed and insightful feedback. Regarding this feedback, clinicians mentioned they appreciated and looked at the individual item feedback in traffic light colors most often. This preference was also found in previous research on the feedback of the QLIC-ON Profile [19].

Although clinicians indicated that the KLIK training sufficiently prepared them to use KLIK in clinical practice, they also indicated that the training did not fully meet their needs. More explanation about the interpretation of PROM results and the use of cut-off scores would increase their sense of competence. In addition, a refresher course every few years would be desirable. For this reason, the KLIK expert team is now revising the KLIK training. More information and tips and tricks about the interpretation and communication of PROM results will be included.

Clinicians indicated that they do not always discuss the PROMs with patients and/or parents due to lack of time, technical problems or lack of clarity regarding the workflow. For some clinicians it is unclear which team member of the multidisciplinary team discusses the PROMs with patients and/or parents or who sends invitations. This indicates that continuous support with the implementation process and annual evaluation meetings with all team members of a multidisciplinary team remains necessary. Also, patients do not always complete PROMs prior to the outpatient consultation. Forgetting, loss of motivation or no Internet access were reasons from the clinicians' perspective. In supporting the implementation process, a commonly heard argument from patients for not completing the PROMs is that the clinician does not discuss the PROMs during the consultation. This indicates how important it is for clinicians to discuss the PROMs with patients and/or parents. In addition, it was mentioned that for patients (or parents) with low health literacy skills and for non-native Dutch speakers it is sometimes difficult to complete the PROMs. Although the most frequently used generic PROMs in KLIK are available in multiple languages, this is not the case for all PROMs. When compiling the PROMs outcome sets with the multidisciplinary teams, more attention should also be paid to the needs of non-native Dutch speakers and patients with low health literacy skills.

Clinicians reported several main barriers for using PROMs via the KLIK portal. The first one is a lack of integration between KLIK and the EHRs. Opening a separate website to view the KLIK ePROfile is an added operation for clinicians, with the consequence that the KLIK ePROfile is sometimes not discussed with patients and/or parents. Therefore, in September 2019 a front-end integration with the two most often used EHRs in the Netherlands, Epic© and HiX© was realized in four hospitals. Clinicians can now view the KLIK ePROfile via the EHR, which increases the user-friendliness and makes it a better fit into the clinical workflow.

Second, clinicians indicated that they are not always satisfied with the content of PROMs. Reasons were mostly focused on the burden of completing PROMs for patients, such as a long completion time, many repetitions in questions and irrelevant questions. These challenges with PROMs correspond with previous research [20]. To address these problems, the National Institute of Health (NIH) developed the Patient-Reported Outcomes Measurement Information System (PROMIS) [21, 22]. PROMIS consists of various dynamic item banks (each measuring a separate construct) that can be administered through computerized adaptive testing (CAT) [20, 23]. By using a CAT, questions are offered based on the person's previous answer. In this way, patients and/or parents only have to answer a few questions per PROMIS construct to get a reliable score. As a result, the burden for patients and/or parents can be reduced [24]. Since November 2019, it is possible to administer the PROMIS item banks via KLIK, by linking KLIK with the Dutch Assessment Center. To realize this, the PROMIS item banks were translated and validated in the Netherlands [11, 16].

Third, clinicians mentioned that the use of PROMs is time intensive. Clinicians indicated that it takes more time to prepare themselves for the consultation and to discuss the PROMs in the consultation room. This is a remarkable finding, since previous research has shown that the use of the QLIC-ON Profile did not lengthen the consultation [9]. In addition, clinicians who are responsible for inviting patients for the KLIK PROM

portal indicated that it takes a lot of effort to motivate patients to complete PROMs. A case manager that supports the KLIK implementation would be helpful.

There were a few limitations to this study. First, not all clinicians that use KLIK in the consultation room have been included in this study, because not all multidisciplinary teams were open to an evaluation meeting despite the importance for the implementation process. However, the experiences of clinicians from different disciplines, working with various disease groups in multiple hospitals and different outcome measure sets were included. Second, completing the VAS of the domains 'overall satisfaction' and 'satisfaction with PROMs and feedback' was not always possible when using a tablet. For these clinicians, it was not possible to move the bar to the desired position, causing a score around 50. Unfortunately, it could not be traced who had had this problem and therefore the results of these questions should be interpreted carefully. Third, the question 'I am satisfied with the PROMs offered' was not always understood by the clinicians. Prior to this question, there was a question about specific PROMs. The explanations showed that some clinicians referred to the specific PROMs when answering this question. That is why the answers to this question of 14 clinicians were not included. Fourth, due to the used method, this study provides no insight into the actions clinicians take with regard to the completed PROMs. In addition, no questions were asked about how clinicians use the information from the completed PROMs in daily clinical care. Therefore, recommendations for future PROM implementation research are to gain more insight into the actions of clinicians with regard to the discussed PROMs and how this can lead to more patient-centered care. The use of video observations in the consultation room may provide this information.

To conclude, the KLIK PROM portal is a valuable tool for clinicians to systematically monitor the functioning of their patients in clinical practice, so that extra support can be offered when needed. Overall, clinicians were enthusiastic about the feedback and user-friendliness of the KLIK PROM portal and the added value of using PROMs in clinical practice. However, some challenges and barriers were also identified. Therefore, a next step is to address the mentioned feedback points in the KLIK portal to improve the user-friendliness. Also, the perspective of the other user group, the patients and parents, is needed to further adapt the KLIK PROM portal to their wishes. Therefore, a similar study will be performed in the near future evaluating the KLIK PROM portal from the patients' perspective, with the ultimate goal to further optimize the KLIK PROM portal and to improve the quality of health care.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the international and/or national research committee (Medical Ethics Committee of the Amsterdam UMC – W18_091 # 18.117) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in this study.

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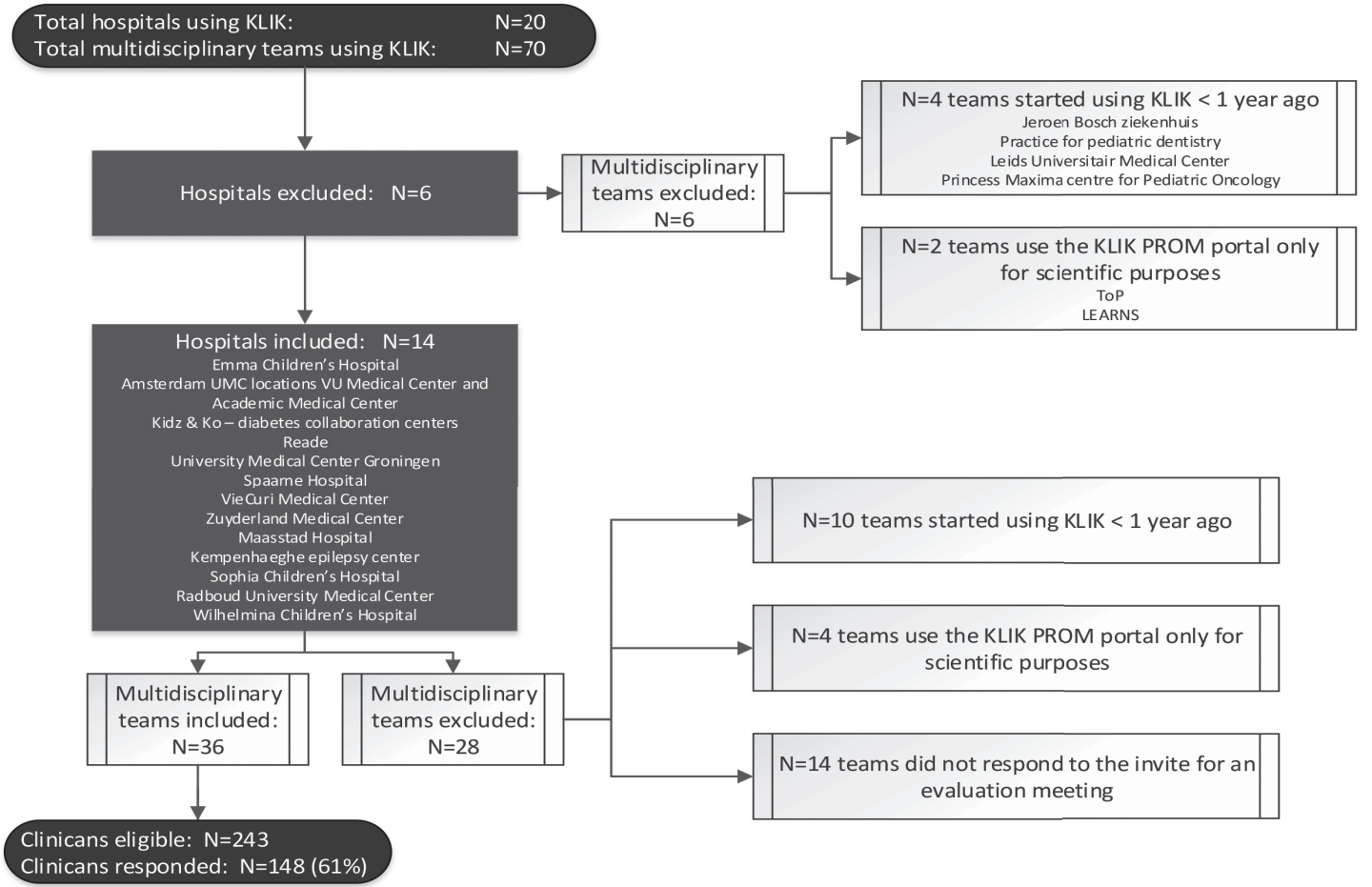
Supplement 1 - Flow diagram of participating hospitals, multidisciplinary teams and clinicians



Supplement 2 - Evaluation questionnaire KLIK

Overall satisfaction					
1. In general, how satisfied are you with the use of KLIK? Not satisfied at all ..... very satisfied *(VAS 0-100)*					
Feeling competent to discuss PROMs	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
2. The KLIK training has prepared me sufficiently to start using KLIK Explanation:	❑	❑	❑	❑	❑
3. I feel competent to discuss the KLIK ePROfile with patients/parents Explanation:	❑	❑	❑	❑	❑
Use of KLIK during the consultation	Always	Usually	Sometimes	Almost never	Never
4. I discuss the KLIK ePROfile with patients/parents Explanation:	❑	❑	❑	❑	❑
When: usually, sometimes, almost never and never, then:					
4a. The reason why I do not always discuss the KLIK ePROfile is: *Open answer*					
5. I discuss the KLIK ePROfile at the ... of the consultation Explanation:	❑ Start	❑ Middle	❑ End		
6. On average, I spend .... % of the consultation on discussing the KLIK PROfile					
❑ I am satisfied with this					
❑ I would like to spend more time on discussing the KLIK PROfile, because ...					
❑ I would like to spend less time on discussing the KLIK PROfile, because ...					

Patient	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
7. All patients are invited to participate in the KLIK PROM portal Explanation:	❑	❑	❑	❑	❑
When: strongly disagree, disagree, neither disagree, nor agree:					
7a. That not everyone is asked to participate is based on: *Open answer*					
8. I estimate that … % of the patients/parents complete the PROMs Explanation:	❑100%	❑75%	❑50%	❑25%	❑0%
Influence of KLIK on the consultation	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
9. KLIK improves my consultation Explanation:	❑	❑	❑	❑	❑
10. With the use of KLIK, I detect problems sooner Explanation:	❑	❑	❑	❑	❑
11. Advantages of KLIK are: *Open answer*					
12. Disadvantages of KLIK are: *Open answer*					
Patient	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
13. I think that patients/parents are satisfied with the use of KLIK Explanation:	❑	❑	❑	❑	❑
14. I think that incentives for patients/parents to use KLIK are: *Open answer*					

15. The most frequently heard reactions of patients/ parents about KLIK are:
    Open answer

Usability of the KLIK PROM portal	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
16. The KLIK PROM portal is easy to use Explanation:	❑	❑	❑	❑	❑
17. The KLIK PROM portal has an attractive lay-out Explanation:	❑	❑	❑	❑	❑
Satisfaction with PROMs and feedback	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
18. I am satisfied with the PROMs offered Explanation:	❑	❑	❑	❑	❑
19. I am satisfied with the feedback of:					
a. Overall KLIK ePROfile	❑	❑	❑	❑	❑
b. Literal answers	❑	❑	❑	❑	❑
c. Traffic light colors	❑	❑	❑	❑	❑
d. Graphs (scores over time and comparison with peers)	❑	❑	❑	❑	❑
Explanation:					
20. I look at the following parts of the feedback in the KLIK ePROfile (multiple answers possible) Explanation:	❑Literal answers	❑Traffic light colors	❑Graph	❑Otherwise	

21. I discuss the following parts of the KLIK ePROfile (multiple answers possible)
    - ❑ Green answers
    - ❑ Orange answers
    - ❑ Red answers
    - ❑ Comparison with peers (graph)
    - ❑ Scores over time (graph)
    - ❑ Other.....

22. I think the following parts of the feedback of the KLIK ePROfile are important:
    a. Literal answers Not important at all .....Very important *(VAS 0-100)*
    b. Traffic light colors Not important at all .....Very important *(VAS 0-100)*
    c. Graphs Not important at all .....Very important *(VAS 0-100)*

Support KLIK expert team	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
23. I know where I can ask my questions regarding the KLIK PROM portal Explanation:	❑	❑	❑	❑	❑
24. There is sufficient support from the KLIK team when I need it Explanation:	❑	❑	❑	❑	❑

CHAPTER 3

Patients' and parents' perspective on the implementation of Patient Reported Outcome Measures in pediatric clinical practice using the KLIK PROM portal

Maud M. van Muilekom*, Lorynn Teela*, Hedy A. van Oers,
Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman

*Authors contributed equally to the manuscript

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Abstract

Introduction

The KLIK Patient Reported Outcome Measures (PROM) portal (www.hetklikt.nu) has been implemented since 2011 in clinical practice in over 20 Dutch hospitals. Patients and/or parents complete PROMs before the outpatient consultation and answers are subsequently discussed by clinicians during consultation. This study aims to provide insight into patients' and parents' perspective on the use of the KLIK PROM portal in order to optimize its implementation in pediatric clinical practice.

Methods

Patients (12-19 years) and parents (of children 0-19 years) from the Emma Children's Hospital were invited to participate. A mixed-method design was used; (1) Focus groups were held and analyzed using thematic analysis in psychology, (2) a questionnaire was sent out and analyzed using descriptive statistics.

Results

(1) Eight patients and 17 parents participated. Patients mentioned that KLIK has an attractive layout. However, PROMs were sometimes considered irrelevant and repetitive. Parents valued that KLIK provides insight into their child's functioning, but they were not satisfied with the extent to which PROMs were discussed by clinicians. (2) 31 patients and 130 parents completed the questionnaire. Overall, patients and parents reported a satisfaction score of 7.9/10 and 7.3/10, respectively. 81% of patients and 74% of parents indicated that KLIK is easy to use.

Conclusion

Patients and parents are generally satisfied with KLIK, however, points of improvement were mentioned. These are currently being addressed by e.g., upgrading the KLIK website, implementing PROMIS item banks in KLIK to reduce irrelevancy and repetitiveness of PROMs, and implementation strategies to improve the discussion-rate. In this way, implementation of the KLIK PROM portal can be further optimized, with the ultimate goal to improve quality of care.

Keywords

Patient Reported Outcomes, questionnaires, patient engagement, pediatrics.

Introduction

Patient Reported Outcome Measures (PROMs) are increasingly used to monitor and discuss symptoms, Health-Related Quality of Life (HRQOL) and psychosocial functioning of patients in the consultation room with the ultimate goal to enable shared-decision making and patient-centered care [1-3]. Using PROMs in clinical practice has been shown valuable, as it results in more awareness for and increased discussion of patient concerns, higher patient satisfaction, better communication between patient and clinician, and improved treatment outcomes [4-9].

A system that facilitates the use of PROMs in clinical practice is the evidence-based KLIK PROM portal (www.hetklikt.nu) [10-13], which has been implemented in over 20 hospitals in the Netherlands since 2011 [14]. With KLIK, pediatric patients and/or their parents, and adult patients complete PROMs before the outpatient consultation. Answers are converted into an electronic KLIK PROfile (KLIK ePROfile) which the clinician discusses with patients and parents during the consultation [14]. The most important stakeholders in the development and implementation process of the KLIK PROM portal are the users; clinicians as well as patients/parents. From the onset of KLIK, clinicians' opinions were asked during these processes. For example, clinicians' preferences for PROM feedback options in the KLIK ePROfile were studied [10], clinicians were involved in the selection of PROs and PROMs for their disease group, and they were consulted in annual evaluation meetings to identify and overcome barriers in the implementation process [14]. Two studies were performed to gain more insight into the experiences of clinicians with KLIK and to identify barriers in the implementation process, with the goal to improve the KLIK PROM portal according to their needs [15, 16]. However, the opinion of the other stakeholder, patient/parents, is also important [17], as engaging patients in KLIK could result in higher patient satisfaction and higher enrollment rates [18-21].

Worldwide, patients are increasingly engaged in PROM development (e.g., item development, comprehensibility) [22] and PROM visualization to patients and clinicians [23]. However, the experiences of patients regarding the use of PROMs in daily clinical practice has received less consideration [24-31]. Available studies explored the experiences of adult patients regarding the use of PROMs in daily clinical practice. Both positive (e.g., improved communication, insight into patient's functioning, and increased awareness of psychosocial problems) [25, 26, 28-31] and negative experiences (e.g., negative and irrelevant questions in PROMs, unclear purpose of using PROMs) [25-27] were identified. To our knowledge, no studies have been performed focusing on the experiences of pediatric patients and their parents with using PROMs in daily clinical practice. To be able to optimize and further implement the KLIK PROM portal, it is also necessary to gain understanding of their wishes and needs. Therefore, the aim of this study is to provide more insight into the perspective of patients and parents on the implementation of PROMs in pediatric clinical practice using the KLIK PROM portal.

Methods

KLIK workflow

The KLIK workflow for pediatric patients and parents consists of several steps; (1) creation of a KLIK account by patients/parents, (2) completion of PROMs by patients/parents before the outpatient consultation, (3) conversion of answers into a KLIK ePROfile, and (4) discussion of the KLIK ePROfile by the clinician during consultation (Figure 1).

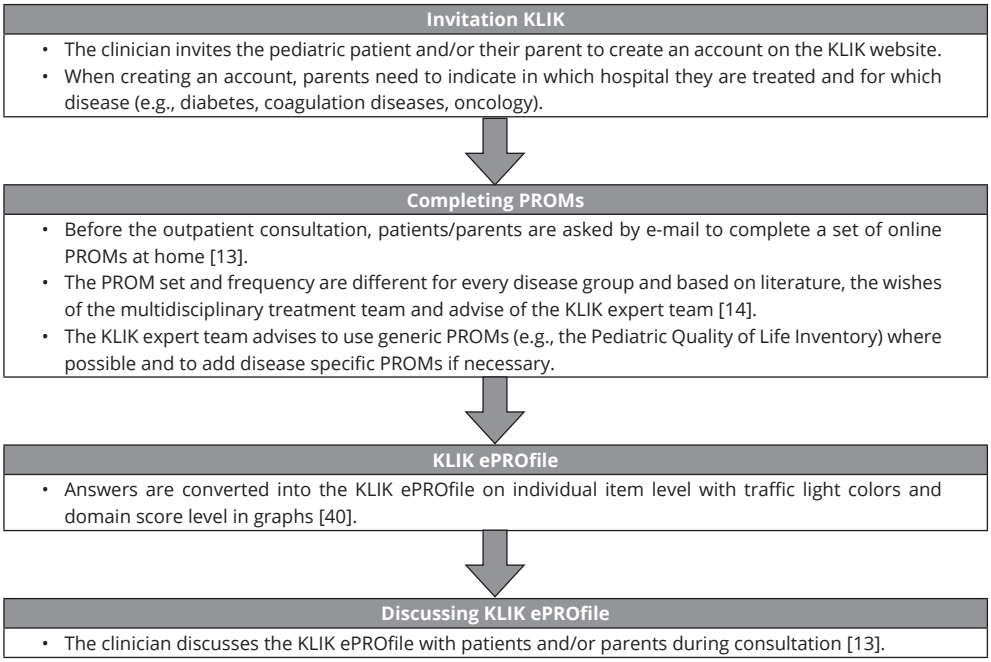

Figure 1. Patient journey of patients and parents using the KLIK PROM portal

Design

This study is part of a larger participation study where KLIK users' (patients/parents) opinion was asked about several aspects of health care and the use of the KLIK PROM portal. This sub-study reports on the evaluation of the KLIK PROM portal. A mixed-method design was used where qualitative and quantitative methodologies were combined: (1) focus groups were held with patients and parents and (2) an evaluation questionnaire was sent out to pediatric patients and parents. The Medical Ethics Committee of the Amsterdam University Medical Centers (Amsterdam UMC-AMC) approved this study. All participants provided informed consent.

Participants

Patients (12-19 years) and parents (of children 0-19 years) who consult a pediatric department of the Emma Children's Hospital Amsterdam UMC that uses KLIK as standard part of care, completed KLIK PROMs at least once (questionnaire) or twice (focus groups),

and were part of the 'KLIK panel' could participate in this mixed-method study. Patients with any chronic health condition could participate in this study as the workflow of the KLIK PROM portal is similar for all patient groups. The 'KLIK panel' consists of patients and parents that indicated, during registration on the KLIK PROM portal, that they give permission to be invited for research projects. Eligible patients/parents were invited by e-mail to take part in the focus groups (March 2018) and/or to complete the evaluation questionnaire (June-December 2019). Socio-demographics (age and gender child), information on chronic health condition of the child and years of using KLIK were obtained from the KLIK PROM portal. All participants received a gift card of 5 euros (focus groups) or 10 euros (questionnaire) after participation.

Procedure

Focus groups

Focus groups with patients and parents were held separately and for each focus group inclusion of three to six participants was pursued [32]. Focus groups consisted of a group discussion guided by two moderators (MvM, LT, HvO, or LH). At the start of the focus group, the aim of the study was explained and a short recapitulation of KLIK was provided. Then, to obtain patients' and parents' opinion about KLIK, positive and negative experiences with KLIK were discussed using the evaluation technique 'Complain and Cheer wall' [33]. Participants were asked to write down their positive experiences on a flip over at one side of the room, what we called the 'Cheer wall', and points of improvement on another flip over at the other side of the room, the 'Complain wall'. Thereafter a group discussion took place and topics on the walls were grouped together into main themes. Duration of each focus group was 60 minutes. All focus groups were audio recorded.

Questionnaire

The questionnaire (separate version for patients and parents, with minor differences regarding language use–Supplement 1) was developed by five researchers of the KLIK expert team and reviewed by five other researchers and one psychologist. Both versions of the questionnaire consisted of 17 closed questions (response options: three- and five-point Likert Scales and Visual Analogue Scales (VAS)) and two mandatory open questions (advantages and disadvantages of KLIK), regarding (1) overall satisfaction with the KLIK PROM portal, (2) completion of PROMs in the KLIK PROM portal, (3) discussing PROMs with the clinician, (4) influence of KLIK on the (preparation of) the consultation, (5) usability of the KLIK PROM portal, and (6) content of PROMs. For three closed questions, an additional mandatory open question was provided, asking about the reason for their answer.

Analyses

Descriptive analyses were performed using the Statistical Package for Social Sciences (SPSS) version 25.0 to characterize the participants.

Regarding the focus groups, all audio recordings were transcribed verbatim and the transcripts were analyzed independently by MvM and LT in MAXQDA (2018) following the thematic analysis in psychology [34]: (1) highlighting relevant parts of the manuscript, (2) organizing data into meaningful groups by generating initial codes, (3) collating initial codes into themes, (4) refining themes into main- and subthemes, (5) defining the final themes. Analyses were discussed until consensus was reached on the themes. Data saturation was considered attained when no new themes emerged during the analyses of the focus groups.

Regarding the questionnaire, SPSS was used for descriptive statistics (percentages) to provide insight into the experiences of patients and parents with the use of the KLIK PROM portal. Open questions of the evaluation questionnaires were analyzed qualitatively by MvM and LT. This was done by clustering the answers of both patients and parents into main themes following the thematic analysis in psychology [34].

Results

Participants

Figure 2 shows the study and participant flowchart of this study. In total, 8 patients (three focus groups) and 17 parents (three focus groups) participated in six focus groups. Regarding the questionnaire, 31 patients (response rate: 21.8%) and 130 parents (response rate: 19.6%) participated. One patient and 5 parents participated in the focus groups and completed the questionnaire. Table 1 shows the sociodemographic characteristics of all participants.

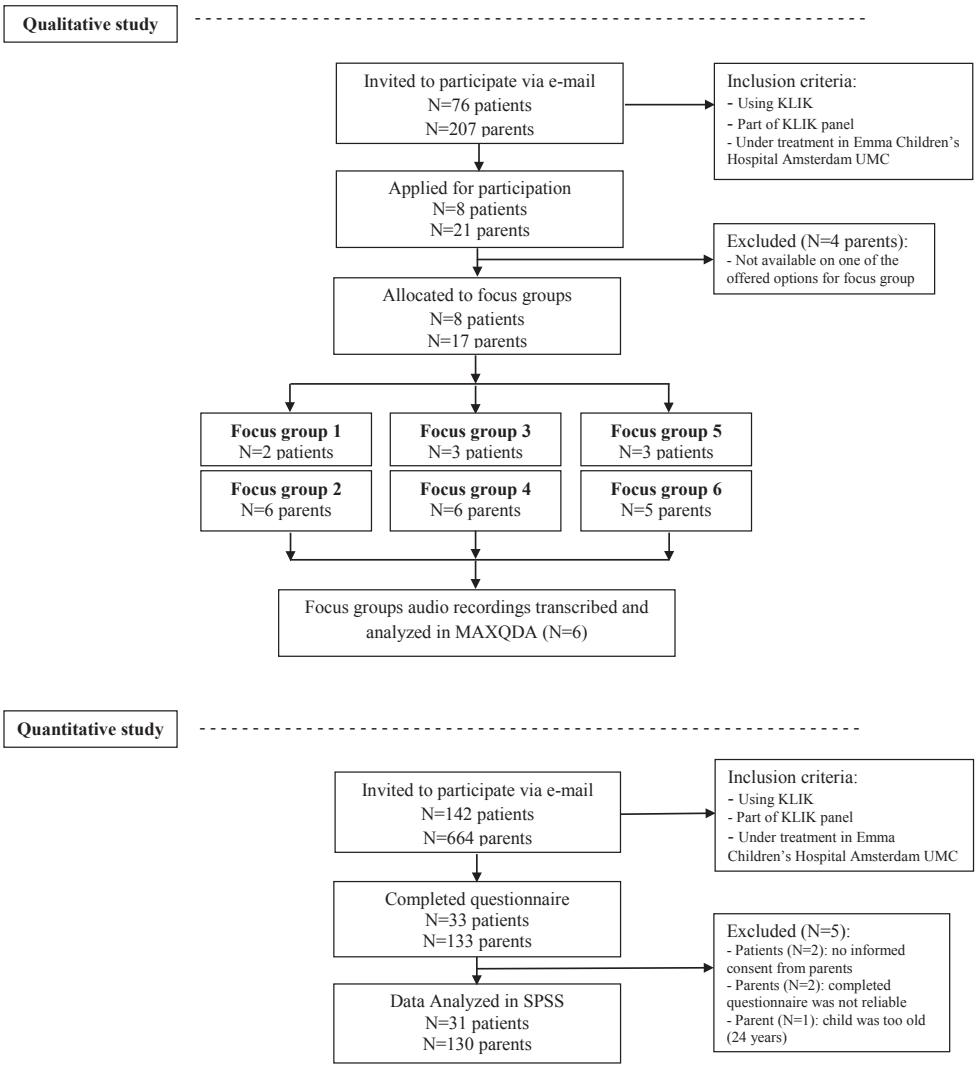

Figure 2. Study and participant flowchart of the qualitative (focus groups) and quantitative study (questionnaire)

Table 1. Sociodemographic characteristics of focus group and questionnaire participants

	Focus groups			Questionnaire		
Patients	***N***	***M***	**Range**	***N***	***M***	**Range**
KLIK user since (years)	8	3.2	1.1-6.1	31	5.2	1.0-8.2
Age	8	15.3	13.1-18.8	31	15.7	12.4-19.2
		%			**%**	
Gender (female)	6	75.0		15	48.4	
Chronic health condition						
Juvenile idiopathic arthritis	2	25.0		7	22.6	
Cystic Fibrosis	2	25.0		1	3.2	
Cancer	2	25.0		0	0	
Gastrointestinal diseases	1	12.5		4	12.9	
Home parenteral nutrition	1	12.5		0	0	
Sickle cell disease	0	0		4	12.9	
Other*	0	0		15	48.4	
Parents	***N***	***M***	**Range**	***N***	***M***	**Range**
KLIK user since (years)	17	2.8	0.8-6.1	130	3.2	0.3-8.1
Age (of child in KLIK)	17	10.4	2.1-16.9	130	9.3	0.9–19.1
		%			**%**	
Chronic health condition (child)						
Cancer	6	35.3		0	0	
Juvenile idiopathic arthritis	2	11.8		13	10.0	
Hemophilia	2	11.7		4	3.1	
Home parenteral nutrition	2	11.7		3	2.3	
Gastrointestinal diseases	1	5.9		20	15.4	
Neonatology follow up	0	0		28	21.5	
Other*	4	23.5		62	47.7	

*Only most common conditions groups (>10% in one of the study groups) are reported, other: cleft lip, endocrinology, nephrology, HIV, dermatology, craniofacial abnormalities, spherocytosis, cystic fibrosis, lysosomal storage disorders, intensive care follow-up, Marfan syndrome, feeding disorders, phenylketonuria, and muscular disorders.

Focus groups

Data saturation was attained as no new themes emerged after analyzing the focus groups. Table 2 (patients) and 3 (parents) depict the most important positive experiences with KLIK and points of improvement for KLIK and corresponding examples of statements. Themes are ranked based on the number of times mentioned (most often to fewest times) by patients and parents during the focus groups.

Table 2. Positive experiences and points of improvement mentioned by patients (N=8) in the focus groups (ranked from most often to fewest times mentioned)

Themes	Positive experiences	Points of improvement
Content of PROMs	'The questions are clear, recognizable and easy to answer' 'All topics are covered in the questionnaires, not only topics about your disease'	'There is a lot of repetition in questions' 'The questions are not relevant for every patient and sometimes questions are difficult to understand' 'It would be good if questions were administered based on previous answers'
Completion time PROMs	'Completing the questionnaires does not take too much time'	'Completing the questionnaires takes a lot of time'
Layout	'The KLIK website looks nice with the colors that are used' 'Nice that you can see a picture of your doctor'	
Discussion by clinician	'The answers in the KLIK ePROfile are discussed by the clinician'	'The clinician often does not discuss the KLIK ePROfile' 'Sometimes the clinician does not ask more questions based on my answers'
Insight patients' functioning	'By completing the questionnaires you see how you are doing' 'It is good that parents know what is going on' 'With KLIK, clinicians know how you are doing'	
Conversation content	'With KLIK, not only physical health, but also mental health is discussed' 'It helps in discussing topics that you would otherwise not think about'	
Preparation of consultation	'Completing the questions before the appointment helps you to come up with topics you want to discuss during the consultation'	'Completing KLIK questionnaires does not help you in preparing for the consultation, it is just something you need to do'
Motivation child		'I think it is not always necessary to complete the KLIK questionnaires' 'I sometimes just do not want to talk about the KLIK topics'
Consultation efficiency	'The consultation is more efficient when KLIK is used, as the doctor immediately has an overview of how you are doing'	
Anonymity and security	'It is good that KLIK is well secured' 'As KLIK PROMs are completed on the computer, it feels more anonymous, which results in completing the PROMs more honestly'	
Ease of use	'It is nice that the KLIK questionnaires can be completed on the computer at home'	'You cannot go back to the questionnaire if you completed all questions'

All quotes were translated into English.

Patients

In all focus groups, patients came up with a broad range of experiences with KLIK, both positive, negative and mixed. Themes that were unanimously rated as positive were that the KLIK website has an attractive *layout* (due to the use of colors and pictures), that KLIK *provides insight* into their daily functioning and that KLIK improves the *conversation content* during the consultation, where a broader range of topics is discussed. Furthermore, patients indicated that the *consultation* is more *efficient* when using KLIK and that they are happy about how *secure* the KLIK website is and how their data remains *anonymous*. There were five themes on which patients disagreed. Some patients rated the *content of PROMs* positively, as they cover all important topics and are clear, while other patients indicated that the questions in the PROMs are difficult to understand, repetitive and not relevant for every patient. In addition, *completion time* was rated by some as good and by others as time-consuming, and the KLIK ePROfile is always *discussed* by the *clinician* according to some patients, but not enough by others. Finally, KLIK helps only some patients in *preparing for the consultation*, and patients were ambiguous about *ease of use* of KLIK. The lack of motivation for completing the KLIK PROMs was only mentioned as a negative experience by some patients.

Parents

Parents mentioned many similar experiences with KLIK as patients (Table 3). Themes that were unanimously rated as positive were that KLIK helps in *preparing for the consultation* and *provides insight into the patients' functioning*, although for some parents this insight was also confronting when many problems were reported. In addition, parents were satisfied that by using KLIK *problems are detected* at an early stage and that support can be provided timely. All other themes were evaluated both positively and negatively. Some parents indicated that they are satisfied with the *content of PROMs*, as all topics are covered and questions are easy to understand, while other parents disagreed and indicated that questions are hard to understand for their child, are confronting and repetitive. Parents also had mixed opinions regarding *ease of use* of KLIK, where some thought completing PROMs online is working great, and others thought this could be improved by developing a KLIK app and linking KLIK to the Electronic Health Records (EHR). Furthermore, *discussion* of the KLIK ePROfile *by clinicians* always happens according to some parents, but not often enough by even more parents. Most parents mentioned that the *conversation content* improves as more and different topics are discussed, while some did not recognize this. *Completion time* is manageable for some, but too long for others and the *layout* of the KLIK website is attractive and child-friendly according to most parents, but could be made more attractive by using visuals according to some parents. Finally, some parents indicated that they do not see the added *value and goal* of KLIK, while others disagreed and indicated that KLIK is of great value to the consultation.

Table 3. Positive experiences and points of improvement mentioned by parents (N=17) in the focus groups (ranked from most often to fewest times mentioned)

Themes	Positive experiences	Points of improvement
Content of PROMs	'The questions are easy to understand for children' 'All important topics are covered in the questionnaires'	'The questions are sometimes not relevant and confronting for children' 'It is annoying that every time the same questions are asked' 'There is no attention for brothers, sisters and the family situation' 'The questions are difficult to understand for young children. I would suggest to make the questions more visual'
Ease of use	'KLIK is easy to use and it is nice that you can complete questionnaires online' 'I like the reminder e-mails that are sent by KLIK'	'KLIK should be connected with the EHRs, so appointments are automatically linked' 'I would like KLIK to be available as an app'
Insight patients' functioning	'It is nice that parents have insight into the functioning of their child over time' 'With KLIK the clinician knows what is going on and can follow the child over time'	
Discussion by clinician	'The clinician takes KLIK seriously and always discusses the answers'	'The KLIK questionnaires are often not discussed by the clinician' 'Especially questionnaires about the functioning of parents are not discussed'
Conversation content	'KLIK is a conversation tool and provides structure and more depth to the conversation' 'It is nice that with KLIK psychosocial functioning is also taken into account'	'Our consultation has already a fixed structure, so KLIK does not help with that'
Preparation of consultation	'KLIK helps to start a conversation with your child or partner about the situation before the consultation' 'KLIK helps to think about how it is going and to prepare questions before the consultation'	
Layout	'The KLIK website is attractive and looks nice for children' 'The layout of KLIK is clear and understandable'	'It would be good if smileys were used to make KLIK more attractive'
Completion time PROMs	'The completion time is manageable and not too long'	'Too many questions have to be completed' 'Before I start completing the questionnaires I would like to see how much time it will take'
Detecting problems	'With KLIK problems are detected early and your child can be referred for help'	
Value and goal	'I like that with KLIK there is the possibility to report difficulties'	'Completing KLIK questionnaires feels not useful when it is going well' 'It is not totally clear what is done with your answers and if they can be used against you by the government'

All quotes were translated into English.

Questionnaire

Overall satisfaction with the KLIK PROM portal

Patients and parents reported an overall satisfaction with the KLIK PROM portal of mean = 7.9 and mean = 7.3, respectively, on a VAS ranging from 0 (not satisfied) to 10 (very satisfied).

Completion of PROMs in the KLIK PROM portal

As shown in Table 4, 78% of the patients and 84% of the parents agreed that they know why there are asked to complete PROMs via the KLIK PROM portal. Patients and parents reported that the frequency in which they are asked to complete these PROMs varies from once every three years to more than four times a year. Most patients and parents were satisfied with this frequency. When patients and parents are asked to complete PROMs, the majority indicated that they almost always do this. Reasons for not completing the PROMs were: lack of time, forgot to complete, little change in functioning since the last PROM completion, and no motivation. Patients and parents spent on average 13.8 and 15.2 min on completing the PROMs, respectively. More than 80% of both patients and parents were satisfied with this completion time.

Table 4. Scores on the domain 'completion of PROMs in the KLIK PROM portal' (patients: *N* = 31, parents: *N* = 130)

			Agree–*N* (%)	**Neutral–*N* (%)**	**Disagree–*N* (%)**
I know why I am being asked to complete KLIK PROMs	Patients		24 (78)	1 (3)	6 (19)
	Parents		109 (84)	13 (10)	8 (6)
		4 times a year–*N* (%)	**2 times a year–*N* (%)**	**Yearly–*N* (%)**	**Other–*N* (%)**
How often are you asked to complete the PROMs in KLIK?	Patients	7 (22)	12 (39)	8 (26)	4 (13)
	Parents	21 (16)	29 (22)	38 (30)	42 (32)
			Yes–*N* (%)	**No, too often–*N* (%)**	**No, too infrequent–*N* (%)**
Are you satisfied with this frequency?	Patients		29 (94)	1 (3)	1 (3)
	Parents		111 (85)	11 (9)	8 (6)
			(Almost) always–*N* (%)	**Sometimes–*N* (%)**	**(Almost) never–*N* (%)**
When you are asked to complete the PROMs in KLIK, how often do you do this?	Patients		28 (90)	3 (10)	-
	Parents		123 (95)	2 (1)	5 (4)
			***M* (range)**		
I spend on average .. minutes on completing the KLIK PROMs	Patients		13.8 (5-30)		
	Parents		15.2 (0-60)		
			Yes–*N* (%)	**No, too long–*N* (%)**	**No, too short–*N* (%)**
Are you satisfied with the completion time?	Patients		25 (81)	6 (19)	-
	Parents		109 (84)	20 (15)	1 (1)

Discussing PROMs with the clinician

About half of the patients and parents indicated that their clinician (almost) always discusses the KLIK ePROfile with them during the consultation (Figure 3). If the clinician does not discuss the completed PROMs, 52% of the patients and 72% of the parents indicated they dare to start the discussion about PROMs themselves.

Figure 3. Scores on the domains 'discussing PROMs with the clinician', 'Influence of KLIK on the (preparation of the) consultation', and 'content of PROMs' (patients: N=31, parents: N=130)

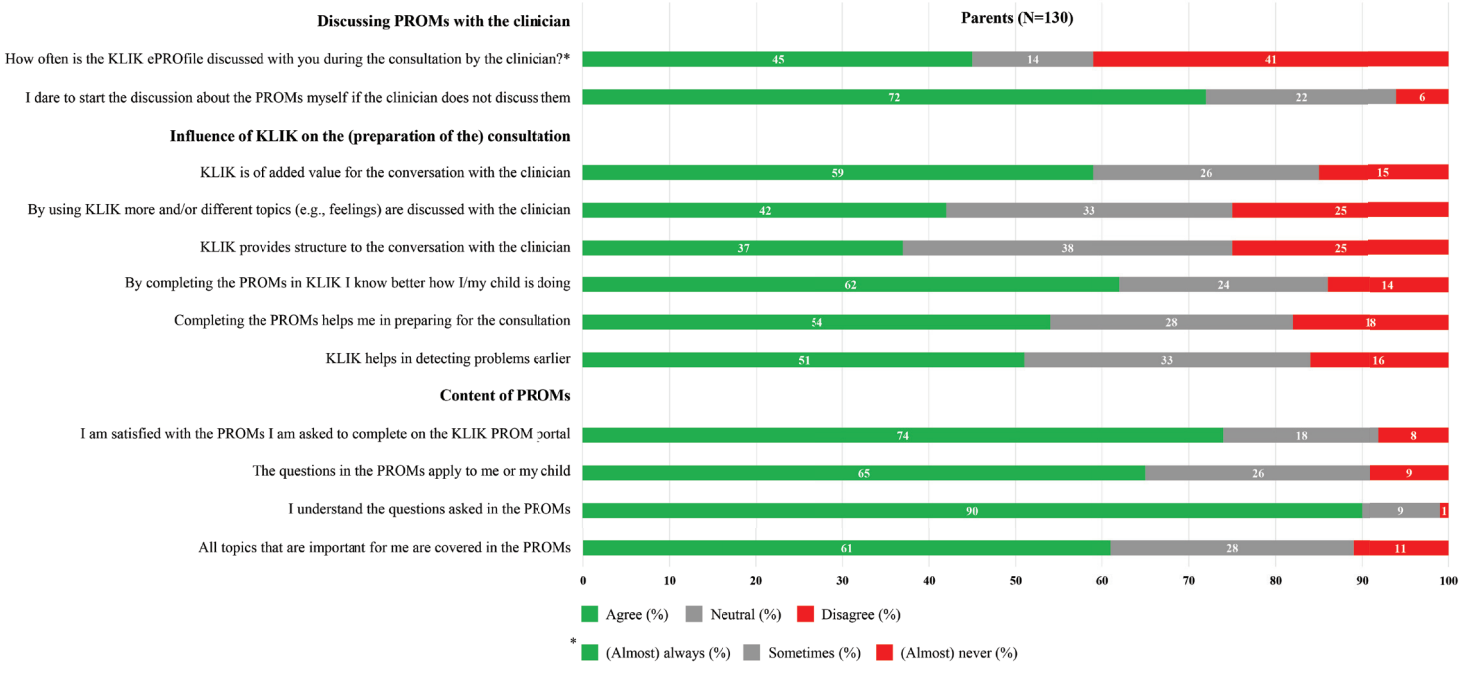

Figure 3. Scores on the domains 'discussing PROMs with the clinician', 'Influence of KLIK on the (preparation of the) consultation', and 'content of PROMs' (patients: N=31, parents: N=130)

Influence of KLIK on the (preparation of the) consultation

KLIK is of added value for the conversation with their clinician, according to 58% of the patients and 59% of the parents (Figure 3). Less than half of the patients and parents indicated that more topics are discussed by using the KLIK PROM portal in comparison with not using the KLIK PROM portal and that the use of KLIK provides more structure to the conversation. Clinicians' failure to discuss the KLIK ePROfile was a frequently mentioned reason why KLIK has no value during the consultation. More than half of the parents reported that the use of KLIK provides them more insight into the functioning of their child and helps in preparing for the consultation (62% and 54% respectively), in contrast to only 39% and 42% of the patients. Patients indicated that they know very well how they are doing, even without completing a PROM.

Table 5 shows the most important advantages and disadvantages of KLIK, as reported in the open questions. The themes are ranked based on the number of times mentioned by patients and parents in the open-ended questions. Main advantages of KLIK for patients and parents were: *easy to use, clinician is better prepared, patients and parents are better prepared*, and *insight into functioning (of my child)*. Main disadvantages of KLIK for patients and parents were: *not easy to use, irrelevant content of PROMs,* and *takes time*. Eleven patients (35%) and 48 parents (37%) did not experience any disadvantages with using the KLIK PROM portal.

Table 5. Advantages and disadvantages of the KLIK PROM portal, mentioned by patients (*N* = 31) and parents (*N* = 130) in the open questions of the evaluation questionnaire

Advantages KLIK PROM portal	**Examples**
Easy to use	'Simple and clear' 'It is easy that you can complete questionnaires online at home'
Clinician is better prepared	'The clinician can see my questions before the appointment at the outpatient clinic' 'The clinician is already aware of my child's health situation and can immediately respond to it'
Patient and parents are better prepared	'It is valuable that you can ask the clinician questions in advance so that you do not forget them' 'Subjects are discussed which you normally do not bring up yourself'
Insight into functioning (of my child)	'KLIK provides insight into how I am doing' 'Provides the opportunity to compare the health situation of my child now with the situation just after diagnosis'
Disadvantages KLIK PROM portal	
Not easy to use	'I keep forgetting my password' 'Annoying that I get multiple reminders'
Irrelevant content of PROMs	'Not all questions apply to our situation' 'It is boring to complete the same questionnaires every time'
Takes time	'Completing the questionnaires takes sometimes more time than I hope' 'It is a lot of work to complete the questionnaires'

All quotes were translated into English.

Usability of the KLIK PROM portal

The KLIK PROM portal is easy to use, according to 81% of the patients (13% neutral and 6% disagree) and 74% of the parents (18% neutral, 8% disagree). In addition, 48% of the

patients (39% neutral, 12% disagree) and 55% of the parents (36% neutral, 9% disagree) indicated that KLIK has an attractive layout.

Content of PROMs

Most patients and parents are satisfied with the PROMs they are asked to complete (Figure 3). Almost all participants indicated that they understand the questions asked in the PROMs. Reasons why patients and parents are not satisfied with the offered PROMs were that the questions in the PROMs do not apply to them or their child, PROMs are too generic, the different questions are very similar, and the PROMs are too long. Some of the patients and parents felt that the offered PROMs do not cover all topics that are important for them. For example they miss topics like growth, parenting support, and side jobs.

Discussion

This study provided insight into the experiences of patients and parents with the implementation of PROMs in pediatric clinical practice using the KLIK PROM portal. Overall, patients and parents were satisfied with the use of KLIK. They indicated that KLIK provides insight into the patient's functioning, helps parents and clinicians in preparing for the consultation, is easy to use, and results in discussion of a broad range of topics (e.g., from disease-specific to psychosocial functioning) during the consultation. However, points of improvement were indicated regarding the content of PROMs, the layout of the KLIK PROM portal, and the discussion of PROMs by the clinician. The results described in this study are in line with previous studies [15, 25, 26].

Although patients and parents responded to the closed question of the evaluation questionnaire that they are generally satisfied with the offered PROMs in KLIK, they mentioned in the focus groups and open-ended questions that the content of PROMs is the most important point of improvement. For example, they indicated that there is repetition in questions, that irrelevant questions are administered, and that the completion time is long, resulting in a burden of completing PROMs. These challenges with PROMs have been mentioned in previous research [16, 35, 36]. To address these challenges, the self-report and proxy-versions of the Patient-Reported Outcomes Measurement Information System (PROMIS®) item banks [37-39] were implemented in the KLIK PROM portal in the past year and are currently used in several clinics [16, 40, 41]. The PROMIS item banks each measure a separate construct that can be administered using Computerized Adaptive Testing (CAT). With CAT, questions are presented to patients based on their previous responses. Hence, patients only have to answer a small number of questions per item bank to obtain a reliable score [42] and have to answer less irrelevant questions. Consequently, the burden of completing PROMs can be reduced.

Another difference between the focus groups and the questionnaire was the rating of the ease of use of the KLIK PROM portal. While in the questionnaire the majority of participants indicated that KLIK is easy to use, in the focus groups especially parents had quite some remarks on how the ease of use could be improved. Parents mentioned that an app would be a valuable addition to the KLIK website in order to complete PROMs

on your mobile phone. Additionally, they would like an integration of KLIK with the EHR so that appointments are automatically linked to KLIK by which PROMs are directly available. To address these suggestions, we made the KLIK PROM portal adaptable for mobile phone use, and realized a front-end (hybrid) integration with the EHR in 2019. With this integration, clinicians can now view the KLIK ePROfile in the EHR and discuss the PROMs more easily. However, to be able to automatically link the appointments to KLIK, a full integration is necessary, which can hopefully be realized in the future.

A final difference between the focus group and questionnaire outcomes was the satisfaction with the layout of the KLIK PROM portal, which was mainly mentioned as a point of improvement in the questionnaire. Patients and parents indicated that the website looks a bit old-fashioned and could be made more attractive by using visuals. For this reason, the homepage of the KLIK website was upgraded recently. The design of the website was changed (e.g., by using visuals and creating a more professional look). In addition, specific information pages are now available for all KLIK users (pediatric patients, parents, adult patients, and clinicians).

Patients and parents mentioned in both the focus groups as the questionnaires that clinicians often do not discuss PROMs during the consultation. This is worrisome, as patients and parents indicated that this is an important reason why KLIK sometimes has no added value for the consultation which consequently may lead to loss of motivation to complete KLIK PROMs. To improve this discussion rate, several implementation strategies were used. For example, the KLIK expert team revised the KLIK training in which more attention is now paid to the importance of discussing PROMs [43] and this topic is discussed more thoroughly during annual evaluation meetings with clinicians [16], with the goal to increase their knowledge, awareness and confidence in discussing PROMs. Additionally, finding champions for each multidisciplinary team to motivate clinicians to use and discuss KLIK PROMs would be beneficial as this was identified as the most important implementation strategy in two KLIK studies [15, 17]. When clinicians do not discuss the completed PROMs, patients and some parents indicated that they do not dare to bring up for them important themes themselves. To empower patients/parents and increase their self-efficacy, educational videos were developed and made available on the KLIK homepage (article in preparation). In these videos tips and tricks are provided how patients and parents can prepare themselves for the consultation and bring up topics they want to discuss with the clinician.

When comparing this study with the KLIK evaluation study with clinicians [16], similar experiences regarding the KLIK PROM portal were mentioned. For example, insight into patients' functioning, improved communication, and better preparation of the consultation were positive points they agreed on, and content of PROMs was the most important point of improvement mentioned by both user groups. However, patients/parents and clinicians mentioned a different PROM completion rate. Patients and parents indicated a very high completion rate, whereas clinicians estimated that this completion rate is much lower and that it takes a lot of effort to motivate patients to complete PROMs [16]. A possible reason for this difference might be a bias in the current sample, as only patients and parents that were part of the KLIK panel were invited for participation. These patients/parents might be more assertive in comparison to the other

KLIK users, which might have resulted in an overestimation of the PROM completion rate. Therefore, continuous support and explanation about the goal of the use of KLIK remains very important to both user groups.

There are some limitations to this study that should be mentioned. First, there was a low response rate in the evaluation questionnaire (around 20%) which was unexpected as this questionnaire was sent to participants of the KLIK panel (who indicated that they were willing to be invited for research projects). Possible reasons for the low response rate might be that (1) the willingness of patients and parents has changed as participation in the KLIK panel was only asked during registration, (2) patients and parents do not actively use the KLIK PROM portal anymore, or (3) patients and parents might be tired of completing surveys. Second, it was also difficult to motivate patients to participate in the focus groups. This resulted in a small number of participants per patient focus group (2 to 3 participants) with two moderators, which may have influenced the dynamics. Additionally, we noticed that pediatric patients found it very difficult to formulate and express their opinion and needed a lot of guidance which could have led to a bias in the results. Third, we used a self-developed questionnaire which makes comparisons with other evaluation studies difficult. However, other studies also made use of self-conducted questionnaires [44] or adapted questionnaires from prior studies [29-31], as the questions needed to be specific about features of the tool used.

In conclusion, pediatric patients and parents were satisfied with the usability and effect of the KLIK PROM portal in clinical care. KLIK provides them insight into their functioning and helps them to communicate with the clinician. However, some points of improvement were also identified, which are currently being addressed. We now have insight into the experiences of the most important stakeholders (patients/parents and clinicians) of KLIK. In the future it is important to continuously evaluate the use of the KLIK PROM portal with all stakeholders (including adult patients) to match their needs. In this way, we can further optimize and implement the KLIK PROM portal in clinical care with the ultimate goal to improve the quality of care.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethics approval

All procedures performed in this study were in accordance with the ethical standards of the international and/or national research committee (Medical Ethics Committee of the Amsterdam UMC – W18_023 # 18.034 and Medical Ethics Committee of the Amsterdam UMC – W19_272 # 19.324) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable

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Supplement 1. Evaluation questionnaire KLIK – Patient version

Overall satisfaction													
1.	In general, how satisfied are you with the use of KLIK?												
	Not satisfied at all	0	1	2	3	4	5	6	7	8	9	10	Very satisfied

Completion of PROMs in the KLIK PROM portal					
2.	I know why I am being asked to complete KLIK questionnaires Explanation:	❑Strongly disagree	❑Disagree	❑Neither disagree nor agree	❑ Agree	❑Strongly agree
3.	How often are you asked to complete the questionnaires in KLIK? Explanation:	❑4 times a year	❑2 times a year	❑Once a year	❑Other	
3a.	Are you satisfied with this frequency?	❑Yes, I am satisfied	❑No, it is too often	❑No, it is too infrequent		
4.	When you are asked to complete the questionnaires in KLIK, how often do you do this? *When: usually, sometimes, almost never and never, then:* 4a. What is the reason that you do not always complete the questionnaires in KLIK? *Open answer*	❑Always	❑Usually	❑Sometimes	❑Almost never	❑Never
5.	I spend on average … minutes on completing the KLIK questionnaires					
5a.	Are you satisfied with the completion time? Explanation:	❑Yes, I am satisfied	❑No, it is too long	❑No, it is too short		

Discussing PROMs with the clinician					
6. How often is the KLIK ePROfile (completed questionnaires on the KLIK website) discussed with you during the consultation by the clinician? Explanation: *When usually, sometimes, almost never and never, then:*	❑Always	❑Usually	❑Sometimes	❑Almost never	❑Never
6a. I dare to start the discussion about the questionnaires myself if the clinician does not discuss them Explanation:	❑ Strongly disagree	❑Disagree	❑Neither disagree nor agree	❑Agree	❑ Strongly agree

Influence of KLIK on the (preparation of the) consultation	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
7. KLIK is of added value for the conversation with the clinician Explanation:	❑	❑	❑	❑	❑
8. By using KLIK more and/or different topics (e.g., feelings) are discussed with the clinician Explanation:	❑	❑	❑	❑	❑
9. KLIK provides structure to the conversation with the clinician Explanation:	❑	❑	❑	❑	❑
10. By completing the questionnaires in KLIK I know better how I am doing Explanation:	❑	❑	❑	❑	❑

11. Completing the questionnaires in KLIK helps me in preparing for the consultation Explanation:	❑	❑	❑	❑	❑
12. KLIK helps in detecting problems earlier Explanation:	❑	❑	❑	❑	❑

13. Advantages of KLIK are:
Open answer

14. Disadvantages of KLIK are:
Open answer

Usability of the KLIK PROM portal	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
15. The KLIK PROM portal is easy to use Explanation:	❑	❑	❑		
16. KLIK has an attractive lay-out Explanation:	❑	❑	❑	❑	❑

Content of PROMs	Strongly disagree	Disagree	Neither disagree nor agree	Agree	Strongly agree
17. I am satisfied with the questionnaires I am asked to complete on the KLIK PROM portal Explanation: *When: strongly disagree, disagree, neither disagree, nor agree:*	❑	❑	❑	❑	❑
17a. Why are you not satisfied? *Open answer*					
18. The questions in the questionnaires apply to me Explanation:	❑	❑	❑	❑	❑

19. I understand the questions asked in the questionnaires Explanation:	❑	❑	❑	❑	❑
20. All topics that are important for me are covered in the questionnaires *When: strongly disagree, disagree, neither disagree, nor agree:*	❑	❑	❑	❑	❑

20a. Which topics do you miss?

Open answer

PART 2

Optimization of PROM use in clinical practice

CHAPTER 4

Pediatric patients report lower health-related quality of life in daily clinical practice compared to new normative PedsQL™ data

Maud M. van Muilekom, Michiel A. J. Luijten, Hedy A. van Oers, Thirsa Conijn, Heleen Maurice-Stam, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman, On behalf of the KLIK collaborator group

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Abstract

Aim

To compare Health-Related Quality of Life (HRQOL) of pediatric patients with newly collected HRQOL data of the general Dutch population, explore responses to individual items and investigate variables associated with HRQOL.

Methods

Children (8-12y) and adolescents (13-17y) from the general population (*N* = 966) and from a pediatric population (*N* = 1209) completed the Pediatric Quality of Life Inventory (PedsQL™) online via the KLIK Patient Reported Outcome Measures portal. PedsQL™ scale scores were compared between groups with independent *t* tests, by age group and gender. Responses to PedsQL™ items were explored using descriptive analyses. Linear regression analyses were performed to determine which variables were associated with HRQOL.

Results

Pediatric patients reported worse HRQOL than the general population on all PedsQL™ scales ($p \leq .001$, $d = 0.20\text{-}1.03$), except social functioning, and a high proportion reported problems on PedsQL™ items, for example, 'I have trouble sleeping'. Younger age, female gender and school absence were negatively associated with HRQOL ($\beta = -0.37\text{-}0.10$, $p \leq .008$).

Conclusions

Pediatric patients reported lower HRQOL than the general population, and school absence, female gender and younger age were associated with lower HRQOL. The results underline the importance to structurally monitor pediatric patients' HRQOL in clinical practice to detect problems and offer the right help on time.

Key words

Clinical practice, health-related quality of life, patient reported outcome measures, pediatric patients, Pediatric Quality of Life Inventory.

Key notes

- Pediatric patients with various chronic health conditions (*N* = 1209) who complete Patient Reported Outcome Measures (PROMs) in clinical practice, report remarkably lower Health-Related Quality of Life (HRQOL) compared to the general population (*N* = 966).
- School absence, female gender and younger age are associated with lower HRQOL.
- Paying attention to and monitoring HRQOL and psychosocial issues (by using PROMs) in clinical practice is thus important.

Introduction

Previous studies have shown that pediatric patients have more psychosocial problems and a lower Health-Related Quality of Life (HRQOL) than their healthy peers [1-4]. It is therefore important to pay attention to and monitor these outcomes in daily clinical practice [5, 6], for example by systematically using Patient Reported Outcome Measures (PROMs). PROMs are validated questionnaires, completed by patients, that measure any aspect of a patients' health status [7, 8].

A system that uses PROMs in daily clinical practice is the evidence-based KLIK PROM portal, implemented since 2011 after two effectiveness studies [9, 10]. With KLIK, pediatric patients and/or parents complete PROMs on the KLIK website (www.hetklikt.nu) at home before an outpatient visit. Answers are converted into an electronic PROfile (KLIK ePROfile) containing several ways of feedback [11], which is discussed during consultation. Currently, >1200 clinicians (e.g., pediatricians, nurses, psychologists) have been trained in using KLIK, and >18000 patients (from >60 different patient groups) in 30 different centers use KLIK [12, 13]. Of the over 300 PROMs available in KLIK, the Pediatric Quality of Life Inventory (PedsQL™)[14, 15] is the most often used PROM. The KLIK ePROfile provides feedback of the PedsQL™ to clinicians over time consisting of individual item and scale score feedback. For individual item feedback traffic light colors are applied to response categories (never/almost never a problem = green, sometimes a problem = orange, often/almost always a problem = red) to indicate possibly concerning responses and for scale score feedback a reference line of a healthy norm group is included (Figure 1)[11].

Using the PedsQL™ in KLIK for >9 years has resulted in a large amount of HRQOL data. As previous studies have mostly focused on comparing HRQOL of pediatric patients with one specific chronic health condition (CHC) to a healthy norm group [5, 16, 17], this large group of pediatric patients with various CHCs as a group compared to a general population can give an overall picture of HRQOL of pediatric patients. This overall picture of HRQOL of a large pediatric patient group with various CHCs was also requested by clinicians in our yearly KLIK evaluation and recent focus groups (e.g., to use as comparative data for rare diseases). Furthermore, this study can provide us with more information on which HRQOL domains pediatric patients and the general population differ, as results from previous studies are inconclusive [4, 14]. Additionally, no previous studies looked at individual items of the PedsQL™, even though this might help explain the possible differences that are found on domain score level. As sociodemographic and school variables are also collected with KLIK, it is possible to investigate which variables are associated with HRQOL. Previous studies showed that older age and female gender [1, 18-20], non-western ethnicity [21], lower parental education [22], school absence [23] and repeating grades [24] were associated with lower HRQOL. This information may help to target and provide interventions to children and adolescents who are most at risk for HRQOL problems. Finally, since the currently used Dutch normative data in KLIK is outdated (collected in 2006-2007) and representativeness for the general population is not optimal as data were only collected in Amsterdam and surroundings [15], we collected new normative data for the present study. The aims of this study were to (A) compare HRQOL scale scores of pediatric patients with newly collected normative data of the general population, (B) explore the

responses (proportion of respondents reporting problems) to individual HRQOL items for pediatric patients and the general population, and (C) investigate which sociodemographic and school variables are associated with HRQOL.

1a

1b

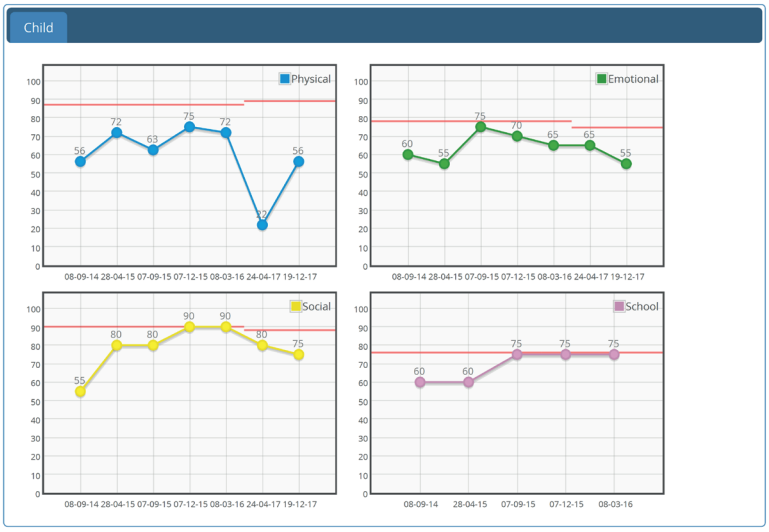

Figure 1. Feedback over time of the PedsQL™ in the KLIK ePROfile: (1a) individual items in traffic light colors, (1b) scale scores including a healthy reference line

Methods

Participants and procedures

General population

Dutch norm data for the PedsQL™ 4.0 for children and adolescents aged 8-17 years in the general population were collected online by research agency TNS NIPO operating under the name of 'Kantar Public ©' between February and April 2018. The Kantar panel consists of families living across the Netherlands that provided informed consent to be approached through e-mail for completing PROMs for a small financial compensation. To obtain at least 1000 respondents, a stratified sample of 2385 children and adolescents was drawn from the Kantar panel. A two-step stratified random sampling technique was used to ensure that the sample was representative (with a maximum deviation of 2.5% of the distribution in the Dutch population, based on the Gold Standard 2017 - Statistics Netherlands, www.cbs.nl/en-gb) on key demographics: sex, ethnicity, social class and educational level. Children and adolescents had to be fluent in Dutch (assessed by Kantar). E-mails were sent to the parents of 2385 children with a login code that granted access to the KLIK research website. After logging in, parents (child 8-15 years) and adolescents (12-17 years) provided informed consent. Thereafter, they were asked to complete their questionnaires (parents - sociodemographic questionnaire, children/adolescents - PedsQL™ 4.0 and school questions) independently.

CHC group

For the CHC group, PedsQL™ data of pediatric patients (8-17 years) using KLIK for clinical purposes for their CHC on the outpatient clinic in the Emma Children's Hospital Amsterdam University Medical Centers (UMC) were used. Patients from the following condition groups were eligible: defecation disorders, oncology, rheumatology, endocrinology, IBD, sickle cell disease, haemophilia, cleft lip, nephrology, HIV, dermatology, craniofacial abnormalities, spherocytosis, cystic fibrosis, lysosomal storage disorders, intensive care follow-up, Marfan syndrome, spina bifida, home parenteral nutrition, feeding disorders and muscular disorders. During registration for KLIK, patients' (12-17 years) and parents' (child 8-15 years) informed consent (IC) was asked to use their data for scientific purposes. Pediatric patients with IC, fluent in Dutch (assessed by clinician), with one of the above mentioned CHCs, and who completed the PedsQL™ 4.0 between June 2011 and October 2017, were eligible for inclusion in the CHC group. The first assessment of HRQOL in KLIK was used to avoid effects that KLIK could have on HRQOL outcomes (as a result of discussing HRQOL issues regularly). Additionally, as the first assessment in KLIK happens in all stages of the disease, both patients recently diagnosed as well as patients with a long disease duration were included. When patients did not have access to a computer, there was a possibility to complete the PROMs on a computer at the outpatient clinic. Patients registered for KLIK who completed questionnaires for clinical purposes, but without IC for scientific research, were considered non-participants.

Mode of administration of the questionnaires was identical for both groups. Anonymity and data security were guaranteed by the websites, compliant with national standards, and information regarding these topics was available on the websites. Data collections were performed with approval of the medical ethics committee of the Amsterdam UMC, location AMC.

Measures

Sociodemographic questionnaire

Parents in both the general population as of pediatric patients using KLIK completed a similar sociodemographic questionnaire online, containing questions concerning the parent (age, country of birth, educational level) and the child (age, gender). Parental educational level was divided into three categories; low (primary education, lower vocational education, lower/middle general secondary education), intermediate (middle vocational education, higher secondary education, pre-university education), and high (higher vocational education, university). In addition, pediatric patients completed questions regarding the following school variables: educational level, grade repetition (no/yes), and school absence (in days) in the last three months. Pediatric patients' CHC type (initially reported by the clinician) was obtained from the KLIK website.

PedsQL™ 4.0

HRQOL was measured with the Dutch version of the generic PedsQL™ 4.0 [14, 15], (self-report [25]) for children (8-12 years) and adolescents (13-17 years). The PedsQL™ contains 23 items in four scales; physical health (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items). A psychosocial health score – combined score of the emotional, social, and school functioning subscales – and a total scale score can be computed. Items are scored on a 5-point Likert scale from 1 'Never a problem' to 5 'Almost always a problem', with a one-week recall period. Answers are transformed into a 0-100 scale, with a higher score representing a better HRQOL. Previous research has shown that reliability and validity of the PedsQL™ are good [14, 15].

Statistical analyses

Descriptive analyses were used to characterize the general population and CHC group. Baseline differences in gender and age between participants and non-participants within both groups and between participants in the general population and CHC group were analyzed for children (8-12 years) and adolescents (13-17 years), using χ^2 tests for dichotomous and categorical variables and independent *t* tests for continuous variables. Effect sizes (Cohen's d) were calculated. Since sample sizes were large in this study, parametric tests could be performed.

To assess reliability of the PedsQL™ versions (8-12 and 13-17 years) in the CHC and general population group, internal consistency estimates (Cronbach's α) were calculated. Estimates of 0.70 or greater were considered sufficient [26]. Thereafter, mean PedsQL™ scale scores and standard deviations were calculated by age group and gender (as gender differences were found within the general population and CHC group). To examine differences on the PedsQL™ scales between the CHC group and general population, independent *t* tests were performed by age group and gender. Effect sizes (Cohen's d) were calculated by dividing the difference in mean scale scores between the general population and the CHC group by the pooled SD. Effect sizes of 0.2 were considered small, 0.5 moderate, and 0.8 large [27]. For individual items, PedsQL™ answer categories were recoded binary (0; never, almost never, sometimes, 1; often, almost always), in

line with previous studies [17, 28]. Thereafter, descriptive analyses (percentages) were performed for each item to explore the proportion of respondents in the CHC group and general population reporting to experience 'often' or 'almost always' a problem on the concerning item. These analyses were also performed by age group and gender.

Finally, to investigate which factors regarding the child (age, gender, school absence, grade retention) and the parent (country of birth, education) are associated with HRQOL in the CHC group, multiple linear regression analyses were performed for each PedsQL™ subscale score. No variables had to be excluded due to multicollinearity (no correlations >0.80). Standardized regression coefficients (β) were reported, where coefficients of 0.1 were considered small, 0.3 moderate and 0.5 large for continuous variables. For binary-coded variables (e.g., gender) regression coefficients of 0.2 were considered small, 0.5 moderate and 0.8 large [29].

The Statistical Package for Social Sciences (SPSS) version 25.0 was used for all analyses.

Results

Sociodemographic characteristics

In Table 1 sociodemographic characteristics of participants and non-participants of the general population and CHC group are presented.

In the general population group, 966 children (8-12 years) and adolescents (13-17 years) participated (response rate = 40.5%). The sample was representative for the Dutch population (maximum deviation of 2.5% on key demographics). Baseline differences in age were found between participants and non-participants in the general population group: participating children (M age = 10.6) were older than non-participating children (M age = 10.2, $p \leq .001$, $d = -.28$) and participating adolescents (M age = 15.5) were older than non-participating adolescents (M age = 15.0, $p \leq .001$, $d = -.39$). No baseline differences in gender were found between participants and non-participants in the general population group.

The CHC group consisted of 1209 pediatric patients aged 8-17 years, under treatment at the Emma Children's Hospital (response rate = 70.2%). For children (8-12 years), the most often reported condition groups were defecation disorders (18.7%) and oncology (16.6%) and for adolescents (13-17 years) rheumatology (24.0%) and endocrinology (15.2%). Baseline differences in age were found between participants and non-participants in the CHC group: participating children (M age = 10.4) were younger than non-participating children (M age = 10.6, $p = .03$, $d = .16$) and participating adolescents (M age = 15.7) were older than non-participating adolescents (M age = 14.8, $p \leq .001$, $d = -.69$). No baseline differences in gender were found between participants and non-participants in the CHC group.

Finally, baseline differences in age were found between participants in the general population and CHC group: participating children were older in the general population group (M age = 10.6) compared to the CHC group (M age = 10.4, $p = .007$, $d = .17$) and participating adolescents were younger in the general population group (M age = 15.5) compared to the CHC group (M age = 15.7, $p = .013$, $d = -.15$). No baseline differences in gender were found between the general population group and CHC group.

Table 1. Sociodemographic characteristics of participants and non-participants of the general population and CHC group

		Participants						Non-participants					
		8-12 years			13-17 years			8-12 years			13-17 years		
GP group	**Child characteristics (N=966)**	***N***	***M***	***SD***	***N***	***M***	***SD***	***N***	***M***	***SD***	***N***	***M***	***SD***
	Age (years)	475	10.6[ce]	1.5	491	15.5[cf]	1.4	717	10.2	1.4	677	15.0	1.4
			%			**%**			**%**			**%**	
	Gender (female)	231	48.6		239	48.7		331	46.2		320	47.3	
	Parent characteristics	***N***	***M***	***SD***	***N***	***M***	***SD***						
	Age (years)	469	43.3	5.7	488	48.2	5.1						
			%			**%**							
	Country of birth	469			488								
	Netherlands	421	89.8		454	93.0							
	Other	48	10.2		34	7.0							
	Educational level[a]	469			488								
	Low	53	11.3		63	12.9							
	Intermediate	224	47.8		237	48.6							
	High	192	40.9		188	38.5							
CHC group	**Child characteristics (N=1209)**	***N***	***M***	***SD***	***N***	***M***	***SD***	***N***	***M***	***SD***	***N***	***M***	***SD***
	Age (years)	589	10.4[de]	1.4	620	15.7[cf]	1.4	274	10.6	1.5	238	14.8	1.1
			%			**%**			**%**			**%**	
	Gender (female)	269	45.7		330	53.2		128	46.7		125	52.5	
	Clinician-reported CHC[b]												
	Defecation disorders	110	18.7		39	6.3		38	13.9		22	9.2	
	Oncology	98	16.6		70	11.3		11	4.0		14	5.9	
	Rheumatology	83	14.1		149	24.0		52	19.0		61	25.6	
	Endocrinology	56	9.5		94	15.2		27	9.9		29	12.2	
	IBD	24	4.1		89	14.4		7	2.6		7	2.9	
	Sickle cell disease	10	1.7		20	3.2		55	20.1		33	13.9	
	Other	208	35.3		159	25.6		84	30.5		72	30.3	
	Parent characteristics	***N***	***M***	***SD***	***N***	***M***	***SD***						
	Age (years)	564	42.7	5.3	449	47.1	4.9						
			%			**%**							
	Country of birth	587			468								
	Netherlands	513	87.4		410	87.6							
	Other	74	12.6		58	12.4							
	Educational level[a]	578			468								
	Low	61	10.6		62	13.3							
	Intermediate	244	42.2		225	48.3							
	High	273	47.2		179	38.4							

Abbreviations: CHC, Chronic Health Condition; GP, General Population.

[a] Highest level completed: Low: primary education, lower vocational education, lower and middle general secondary education; Intermediate: middle vocational education, higher secondary education, pre-university education; High: higher vocational education, university.

[b] Only most common conditions groups (>10% in one of the age groups) are reported, other: hemophilia, cleft lip, nephrology, HIV, dermatology, craniofacial abnormalities, spherocytosis, cystic fibrosis, lysosomal storage disorders, Intensive Care follow-up, Marfan syndrome, spina bifida, home parenteral nutrition, feeding disorders and muscular disorders.

[c] Participants differed significantly from non-participants at $p \leq .001$, range $d = .28$-$.69$,

[d] Participants differed significantly from non-participants at $p = .03$, $d = .16$,

[e] GP differed significantly from CHC at $p = .007$, $d = .17$,

[f] GP differed significantly from CHC at $p = .013$, $d = .15$.

Reliability

All internal consistency estimates were sufficient. In the CHC group, Cronbach's alpha for the 8-12 version ranged from .70-.90 and for the 13-17 version from .75-.92. In the general population group, Cronbach's alpha ranged from .76-.91 for the 8-12 version and from .82-.93 for the 13-17 version.

PedsQL™ scale scores CHC group versus general population

In Table 2 the PedsQL™ scale scores of the general population and CHC group split by age group and gender are provided.

Children (8-12 years)

Children with CHCs reported significantly lower HRQOL on five out of six PedsQL™ scales than the general population ($p \leq .001$, range d=.40-.83). Boys and girls with CHCs reported significantly lower HRQOL on five out of six and six out of six PedsQL™ scales than boys and girls in the general population ($p \leq .003$, range d = .26-.98).

Adolescents (13-17 years)

Adolescents with CHCs reported significantly lower HRQOL on five out of six PedsQL™ scales than the general population ($p \leq .001$, range d = .20-.88). Boys and girls with CHCs reported significantly lower HRQOL on four out of six PedsQL™ scales than boys and girls in the general population ($p \leq .001$, range d = .28-1.03).

PedsQL™ item scores CHC group and general population

In Table 3 the proportion of respondents reporting problems on PedsQL™ items in the general population and CHC group split by age group and gender are provided.

Children (8-12 years)

The items 'I hurt or ache', 'I have low energy', and 'I have trouble sleeping' were the most reported problems by children with CHCs (15.8%-23.3%), especially by girls with CHCs (19.3%-25.7%). The items 'I worry about what will happen to me', 'I cannot do things that other kids my age can do' and 'I miss school to go to the doctor or hospital' were other often reported problems by children with CHCs (13.6%-13.8%). Children in the general population rated these items less often to be a problem (0.4%-7.2%).

Adolescents (13-17 years)

The items 'I have low energy', 'I hurt or ache', 'It is hard for me to run' and 'It is hard for me to do sports activity or exercise' were the most reported problems by adolescents with CHCs (19.7%-26%), especially by girls with CHCs (27.3%-33.6%). Additionally, the items 'I have trouble sleeping', 'I cannot do things that other teens my age can do', 'I forget things', and 'I miss school to go to the doctor or hospital' were other often reported problems by adolescents with CHCs in all three groups (14.8%-18.7%). Adolescents in the general population rated these items less often to be a problem (2%-10.4%).

Table 2. PedsQL™ mean scale scores of the general population versus CHC group by age group and gender

		GP group			CHC group			GP vs CHC	
	PedsQL™ scale	***N***	**M**	***SD***	***N***	**M**	***SD***	***p***	***d***
Age group 8-12	Total score	475	85.34	11.66	589	76.19	15.16	**.000**	.67
	Physical health	475	92.59	11.17	589	78.83[b]	19.94	**.000**	.83
	Psychosocial health	475	81.48[a]	13.84	589	74.78	15.41	**.000**	.45
	Emotional functioning	475	78.17	17.09	589	70.90	19.40	**.000**	.40
	Social functioning	475	83.49[a]	16.87	589	81.35	17.62	.044	.12
	School functioning	475	82.77[a]	15.44	589	72.09	18.28	**.000**	.63
Age group 8-12 female	Total score	231	86.75	11.11	269	75.18	15.14	**.000**	.87
	Physical health	231	92.52	11.64	269	76.21	19.99	**.000**	.98
	Psychosocial health	231	83.67	12.65	269	74.63	15.30	**.000**	.64
	Emotional functioning	231	79.13	16.61	269	68.94	19.79	**.000**	.55
	Social functioning	231	86.19	15.17	269	80.99	17.19	**.000**	.32
	School functioning	231	85.69	14.02	269	73.96	17.76	**.000**	.73
Age group 8-12 male	Total score	244	84.01	12.03	320	77.04	15.16	**.000**	.50
	Physical health	244	92.65	10.74	320	81.04	19.66	**.000**	.71
	Psychosocial health	244	79.40	14.60	320	74.91	15.53	**.001**	.30
	Emotional functioning	244	77.25	17.52	320	72.55	18.94	**.003**	.26
	Social functioning	244	80.94	18.01	320	81.66	17.98	.641	-.04
	School functioning	244	80.00	16.22	320	70.52	18.59	**.000**	.54
Age group 13-17	Total score	491	84.51[c]	13.49	620	74.99[d]	16.22	**.000**	.63
	Physical health	491	90.66[c]	13.35	620	73.62[d]	22.89	**.000**	.88
	Psychosocial health	491	81.24	15.48	620	75.72[d]	15.22	**.000**	.36
	Emotional functioning	491	80.37[c]	19.45	620	76.54[d]	19.25	**.001**	.20
	Social functioning	491	85.22	16.99	620	83.41[d]	16.87	.077	.11
	School functioning	491	78.12	17.76	620	67.20	19.17	**.000**	.59
Age group 13-17 female	Total score	239	82.74	14.67	330	71.10	16.73	**.000**	.73
	Physical health	239	88.51	14.92	330	67.64	23.44	**.000**	1.03
	Psychosocial health	239	79.67	16.63	330	72.94	16.08	**.000**	.41
	Emotional functioning	239	76.97	21.23	330	72.83	19.71	.017	.20
	Social functioning	239	83.31	17.99	330	80.50	17.90	.066	.16
	School functioning	239	78.72	17.74	330	65.48	20.15	**.000**	.69
Age group 13-17 male	Total score	252	86.19	12.05	290	79.42	14.42	**.000**	.51
	Physical health	252	92.70	11.33	290	80.43	20.24	**.000**	.73
	Psychosocial health	252	82.72	14.18	290	78.88	13.53	**.001**	.28
	Emotional functioning	252	83.59	17.03	290	80.76	17.84	.060	.16
	Social functioning	252	87.04	15.82	290	86.72	14.97	.809	.02
	School functioning	252	77.54	17.79	290	69.16	17.82	**.000**	.47

A higher score (0-100) indicates a better HRQOL. Differences at $p \leq .008$ are considered significant, Bonferroni corrected for multiple testing by dividing .05 by the amount of tests [6]. Significant *p*-values for the general population group versus the CHC group are shown in bold.

Abbreviations: CHC, Chronic Health Condition; *d,* effect size; GP, General Population.

[a] Females scored significantly higher than males within the age group 8-12 of the GP.

[b] Females scored significantly lower than males within the age group 8-12 of the CHC group.

[c] Females scored significantly lower than males within the age group 13-17 of the GP.

[d] Females scored significantly lower than males within the age group 13-17 of the CHC group.

Table 3. Proportion of children and adolescents reporting 'often a problem' or 'almost always a problem' on the PedsQL™ items in the general population and the CHC group by age group and gender

PedsQL™ scale	Items	8-12 years						13-17 years					
		Total		Female		Male		Total		Female		Male	
		GP *N* = 475	CHC *N* = 589	GP *N* = 231	CHC *N* = 269	GP *N* = 244	CHC *N* = 320	GP *N* = 491	CHC *N* = 620	GP *N* = 239	CHC *N* = 330	GP *N* = 252	CHC *N* = 290
		%	%	%	%	%	%	%	%	%	%	%	%
Physical health	It is hard for me to walk more than one block	0.8	5.9	1.3	7.4	0.4	4.7	0.6	7.3	0.4	7.9	0.8	6.6
	It is hard for me to run	1.7	11.7	2.2	12.6	1.2	10.9	4.5	22.4	6.3	30.9	2.8	12.8
	It is hard for me to do sports activity or exercise	1.9	12.6	2.2	13.8	1.6	11.6	3.5	19.7	5.0	27.3	2.0	11.0
	It is hard for me to lift something heavy	1.5	9.5	1.7	11.2	1.2	8.1	1.8	13.9	2.5	19.4	1.2	7.6
	It is hard for me to take a bath or shower by myself	1.9	5.9	2.2	4.5	1.6	7.2	1.4	3.4	1.3	3.3	1.6	3.4
	It is hard for me to do chores around the house	1.9	6.6	1.7	6.7	2.0	6.6	3.3	8.4	4.2	8.5	2.4	8.3
	I hurt or ache	5.1	19.4	5.6	25.7	4.5	14.1	5.1	23.1	7.1	30.9	3.2	14.1
	I have low energy	1.1	15.8	0.9	19.3	1.2	12.8	6.5	26.0	10.0	33.6	3.2	17.2
Emotional functioning	I feel afraid or scared	2.9	6.1	2.6	6.3	3.3	5.9	4.1	2.4	6.3	3.6	2.0	1.0
	I feel sad or blue	3.4	7.3	3.9	8.6	2.9	6.3	6.3	6.9	9.2	9.7	3.6	3.8
	I feel angry	5.1	10.5	2.2	8.9	7.8	11.9	4.3	6.0	5.9	6.1	2.8	5.9
	I have trouble sleeping	7.2	23.3	7.4	25.3	7.0	21.6	10.4	16.8	14.2	20.3	6.7	12.8
	I worry about what will happen to me	4.8	13.8	5.2	17.5	4.5	10.6	6.9	7.7	9.6	8.5	4.4	6.9
Social functioning	I have trouble getting along with other kids/teens	3.4	4.9	1.7	4.5	4.9	5.3	4.1	2.3	5.9	2.4	2.4	2.1
	Other kids/teens do not want to be my friend	7.4	4.9	6.5	4.8	8.2	5.0	5.5	2.4	7.9	2.4	3.2	2.4
	Other kids/teens tease me	2.7	4.4	2.2	4.5	3.3	4.4	1.8	1.1	2.1	1.2	1.6	1.0
	I cannot do things that other kids/teens my age can do	3.4	13.6	3.5	11.2	3.3	15.6	5.5	18.7	6.3	22.4	4.8	14.5
	It is hard for me to keep up when I play with other kids/It is hard for me to keep up with my peers	2.7	6.1	0.9	7.4	4.5	5.0	3.5	11.3	4.2	15.8	2.8	6.2
School functioning	It is hard to pay attention in class	6.7	13.1	4.8	10.0	8.6	15.6	9.8	12.4	10.9	13.9	8.7	10.7
	I forget things	6.1	12.9	3.9	9.7	8.2	15.6	10.2	17.9	9.6	20.6	10.7	14.8
	I have trouble keeping up with my schoolwork	7.2	12.6	4.3	8.2	9.8	16.3	10.0	15.2	8.8	15.5	11.1	14.8
	I miss school because of not feeling well	0.8	7.1	0.4	7.1	1.2	7.2	1.6	11.5	2.1	14.5	1.2	7.9
	I miss school to go to the doctor or hospital	0.4	13.8	0.4	14.5	0.4	13.1	2.0	14.8	3.8	16.1	0.4	13.4

Abbreviations: CHC, Chronic Health Condition; GP, General Population.

Variables associated with PedsQL™ scale scores within the CHC group 8-17 years

In Table 4 the regression analyses outcomes are presented regarding the variables associated with the PedsQL™ scales in the CHC group. Higher age was significantly associated with higher scores for psychosocial health, emotional functioning and social functioning (β-range: 0.12-0.20, $p \leq .001$). Being a boy was significantly associated with higher scale scores (β-range: 0.10-0.19, $p \leq .008$), except for school functioning. More school absence was significantly associated with lower scores on all scales (β-range: -0.37-0.20, $p \leq .001$). Grade retention was significantly associated with a lower score on school functioning (β = -0.09, $p \leq .008$).

Table 4. Standardized regression coefficients (β) of variables associated with PedsQL™ scales in the CHC group (N = 1209).

	Total score	Physical health	Psychosocial health	Emotional functioning	Social functioning	School functioning
Predictors	*β*	*β*	*β*	*β*	*β*	*β*
Age	0.05	-0.06	0.12[b]	0.22[b]	0.13[b]	-0.07
Gender (boy)	0.16[b]	0.19[b]	0.10[a]	0.15[b]	0.10[a]	0.00
Parental country of birth (foreign country)	0.04	0.04	0.04	0.05	-0.02	0.06
Parental education (high)	0.07	0.08	0.06	0.05	0.05	0.05
School absence	-0.37[b]	-0.37[b]	-0.31[b]	-0.22[b]	-0.20[b]	-0.35[b]
Grade retention (yes)	-0.05	-0.01	-0.08	-0.07	-0.04	-0.09[a]
R^2	.17	.19	.12	.11	.06	.15
F Test	27.14[b]	31.49[b]	17.93[b]	15.94[b]	8.67[b]	23.28[b]

Abbreviations: CHC, Chronic Health Condition; *F* test, Statistic of Multiple Linear Regression analysis; R^2, Explained variance.

[a]Differences at $p \leq .008$ are considered significant, Bonferroni corrected for multiple testing by dividing .05 by the amount of tests [6].

[b]Difference at $p \leq .001$.

Discussion

In this study, PedsQL™ data of pediatric patients with CHCs, collected with KLIK in clinical practice, was compared to newly collected normative PedsQL™ data of the general Dutch population. Pediatric patients reported worse HRQOL on nearly all PedsQL™ scales, especially on physical health, compared to the general population, with moderate to large effect sizes. Additionally, a high proportion of pediatric patients reported problems on the PedsQL™ items. School absence, younger age, and being a girl were negatively associated with the HRQOL scales, with small to moderate regression coefficients.

Our results regarding the lower PedsQL™ scores for the CHC group are in accordance with previous literature [1, 2, 4, 30]. In contrast with earlier studies [1, 4], no differences were found between the CHC group and general population on the social functioning scale. However, pediatric patients in our sample did report quite some problems on individual item

level for social functioning. Pediatric patients reported difficulties on items with a physical component (e.g., I cannot do things that other kids/teens my age can do). This implicates that pediatric patients perceive difficulty to participate in the same activities as their peers. Not many problems were reported on items regarding social acceptance (e.g., Other kids/teens do not want to be my friend), which matches the outcome of a large meta-analysis where no differences were found on the social acceptance scale as well [4]. It is known that social acceptance problems (e.g., being bullied) are more often reported by patients that have external visible CHCs like craniofacial disorders, osteogenesis imperfecta and spina bifida [19, 31]. Many of the CHCs in our heterogeneous sample were not visibly present, which might explain why not many problems were reported on these items. In contrast to the social functioning scale, this study showed differences on the emotional functioning scale, while previous studies did not report this difference [5, 15, 17]. When looking at the individual items of this scale, the difference might be explained by the higher proportion of pediatric patients reporting to have sleep and worrying problems. Another interesting finding was found in the regression analyses, where higher age was associated with better HRQOL. While this finding is in contrast with previous studies showing that higher age was associated with lower HRQOL in two general population groups [18, 20] and a chronic conditions group (gastrointestinal disorders) [1], a recent large meta-analysis in children with CHCs did not find an effect of age on HRQOL at all [19]. A possible explanation for the positive association found in the current study could be the differences in CHCs between the younger (e.g. defecation disorders and cancer) and older patients (e.g. rheumatology and endocrinology). However, the study by Pinquart [19] displayed that these particular patient groups show similar declines in HRQOL compared to the general population. It would be interesting to further investigate how the increase in HRQOL over age can be explained.

The results of this study however underline that HRQOL of pediatric patients is affected and that they need support in adapting to their CHC using a multidisciplinary approach. Clinicians should thus monitor and discuss HRQOL in clinical practice. One way to do this, is by using PROMs. From our experience with implementing PROMs in clinical practice and annual evaluation meetings with clinicians, we know that clinicians can be reluctant to ask pediatric patients to complete PROMs in clinical practice as they doubt if children will report problems. However, this study indicated that pediatric patients do report HRQOL problems when completing PROMs in clinical practice and this information can thus be used during a doctor's visit. Discussion of both HRQOL scales and items is suggested as problems were reported on both levels. Clinicians can use the individual items as a conversation tool, as items provide concrete examples about which the clinician can ask questions. In addition, clinicians should be informed that patients with female gender, younger age, and more school absence might be more vulnerable for having HRQOL problems. This might help clinicians in judging which patients need extra attention.

Some limitations to this study should be mentioned. First, differences in age were found between several groups. However, these differences were very small and analyses were therefore conducted in two age groups. Second, the representativeness of the CHC group cannot be guaranteed (e.g. due to regional data collection and disproportionate distribution of CHCs) and information about non-participants with a CHC was lacking

because only patients who completed questionnaires on the KLIK website and gave permission to use their data for scientific purposes were included. Third, an online, unsupervised data collection method was used for both the general population and CHC group, by which we cannot guarantee that children and adolescents completed the questionnaires themselves. Fourth, the data collections were performed on different time scales, namely six years (in all four seasons) for the CHC group and three months (in Spring only) for the general population. Therefore, it could be that seasonal variations in HRQOL might partly account for the lower HRQOL scores that were found in the CHC group [32]. Fifth, only a limited number of variables was included in the regression model, even though previous research showed that factors like pain [5], fatigue [33] and disease duration [19] are also associated with HRQOL. Additionally, in the regression analyses some variables might have been prone to bias when reported by the child. For example, school absence (days missed) is a variable that children may not keep track of. Finally, no analyses could be performed on disease-specific functioning of patient groups, as the sample sizes of individual CHC subgroups were too small.

Clinical implications

As a result of this study, new normative data have become available. We therefore updated the KLIK ePROfile (Figure 2) by replacing the reference line based on outdated HRQOL data of the healthy Dutch population by the reference line based on the newly collected PedsQL™ data of the general population, and by adding a reference line representing the PedsQL™ scale scores of the CHC group to the graphs. Gender (and age)-specific reference lines are shown, since differences in HRQOL scores were found between boys and girls. Finally, information about school absence (days missed) was added as this factor was negatively associated with HRQOL outcomes. In line with these updates, the KLIK training for clinicians was updated with information on which PedsQL™ scales and items most problems are reported and which factors are associated with HRQOL. This may help clinicians in discussing a HRQOL PROM during the consultation.

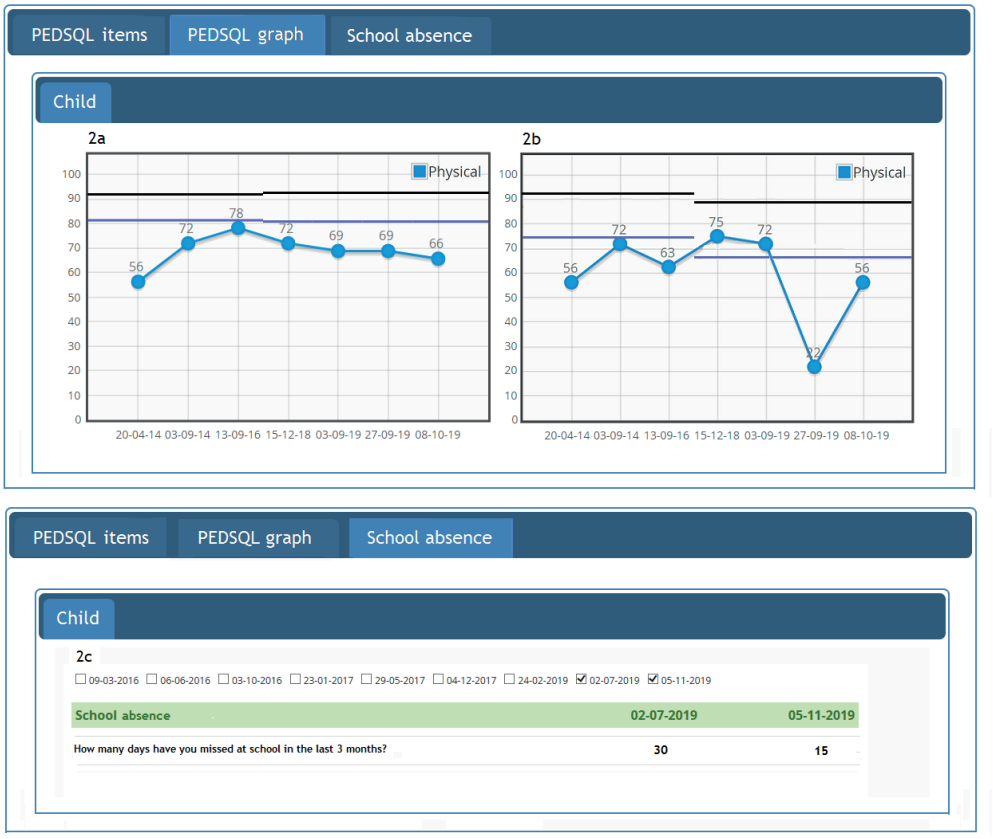

Figure 2. Updated feedback of the PedsQL™ over time in the KLIK ePROfile by providing reference lines of the general population (upper line) and CHC group (lower line) for boys (2a) and girls (2b) separately and per age group (shown by shift of reference line) and information about school absence of the patient (2c).

Conclusions

This study showed that pediatric patients, who complete PROMs in daily clinical practice, experience more difficulties than the general population in HRQOL. School absence, female gender and younger age were negatively associated with HRQOL. It is therefore important to structurally monitor HRQOL by using and discussing PROMs in daily clinical practice (e.g., by using the updated KLIK PROM portal) and to take into account the associated factors, to detect problems and offer the right help on time.

Abbreviations

CHC – Chronic Health Condition
HRQOL – Health-Related Quality of Life
IC – Informed Consent
PedsQL™ – Pediatric Quality of Life Inventory
PROM – Patient Reported Outcome Measure

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Conflicts of interest

All authors have no financial or other conflicts of interest to disclose.

Data availability statement

Data are available upon reasonable request.

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CHAPTER 5

Psychometric properties of the Patient-Reported Outcomes Measurement Information System (PROMIS®) pediatric Anger scale in the Dutch general population

Maud M. van Muilekom, Michiel A. J. Luijten, Raphaele R. L. van Litsenburg, Martha A. Grootenhuis, Caroline B. Terwee, Lotte Haverman

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Abstract

This study aimed to validate the PROMIS® pediatric v2.0 Anger scale in the Dutch general population, provide reference data, and compare reliability and relative efficiency between the full-length scale, its short-form, computerized adaptive test (CAT) and Pediatric Quality of Life Inventory (PedsQL™) emotional functioning (EF) subscale scores. Children (*N* = 1,328), representative of the Dutch population, were asked to complete the PROMIS pediatric Anger scale (8-18 years) and PedsQL™ (8-17 years). A graded response model (GRM) was fit to the data. Structural validity was assessed by checking item-fit statistics (S-X^2, $p < .001$ = misfit). For construct validity, a moderate correlation (Pearson's $r > 0.50$) was expected between the Anger scale and PedsQL™ EF subscale score. Dutch mean *T* score based on the U.S. model was calculated to provide reference data and cut-offs. Standard error of measurement (*SE*(θ)) was used to assess reliability (*SE*(θ) < .32 = .90 reliability). Relative efficiency was calculated (1 - $SE(\theta)^2$)/*N* items) to compare how good the measures performed relative to the amount of items administered. In total, 527 children completed the PROMIS pediatric Anger scale, of which 482 completed the PedsQL™. Structural validity was sufficient as no items displayed misfit (S-X^2 = 22.9-40.3, $p > .001$). The Anger scale score correlated moderately (Pearson's $r = .64$) with the PedsQL™ EF subscale score. Dutch mean T-score was 44.20 (SD = 11.39), with cut-offs of >52.2 for moderate and ≥62.3 for severe symptoms. Reliable measurements were obtained at the population mean and >2SD in the clinically relevant direction. CAT outperformed all other measures in efficiency. The PROMIS pediatric Anger scale displayed sufficient psychometric properties within the Dutch population and reference data are available.

Key words
Validity, reliability, computerized adaptive testing, item response theory, aggression.

Public Significance Statements
This study provides evidence that the PROMIS pediatric Anger scale has good psychometric properties in the Dutch general population. This scale can thus be implemented in clinical practice and for pediatric research in the Netherlands to solve the problem that validated Patient Reported Outcome Measures (PROMs) assessing anger in a pediatric population are missing, improve interpretability and comparison of scores and reduce the burden of completing PROMs for pediatric patients.

Introduction

Patient Reported Outcome Measures (PROMs) are increasingly used in pediatric clinical practice, to monitor physical, mental and social health outcomes, include the patient's voice, and facilitate shared decision-making and patient-centered care [1, 2]. Although completion of PROMs before the outpatient consultation and subsequent discussion of outcomes with the clinician has been shown beneficial in enhancing patient-clinician communication, increasing patient satisfaction and improving patient outcomes [3, 4], implementation of PROMs in this setting remains challenging. For example, currently used PROMs are often considered burdensome due to questionnaire length and irrelevance and repetitiveness of questions [5, 6]. Additionally, content and scoring methods differ between PROMs measuring the same domains of functioning. As a consequence, when patients have multiple chronic conditions and thus complete different PROMs for multiple diseases (which is extra burdensome for patients), domain scores are often incomparable between PROMs and there is question of unstandardized interpretation of scores [7]. Finally, psychometric properties are often not documented or disappointing and some domains such as anger, are not covered by existing validated pediatric PROMs, resulting in difficulties for clinicians to choose the best PROM for a specific purpose.

The Patient-Reported Outcomes Measurement Information System (PROMIS®) item banks offer an opportunity to address these challenges. These measures were developed for children and adults, measuring generic, relevant domains of physical, mental and social health [8]. PROMIS item banks consist of a large selection of items that measure the same domain (e.g., anger) across a wide range of functioning, and were developed with item response theory (IRT) [9]. With IRT modeling, item difficulty and discriminative ability are taken into account when calculating domain *T* scores and items and persons can be scaled onto a single metric, which improves the interpretability and comparison of scores. Due to the ordering of items by their difficulty and discriminative ability, short-forms can be developed and computerized adaptive testing (CAT) is enabled. CATs select items based on responses to previously completed items by a patient, while taking into account the level of functioning of a patient, resulting in a reduction of questionnaire length and selection of more relevant questions [9, 10].

To use the PROMIS pediatric measures in the Netherlands, the Dutch-Flemish PROMIS national center translated the pediatric item banks (v1.0 and v2.0) into Dutch-Flemish [11] and validated them in a Dutch clinical sample [12]. However, the PROMIS pediatric measures need to be validated in the Dutch general population as well. Therefore, this study aims to assess validity, reliability and relative efficiency of one of the Dutch-Flemish PROMIS pediatric measures, the v2.0 Anger scale, in the Dutch general population, and to obtain reference data and cut-off values for minimal, moderate, and severe anger. If the psychometric properties of the PROMIS pediatric Anger scale are sufficient, this measure can be implemented for use in clinical practice, solving the problem that currently validated PROMs assessing anger in a pediatric population are missing.

Methods

Procedure and participants

Between December 2017 and April 2018, children (8-18 years, *N* = 1,328), representative of the Dutch population on key demographics, were asked to complete the PROMIS pediatric Anger scale and the Pediatric Quality of Life Inventory (PedsQL™) as part of a larger study by marketing agency Kantar Public. Eighteen-year olds did not complete the PedsQL™. After receiving an invitation email with a link to the study website (onderzoek.hetklikt.nu/promis), participants could log in and complete the questionnaires. Parents (of children aged 8-15 years) and adolescents (aged ≥12 years) provided informed consent. See Luijten et al. (2021) for the full data collection procedure [13]. This study was approved by the Medical Ethics Committee of the Amsterdam UMC, location AMC.

Measures

Sociodemographic questionnaire

Parents completed a sociodemographic questionnaire with questions about their child (age, gender, country of birth) and themselves (age, gender, and educational level).

PROMIS pediatric Anger 9a v2.0 scale

The PROMIS pediatric Anger v2.0 scale [14] is a 9-item measure that assesses self-reported angry mood, negative social cognitions, and efforts to control anger in children aged 8-18 years. Participants respond to statements (e.g., "I felt mad") with response options ranging from 1 ("*Never*") to 5 ("*Always*"), with a 1-week recall period. A short-form version (v2.0 – Anger 5a), containing 5 items, also exists, whereof for this study the responses were extracted from the completed full-length scale. Total scores of the full-length scale and short-form were calculated by applying the U.S. IRT model to the data and estimating the level of anger (theta; θ; based on [14]). The theta was transformed into a *T* score, where 50 is the mean (with *SD* of 10) of the U.S. calibration sample (combination of general population and clinical sample). A higher score represents more anger.

Pediatric Quality of Life Inventory™ (4.0)

The PedsQL™ is a generic questionnaire that measures self-reported Health-Related Quality of Life (HRQOL) of children aged 8-18 years [15, 16]. It contains 23 items in four HRQOL subscales; physical health (N_{items} = 8), emotional functioning (N_{items} = 5), social functioning (N_{items} = 5) and school functioning (N_{items} = 5). Items are scored from 1 "*Never a problem*" to 5 "*Almost always a problem*", with a 1-week recall period. Item scores are transformed into a 0-100 scale, where higher scores represent a better HRQOL. Previous research has shown that reliability and validity of the PedsQL™ scores is good in the Netherlands [16, 17].

Statistical analyses

To describe the sociodemographic characteristics of participating children, descriptive analyses were performed using the Statistical Package for Social Sciences (SPSS) version 26.0. All further analyses were performed in R.

First, a graded response model (GRM; an IRT model for items with ordinal response categories) was fitted, requiring that several assumptions are met: unidimensionality, local independence and monotonicity. *Unidimensionality* was assessed by performing a confirmatory factor analyses (CFA) with weighted least square mean- and variance-adjusted (WLSMV) estimator, using the R-package "Lavaan (v0.6-3)" [18]. An acceptable CFA fit was represented by a Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI) value of >0.95, a standardized root mean square residual (SRMR) value <0.10, and a root mean square error of approximation (RMSEA) value <0.08 [19]. By looking at the residual correlations, *local independence* was assessed, where item pairs were considered locally independent with a residual correlation <0.20 [20]. Finally, *monotonicity* was assessed by Mokken scaling [20-22], where the assumption was considered met when item *H* values of all items were ≥0.30 and the *H* value of the entire scale was ≥0.50.

When all GRM assumptions were met, a GRM was fitted to the data to estimate discrimination (α) and threshold (β) parameters, using the Expectation-Maximization (EM) algorithm within the R-package "mirt (v1.29)" [23]. The α parameter indicates the ability of an item to distinguish between participants with a different level of anger (θ) and the β parameters represent the required level of anger of a person to select a higher response category over a lower one. To assess structural validity, item fit was determined by using the S-X^2 statistic, where a *p*-value of <.001 for an item is considered as item misfit, based on PROMIS convention [20].

To assess construct validity, the PROMIS Anger *T* score, based on U.S. parameters, was correlated with the PedsQL™ subscale scores using Pearson's *r* for continuous variables. A moderate correlation (Pearson's *r*: 0.50 to 0.70) was expected between *T* scores and the PedsQL™ emotional functioning subscale score and lower correlations (Δr > 0.10, Pearson's *r* < 0.50; tested for significance) for the other PedsQL™ subscale scores [24]. Construct validity was considered sufficient if 75% of the hypotheses were met [13]. Dutch mean *T* score (with one decimal value based on the scoring manual on healthmeasures.net) of the PROMIS pediatric Anger scale was calculated based on the U.S. model to provide reference data. Cut-offs were determined by examining the *T* score percentiles (minimal: ≤74th percentile, moderate: 75-94th percentile, and severe: ≥95th percentile) in accordance with PROMIS conventions [25].

To investigate reliability of the PROMIS Anger full-length scale and short-form scores, θ estimates and *SE*(θ) were calculated using the Expected A Posteriori (EAP) estimator, where a *SE*(θ) score of 0.32 or lower was considered a reliable measurement (corresponding to a reliability of 0.90 or higher, based on formula $SE(\theta) = S\sqrt{1 - r_{xx}}$ [26]). Post hoc CAT simulations were performed with the R-package "catR (v3.16)" [27] to assess how a CAT would function when Dutch model parameters are applied, using maximum posterior weighted information (MPWI) selection criterion and EAP estimator [28]. The stopping rule for the CAT was an *SE*(θ) <0.32 [26]. Thereafter, reliability of scores was compared between the full-length scale, short-form, CAT and the PedsQL™ emotional functioning subscale, by fitting a GRM model based on Dutch parameters to the PedsQL™ data and calculating and presenting the θ estimates and *SE*(θ) in a reliability plot. In addition, percentage of participants reliably measured (*SE*(θ) <0.32) was calculated for the PROMIS measures and the PedsQL™ emotional functioning subscale. Finally,

relative efficiency was calculated ($1\text{-}SE(\theta)^2/N_{items}$) for each measure (full-length scale, short-form, CAT and PedsQL™ emotional functioning) and subsequently compared to the other measures by dividing the mean efficiency of one measure by the other.

Results

In total, 527 children (response rate of 39.7%), representative of the Dutch general population on key demographics (described in; [13]), completed the PROMIS Anger scale of which 482 children (aged 8-17 years) also completed the PedsQL™ 4.0. Sociodemographic characteristics of the sample are presented in Table 1.

Table 1. Sociodemographic characteristics of the PROMIS Anger scale sample for the main analyses and the relative efficiency analysis

Sociodemographics	Main analysis sample (*N* = 527)	Relative efficiency analysis (*N* = 482)*
	***M* (*SD*)**	***M* (*SD*)**
Age (years)	13.6 (3.1)	13.1 (2.8)
	%	**%**
Gender (female)	48.4	48.7
Country of birth		
Netherlands	82.7	83.2
Western country	12.2	12.0
Non-western country	5.1	4.8
Educational level (parent)**		
Low	13.7	13.3
Intermediate	48.4	47.4
High	37.9	39.3

Note: * = Used for calculating relative efficiency between the PROMIS full-length scale, short-form, CAT and the PedsQL™ emotional functioning subscale. Eighteen-year olds did not complete the PedsQL™. ** = Highest level completed: Low: primary education, lower vocational education, lower and middle general secondary education; Intermediate: middle vocational education, higher secondary education, preuniversity education; High: higher vocational education, university.

All assumptions for fitting a GRM were met. Unidimensionality was satisfied by the CFA (CFI = 0.99, TLI = 0.99, SRMR = 0.03, RMSEA = 0.06), all items showed to be locally independent and the entire scale displayed sufficient monotonicity (H_{scale} = 0.71). Structural validity was sufficient as no items displayed misfit (S-X^2 range = 22.88-40.31, *p* value >.001).

The *T* score of the Anger scale had a moderate correlation (Pearson's *r* = -0.65) with the PedsQL™ emotional functioning subscale sum score, indicating sufficient construct validity. Correlations with the PedsQL™ physical, social and school functioning subscale sum scores were significantly lower, namely -0.37, -0.49, and -0.45, respectively, *p* values <.001. All hypotheses regarding construct validity were met. Dutch mean *T* score was 44.2 (*SD* = 11.4). No/minimal symptoms were represented by a *T* score ≤52.1, moderate symptoms by *T* scores ranging from 52.2 to 62.2 and severe symptoms by a *T* score ≥62.3, corresponding respectively to the ≤74th, 75-94th and ≥95th percentile of *T* scores in the Dutch general population.

The model based on Dutch parameters (range α = 2.4–4.6, range $B_{1\text{-}min}$–$B_{4\text{-}max}$ = -0.6–3.0) provided reliable measurements at the sample mean (θ = 0) and more than

two *SD* in the clinically relevant direction. All PROMIS Anger measures scores had higher reliability in comparison with the PedsQL™ emotional functioning subscale score (Figure 1). A majority of the participants were reliably estimated by the full-length scale (72.1%), short-form (64.5%) and post-hoc CATs (72.1%, see Table 2). For the PedsQL™ emotional functioning subscale 42.7% was reliably measured. Finally, the post hoc CAT outperformed the PROMIS full-length scale, short-form and PedsQL emotional functioning subscale in relative efficiency (Table 3).

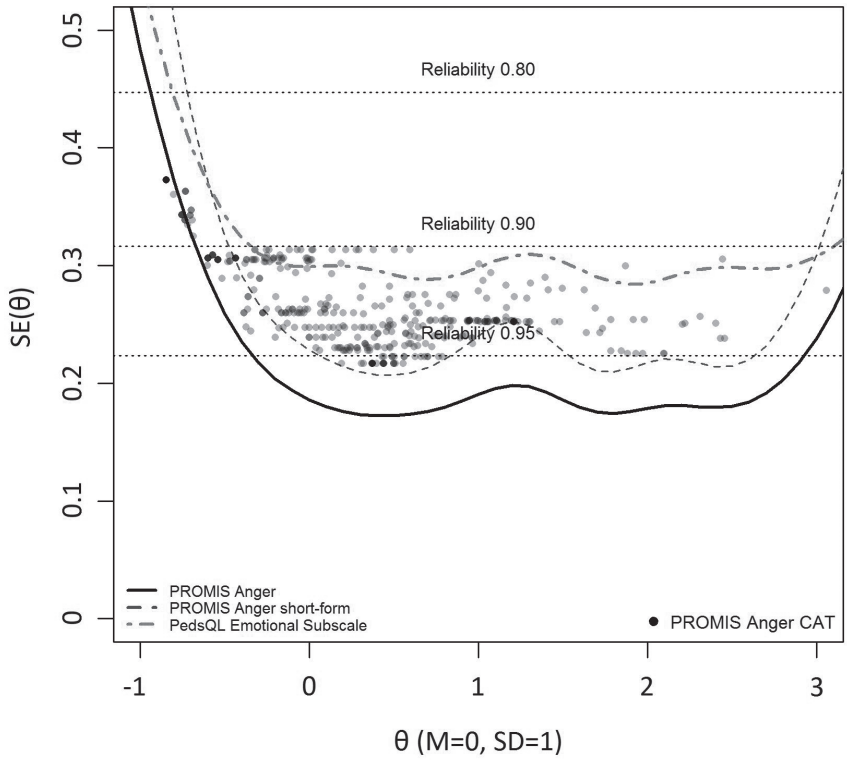

Figure 1. Standard error of measurement (*SE*(θ)) of the full-length scale, short-form and CAT of the PROMIS Anger scale and the PedsQL™ emotional functioning subscale, using the Dutch model parameters.

Table 2. Reliability of measurements and amount of items administered for the PROMIS pediatric Anger full-length scale, short-form and computerized adaptive test and the PedsQL™ Emotional functioning subscale in the Dutch general population (*N* = 527).

Measure Characteristics	PROMIS Anger FL	PROMIS Anger SF	PROMIS Anger CAT	PedsQL™ EF**
M SE(θ)	0.286	0.352	0.327	0.377
SE(θ) <0.32 %*	72.1	64.5	72.1	42.7
(*M*) amount of items	9	5	5.5	5

Note: * = Percentage of participants that were measured reliably (<0.32 *SE*(θ)). *SE*(θ): standard error of measurement. ** = Based on *N* = 482. FL = full-length scale. SF = short-form. CAT = computerized adaptive test. EF = emotional functioning.

Table 3. Relative efficiency of the PROMIS pediatric Anger full-length scale, short-form, and CAT compared to the emotional functioning subscale of the PedsQL™ (*N* = 527*).*

Measure	PedsQL™ Emotional Functioning	PROMIS Anger full-length scale	PROMIS Anger short-form
PROMIS Anger full-length scale	1.35*	-	-
PROMIS Anger short-form	1.49*	1.11	-
PROMIS Anger CAT	1.75*	1.28	1.16

Note: * = Based on *N* = 482. A relative efficiency ratio > 1 indicates that the row has a higher efficiency than the column.

Discussion

This study investigated the psychometric properties of the PROMIS pediatric v2.0 Anger scale in a representative general population sample and obtained reference data and cut-off values for minimal, mild, and severe anger. The Anger scale performed very well in the Dutch general population. Structural validity was sufficient as no items displayed misfit and construct validity was also sufficient as the scale score correlated moderately with the PedsQL™ emotional functioning subscale score. Additionally, results showed that the scale provides reliable measurements at the Dutch population mean and more than two *SD* in the clinically relevant direction. Finally, the CAT administration of the PROMIS Anger scale outperforms the other measures in relative efficiency.

Findings in this study were in accordance with results of the development study of the PROMIS pediatric Anger scale in the U.S [14]. Similar unidimensionality and item-fit values and model parameters were found. Additionally, regarding the mean *T* score, Dutch children scored on average lower on Anger compared to the U.S. calibration population. However, the calibration sample consisted of clinical and general population participants. Recent research in the U.S. general population has also shown lower median *T* scores on Anger than the U.S. calibration sample [25]. Furthermore, results found in this study were also similar to the results of the validation study of the Anger scale v1.0 in a Dutch clinical sample [12], where sufficient unidimensionality, structural validity, construct validity and reliability were found for the PROMIS pediatric Anger scale scores as well.

Interestingly, it was found in this study that the CAT administration of the Anger scale was most efficient, although currently no CAT version is available for the Anger scale [29]. This study provides evidence that even with a scale that has only nine items (and the short-form only five), CAT administration is more efficient (on average 5.5 items

necessary for a more reliable score), indicating that it is possible to make the Anger scale available as CAT.

There are some limitations to this study that should be taken into account. First, although reliability of the PROMIS pediatric Anger scale score was sufficient, still a substantial percentage of participants (27.9%) was not reliably measured. This could be due to the large group of participants (20.1%) with no anger symptoms that reported "never" to all items of the scale, resulting in no variance in responses and thus in a floor effect. However, having precise measurements in the clinical range is more important than the measurement precision at a healthy level of functioning. As the participants were from a general population sample this floor effect can be expected. A recently published study showed a similar floor effect (16%) in the U.S. general population for the PROMIS pediatric Anger scale [25]. To reduce this floor effect, the scale might require more "easy" items at the low-end of the scale to reliably measure these participants.

A second limitation concerns the use of the emotional functioning subscale of the PedsQL™ for the assessment of construct validity. This subscale contains only one question about anger and might thus not represent the anger domain accurately. However, the PedsQL™ was considered most suitable as there are currently no other appropriate PROMs available that accurately measure anger in a pediatric population. This was among the reasons why the American Psychiatric Association (APA) selected this PROMIS measure to be used as the standard level-2 assessment for monitoring and evaluating disorders diagnosed with the Diagnostic and Statistical Manual of Mental Disorders (DSM-V).

Third, as an online, unsupervised data collection method was used, it cannot be guaranteed that children and adolescents completed the questionnaires without help of their parents.

In conclusion, this study provides evidence that the PROMIS pediatric Anger scale has good psychometric properties in the Dutch general population. This PROMIS scale can thus be implemented in clinical practice and for pediatric research in the Netherlands in its full-length, short-form or CAT (when available) through the Dutch-Flemish Assessment Center (www.dutchflemishpromis.nl) to improve interpretability and comparison of scores and reduce the burden of completing PROMs for pediatric patients.

Author Note

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Compliance with APA ethical principles

I certify that we have complied with the APA ethical principles regarding research with human participants and/or care and use of animals in the conduct of the research presented in this manuscript.

Ethics approval

All procedures performed in this study were in accordance with the ethical standards of the international and/or national research committee (Medical Ethics Committee of the Amsterdam UMC, location AMC – reference number W20_136 # 20.175) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all individual participants and/or legal guardians included in this study.

Consent for publication

Not applicable.

Availability of data

Data are available upon reasonable request.

Code availability

Code is available upon reasonable request.

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CHAPTER 6

The impact of lockdown during the COVID-19 pandemic on mental and social health of children and adolescents

Maud M. van Muilekom*, Michiel A. J. Luijten*, Lorynn Teela, Tinca J. C. Polderman, Caroline B. Terwee, Josjan Zijlmans, Leonie Klaufus, Arne Popma, Kim J. Oostrom, Hedy A. van Oers, Lotte Haverman

*Authors contributed equally to the manuscript

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Abstract

Purpose

During the COVID-19 pandemic in the Netherlands, governmental regulations resulted in a lockdown for adults as well as children/adolescents. Schools were closed and contact with other people was limited. In this cross-sectional, population-based study, we aimed to investigate the mental/social health of children/adolescents during COVID-19 lockdown.

Methods

Two representative samples of Dutch children/adolescents (8-18 years) before COVID-19 (2018, *N* = 2401) and during lockdown (April 2020, *N* = 844) were compared on the Patient-Reported Outcomes Measurement Information System (PROMIS) domains: Global Health, Peer Relationships, Anxiety, Depressive Symptoms, Anger, Sleep-Related Impairment by linear mixed models and calculating relative risks (RR (95% CI)) for the proportion of severe scores. Variables associated with worse mental/social health during COVID-19 were explored through multivariable regression models. The impact of COVID-19 regulations on the daily life of children was qualitatively analyzed.

Results

Participants reported worse PROMIS *T*-scores on all domains during COVID-19 lockdown compared to before (absolute mean difference range 2.1–7.1 (95% CI 1.3-7.9). During lockdown more children reported severe Anxiety (RR = 1.95 (1.55–2.46) and Sleep-Related Impairment (RR = 1.89 (1.29–2.78) and fewer children reported poor Global Health (RR = 0.36 (0.20–0.65)). Associated factors with worse mental/social health were single-parent family, ≥ three children in the family, negative change in work situation of parents due to COVID-19 regulations, and a relative/friend infected with COVID-19. A large majority (> 90%) reported a negative impact of the COVID-19 regulations on daily life.

Conclusion

This study showed that governmental regulations regarding lockdown pose a serious mental/social health threat on children/adolescents that should be brought to the forefront of political decision making and mental healthcare policy, intervention and prevention.

Introduction

The COVID-19 pandemic has an enormous impact on society as a whole, and on children and adolescents in particular. Although children and adolescents are less affected by morbidity and mortality [1], the restrictions imposed by governments worldwide profoundly impact their daily life, including their mental and social health [2].

In the Netherlands, the first COVID-19 patient was identified on February 27th 2020 and restrictions were imposed by the government starting on March 12th 2020. People were asked to stay inside and work from home as much as possible, to comply to social distancing (1.5 m), and all large events were canceled. On March 15th, a 'partial' lockdown was implemented (www.government.nl/topics/coronavirus-covid-19). All schools and child care facilities were closed (except for children whose parents had an occupation classified as essential), as well as sports and leisure facilities, bars, and restaurants. However, children were still allowed to play outside, and visitors up to three persons were permitted at home. On May 11th primary schools were partially reopened and on June 2nd secondary schools followed.

During the lockdown, children and adolescents were experiencing physical isolation from their classmates, friends, teachers, and other important adults (e.g., grandparents). This might not only result in feelings of loneliness, but could potentially lead to precarious situations for children from unsafe domestic situations, due to a lack of escape possibilities. In addition, children and adolescents may experience mental health problems due to the COVID-19 pandemic itself, such as increased anxiety, as they might fear that they or their loved ones will get infected or they might worry about the future of the world.

Several cross-sectional and longitudinal studies on the effects of the COVID-19 pandemic on mental health in adults have now been published. Increased levels of anxiety, depression, suicidal ideation and (post-traumatic) stress, decreased psychological well-being, and a high percentage of sleep problems have been reported [3-10]. Poor mental health was associated with female gender, younger age, low educational level, living alone/being divorced, having no work, low income, a socially disadvantaged background, and having an infected relative with COVID-19 [3-10].

However, studies on the effects of the COVID-19 lockdown on social and mental health of children and adolescents are yet sparse. Two reviews reflect on the possible effects of social isolation, and they have painted an image of loneliness, anxiety and depression [11, 12]. Additionally, current opinion papers regarding the COVID-19 outbreak have described increased tension at home and child abuse as possible consequences during the lockdown [13, 14]. Several authors fear that the lockdown will magnify existing health disparities and that certain communities (e.g., with migrant background and low socioeconomic status) will be more vulnerable to develop mental and social health issues [12, 15, 16].

One systematic review on the effects of previous pandemics on mental health of children and adolescents is available, indicating that social isolation and quarantining have a negative impact on anxiety, depressive, and fear symptoms [2]. Additionally, three cross-sectional survey studies are currently available from China, focusing on the impact on mental health of the COVID-19 pandemic and lockdown specifically. They reported prevalences of anxiety and depressive symptoms of 19% and 23% respectively for primary school children [17], of 37% and 44% respectively for high school children [18],

and clinically elevated depressive symptoms scores for > 22% of children and adolescents [19] during the COVID-19 lockdown. Especially girls, older children, children living in an urban region, and children having a COVID-19 infected friend/relative appeared to be most prone to mental health problems [18, 19]. The reported prevalences were higher compared to pre-COVID-19 established cut-offs and percentages in China, however none of these differences were statistically tested. Recently published studies have shown that children did report statistically significant lower health-related quality of life and higher anxiety and depression levels than before the pandemic [20-23].

A better understanding of how the governmental restrictions during the COVID-19 pandemic affect children's and adolescents' mental and social health can help guide future interventions and inform policy makers. The current study compares the mental and social health of a representative sample of Dutch children and adolescents during the COVID-19 lockdown to earlier collected before COVID-19 reference data. The aims of this study were to: (1) quantify differences in mental and social health of children and adolescents before and during the COVID-19 lockdown, (2) identify factors that are associated with poorer mental and social health during the COVID-19 lockdown, (3) examine the change in overall atmosphere at home before and during the COVID-19 lockdown, and (4) qualitatively assess the impact of the COVID-19 lockdown on the daily life of children and adolescents.

Methods

Participants and procedure

Before COVID-19

As part of a larger Patient-Reported Outcome Measurement Information System (PROMIS) validation study, two studies were conducted between December 2017 and July 2018 in the Dutch general population to collect representative data of children and adolescents (8-18 years) on physical, mental, and social aspects of health [24, 25]. A two-step random stratified sampling method was used to ensure representativeness on key demographics. Parents participating in existing panels were approached by two independent online research agencies ('Kantar Public' or 'Panel Inzicht'). Both panels consist of families living across the Netherlands, that provided informed consent to be approached through e-mail for completing questionnaires for a small financial compensation. Children were subsequently approached by their parents to complete self-report questionnaires. Children completed the questionnaires through our research website of the KLIK Patient Reported Outcome Measures (PROM) portal [26] or the panel website. Parents were asked to complete a sociodemographic questionnaire. All children and parents provided informed consent and the studies were approved by the Medical Ethics Committee Amsterdam UMC. The samples were representative of the Dutch general population within 2.5% on most key demographics (age, gender, ethnicity, region, and educational level) compared to population numbers in 2017 (Gold Standard – Statistics Netherlands, www.cbs.nl/en-gb) [24]. Marital status and parental educational level data were differently categorized in the before COVID-19 data collection of the PROMIS Anxiety and Depressive Symptoms domains and therefore not usable for this study [25].

During COVID-19

During the COVID-19 lockdown, between April 10th and May 5th 2020, data were collected by 'Panel Inzicht' from another sample of children and adolescents from the Dutch general population. The aim was to collect data on the same measures in a representative sample of approximately 1000 children with similar characteristics (within 2.5% of the previously mentioned key demographics) as the before COVID-19 sample. Data collection procedures were similar as in 2018, with the addition of a few COVID-19 specific questions for children, adolescents and parents. Children and parents provided informed consent and the study was approved by the Medical Ethics Committee Amsterdam UMC.

Measures

Sociodemographic questionnaires

Parents completed questions about themselves (region of residence, country of birth, educational level, marital status, and number of children) and their child (age, gender).

PROMIS pediatric measures

PROMIS item banks and scales were developed and validated, to measure generic unidimensional domains (e.g., anxiety) of physical, social or mental health using modern psychometric techniques. The item banks can be administered as Computerized Adaptive Test (CAT), where items are selected based on responses to previously completed items, resulting in a reliable score with a few items [27]. Six Dutch-Flemish PROMIS pediatric measures (Scale V2.0 – Anger [28], CAT V2.0 - Peer Relationships [29], Scale V1.0 - Global Health (7+2) [30], CAT V1.0 - Sleep-related Impairment [31], CAT V2.0 – Anxiety [32], and CAT V2.0 - Depressive Symptoms [32]) were completed by children and adolescents. These measures have been selected by the American Psychiatric Association (APA) as level-2 assessment measures for monitoring and evaluating psychiatric disorders from the DSM-5. All PROMIS measures use a 7-day recall period, and items are scored on a five-point Likert scale. All items range from 'never' to '(almost) always' except for Global Health, where response categories differ for each item (e.g. 'excellent' to 'poor'). Total scores are calculated by transforming the item scores into a *T*-score which has a mean of 50 and standard deviation (SD) of 10 in the U.S. general population. For all measures higher scores represent more of the construct. For Anger (9 items) and Global Health (7+2 items) all items were administered. The US item parameters were used in the CAT algorithm and *T*-score calculations, as by PROMIS convention.

COVID-19–related additional questions

Three closed-ended questions were added for parents about whether there was a negative change in work situation of one of the parents/caregivers due to COVID-19 regulations (e.g., loss of income, reduced number of working hours, unemployment), whether a friend or relative had been infected with COVID-19 and if the child still attended child care/school during lockdown (e.g., both parents performing essential occupations).

Children and adolescents were asked to complete three COVID-19-specific questions: 'How did you experience the atmosphere at home before the schools were

closed?' and 'How do you experience the atmosphere at home now?' rated on a visual analogue scale (VAS) ranging from 0 'Not pleasant at all' to 100 'Very pleasant', and an open-ended question 'How are the corona-regulations for you?'.

Statistical analyses

For all statistical analyses the Statistical Package for Social Sciences (SPSS), version 26.0, was used.

First, descriptive analyses (mean and percentages) were used to characterize the participants in the different samples. To compare samples, independent T-tests (for continuous variables) or chi-square tests of independence (for categorical variables) were performed. Effect sizes were calculated for continuous variables (Cohen's *d*) and categorical variables (risk ratio or Cramer's *V*).

Second, to test whether mental and social health of the sample during COVID-19 differed from the sample before COVID-19 on PROMIS *T*-scores, a one-way analysis of covariance (ANCOVA) was performed per PROMIS domain, adjusted for differences in sociodemographic characteristics. Mean differences (95% CI) were reported.

Percentages of children and adolescents reporting 'severe' symptoms or 'poor' functioning on the PROMIS measures before and during the COVID-19 lockdown were compared. Severe symptoms or poor functioning was defined as a *T*-score 1.5 SD above or below the mean *T*-score before COVID-19 respectively, except for Peer Relationships, where 2 SD was used as cut-off for poor functioning (see www.healthmeasures.net). Differences in proportions of severe scores were tested using chi-squares tests of independence and the relative risk (RR) with 95% confidence intervals (95% CI) were reported. The RR represents the risk of a child measured during the COVID-19 lockdown having a severe score compared to before COVID-19. A ratio > 1 indicates more risk.

Third, to determine which variables were significantly associated with mental and social health during the COVID-19 lockdown, a multivariable linear regression analysis was performed for each PROMIS domain. The following variables were included as independent variables: age, gender, parental country of birth, marital status, region, number of children in the family, parental educational level, change in work situation due to COVID-19 regulations, infected relative/friend with COVID-19 and if the child still attended child care/school during lockdown. No multicollinearity was present between these variables (all correlations < 0.50). Per domain the effect size of all independent variables was reported, expressed as unstandardized regression coefficient *B* (95% CI).

Fourth, to investigate changes in atmosphere at home a paired T-test was used to test the difference between the two single items. Mean difference (95% CI) was reported.

Fifth, to assess the impact of the COVID-19 lockdown on the daily life of children, the open ended question 'How are the corona-regulations for you?' was qualitatively analyzed (by LT and HAvO) using thematic analysis [33]. The answers were categorized into positive, neutral or negative experiences and thereafter clustered into themes. Themes were ranked according to their frequency of occurrence (high to low).

Results

Sociodemographic characteristics

During the COVID-19 lockdown, 844 children participated. This sample showed similar characteristics (most variables within 2.5% from each other) compared to the sample collected before COVID-19 (total *N* = 2401). Significant differences were found on four variables (Table 1); age (during M = 13.4 (SD = 2.80) versus before M = 13.1 (SD = 3.14), mean difference = 0.3; 95% CI -0.54 to -0.06, *d* = 0.10), at least one parent born in a foreign country (during 11.8% versus before 20.2%, $\chi^2(1) = 29.884$, $P < 0.001$, RR = 0.58), parents with a low educational level (during 9.0% versus before 12.8%, $\chi^2(2) = 7.470$, $P = 0.024$, Cramer's $V = 0.06$), and families with one child (during 25.5% versus before 15.5%, $\chi^2(2) = 44.728$, $P < 0.001$, Cramer's $V = 0.12$).

Table 1. Sociodemographic characteristics of participants per group

	General population sample during COVID-19	General population sample before COVID-19
N[a]	844	2401
Mean age in years (SD)*	13.4 (2.8)	13.1 (3.1)
	%	%
Gender (male)	47.4	50.3
Region[b]		
North	12.6	10.6
East	22.2	23.8
South	25.0	23.2
West	40.3	42.4
Number of children in family*		
1 Child	25.5	15.5
2 Children	46.6	49.8
3 Children or more	27.9	34.7
Country of birth parents*		
Both parents Netherlands	88.2	79.8
At least one parent in foreign country	11.8	20.2
Marital status parents		[c]
Two parent family	82.0	84.7
Single parent family	18.0	15.3
Educational level parents*[d]		[c]
Low	9.0	12.8
Intermediate	51.8	48.2
High	39.2	38.9
Corona-specific variables		
Infected relative/friend (yes)	23.7	.
Negative change in work situation (yes)	26.2	.
Daycare/school attendance child (yes)	5.5	.

SD standard Deviation
*Significant difference between the two samples with $P < 0.05$
[a]Due to missing values, number of respondents vary across different sociodemographic variables.
[b]Region: North = Groningen, Friesland, Drenthe; East = Overijssel, Gelderland, Flevoland; South = Zeeland, Noord-Brabant, Limburg; West = Utrecht, Noord-Holland, Zuid-Holland.
[c]Based on *N* = 1082 due to missing values of these variables for the PROMIS Anxiety and Depressive Symptoms measures.
[d]Educational level parents, Low = primary, lower vocational education, lower and middle general secondary education; Intermediate = middle vocational education, higher secondary education, pre-university education; High = higher vocational education, university.

Differences in mental and social health in children and adolescents during versus before the COVID-19 lockdown

During the COVID-19 lockdown, children and adolescents reported worse *T*-scores than children and adolescents before the COVID-19 lockdown on all PROMIS domains, after controlling for age, parental country of birth, parental educational level and number of children (absolute mean difference range, 2.06–7.05; absolute 95% CI range, 1.25–7.86) (Table 2). Largest differences were found for Anxiety (mean difference = 7.1, 95% CI 6.2–7.9) and Depressive Symptoms (mean difference = 4.9; 95% CI 4.0–5.7).

Table 2. Mean PROMIS *T*-scores and significant mean differences in the general population during and before COVID-19, adjusted for age, parental country of birth, parental educational level and number of children

	General population sample during COVID-19			General population sample before COVID-19					Mean difference (95% CI)[b]
	N	M	SD	*N*	M	SD	*P*[a]	η^2	
PROMIS Global Health[c]	813	46.2	6.9	1082	48.3	9.8	<0.01	0.01	-2.1 (-2.9 to -1.3)
PROMIS Peer Relationships[c]	813	44.3	7.0	527	46.9	9.5	<0.01	0.02	-2.6 (-3.5 to -1.7)
PROMIS Anxiety[d]	813	50.5	7.6	1318	43.8	9.7	<0.01	0.12	7.1 (6.2 to 7.9)[e]
PROMIS Depressive Symptoms[d]	813	49.4	8.0	1318	44.7	10.6	<0.01	0.05	4.9 (4.0 to 5.7)[e]
PROMIS Anger[d]	813	47.3	8.2	527	44.2	11.4	<0.01	0.02	3.1 (2.0 to 4.1)
PROMIS Sleep Related Impairment[d]	813	49.9	8.7	527	47.6	10.0	<0.01	0.02	2.5 (1.5 to 3.5)

η^2 Amount of variance explained by group membership, *CI* confidence interval, *M* mean, *SD* standard deviation
[a]*P*-value of the main effect of the ANCOVA
[b]Adjusted mean differences and CI
[c]Higher scores indicate better functioning
[d]Higher scores indicate more symptoms
[e]Not corrected for parental educational level due to missing values

Significantly more children reported severe Anxiety (during 16.7% versus before 8.6%; RR, 1.95; 95% CI 1.55–2.46) and severe Sleep-Related Impairment (during 11.5% versus before 6.1%; RR, 1.89; 95% CI 1.29–2.78) during the COVID-19 lockdown than before COVID-19 (Table 3). Fewer children reported poor Global Health (during 1.7% versus before 4.6%; RR, 0.36; 95% CI 0.20–0.65).

Variables associated with poor mental and social health in children and adolescents during the COVID-19 lockdown

Lower Global Health was associated with a single-parent family (*B* = -3.00; 95% CI -4.23 to -1.76). Lower Peer Relationships were reported by boys compared to girls (*B* = -1.25; 95% CI -2.23 to -0.27). Increased Anxiety was associated with age (*B* = -0.34; 95% CI -0.53 to -0.15), a single-parent family (*B* = 1.46; 95% CI 0.11–2.81), an infected relative or friend (*B* = 1.94; 95% CI 0.72–3.16), and parents with a negative change in work situation (*B* = 3.01; 95% CI 1.84–4.18). More Depressive Symptoms was associated with highly educated parents (where intermediate differed from lower; *B* = 2.24; 95% CI 0.23–4.24) and parents with a negative change in work situation (*B* = 2.45; 95% CI 1.20–3.70). More Anger was associated with age (*B* = -0.47; 95% CI -0.67 to -0.28), highly educated parents (where

intermediate differed from lower; *B* = 2.30, 95% CI 0.27–4.33 and high differed from lower; *B* = 2.10; 95% CI 0.01–4.19), three or more children (*B* = 2.07; 95% CI 0.52–3.62) and parents with a negative change in work situation (*B* = 1.71; 95% CI 0.45–2.98). Finally, more Sleep-Related Impairment was related to the country of birth of parents (≥ one foreign parent; *B* = 1.95; 95% CI 0.13–3.77), a single-parent family (*B* = 2.07; 95% CI 0.53–3.62) and parents with a negative change in work situation (*B* = 2.53; 95% CI 1.19–3.87) (Table 4).

Table 3. Percentage of participants with poor functioning or severe symptoms (> 1.5 SD) on the PROMIS domains for both samples

	General population sample during COVID-19	General population sample before COVID-19	Relative risk (95% CI)
	%	%	
PROMIS Global Health*	1.7	4.6	0.36 (0.20–0.65)
PROMIS Peer Relationships[a]	1.9	1.9	0.99 (0.46–2.19)
PROMIS Anxiety*	16.7	8.6	1.95 (1.55–2.45)
PROMIS Depressive Symptoms	7.1	8.2	0.87 (0.64–1.18)
PROMIS Anger	3.7	5.5	0.67 (0.41–1.09)
PROMIS Sleep-Related Impairment*	11.5	6.1	1.89 (1.29–2.78)

CI Confidence interval
*Significant difference between during and before with *P* value < 0.01
[a]For Peer Relationships a cut-off of 2 SD was used, as per HealthMeasures guidelines.

Changes in atmosphere at home during the COVID-19 lockdown

Children and adolescents reported a worse atmosphere (mean difference = -3.1; 95% CI -4.1 to -2.1) at home during the COVID-19 lockdown (M = 78.2, SD = 17.9) than before COVID-19 (M = 81.4, SD = 16.0).

Impact of COVID-19 regulations on the daily life of children

The majority (~ 90%) of children indicated that the COVID-19 lockdown had a negative impact on their daily life. The most often mentioned issues (> 50 children) were: (1) missing contact with friends, (2) not allowed to go to school, (3) missing freedom, (4) not allowed to participate in sports, (5) missing joyful activities (e.g., birthdays, holidays, parties, shopping), (6) difficulties with homeschooling, (7) missing extended family, and (8) boredom (Table 5). A minority of children did not experience any difficulties with the COVID-19 lockdown regulations (~ 7%) (e.g., *'It does not bother me'*) or reported positive consequences (~ 3%) (e.g., *'I really like that I can play with children in my neighborhood all day long'*).

Table 4. Variables associated with mental and social health in children and adolescents during the COVID-19 lockdown

	Global Health[a]	Peer Relationships[a]	Anxiety[b]	Depressive Symptoms[b]	Anger[b]	Sleep-Related Impairment[b]
Covariates	*B*	*B*	*B*	*B*	*B*	*B*
Age	-0.03	0.11	-0.34**	-0.19	-0.47**	-0.09
Male	0.50	-1.25*	-0.32	-0.56	0.12	-1.11
Region[c]						
West	Ref	Ref	Ref	Ref	Ref	Ref
North	-0.22	-0.19	-0.50	-1.18	-0.97	-0.52
East	-0.88	-0.07	0.32	0.21	-0.17	0.38
South	-0.78	-0.32	-0.03	-0.69	-0.74	-0.94
Foreign country of birth parents	-0.33	-0.60	0.45	0.32	0.37	1.95*
Educational level parents[d]						
Low	Ref	Ref	Ref	Ref	Ref	Ref
Intermediate	-0.68	0.78	1.60	2.24*	2.30*	1.19
High	0.87	1.51	1.12	1.94	2.10*	0.02
Single parent family	-3.00**	-0.76	1.46*	1.02	0.91	2.07**
Number of children in family						
1 Child	Ref	Ref	Ref	Ref	Ref	Ref
2 Children	0.37	-0.81	0.31	0.08	1.29	0.11
3 or more children	0.60	0.16	-0.14	-0.17	2.07**	1.26
Negative change in work situation	-0.88	-0.46	3.01**	2.45**	1.71**	2.53**
Infected relative/ friend with COVID-19	0.96	0.84	1.94**	1.11	0.11	0.99
Daycare/school attendance child	-0.65	0.20	1.20	2.04	1.15	2.73

B unstandardized regression coefficient of multivariable linear regression model
***P* value < 0.01, **P* value < 0.05
[a]Higher scores indicate better functioning
[b]Higher scores indicate more symptoms
[c]Region: North = Groningen, Friesland, Drenthe; East = Overijssel, Gelderland, Flevoland; South = Zeeland, Noord-Brabant, Limburg; West = Utrecht, Noord-Holland, Zuid-Holland
[d]Educational level parents divided into three categories: Low = primary, lower vocational education, lower and middle general secondary education; Intermediate = middle vocational education, higher secondary education, pre-university education; High = higher vocational education, university

Table 5. Themes regarding the negative impact of COVID-19 regulations ranked according to their frequency of occurrence (high to low)

Themes	Illustrative quotes as reaction to the question 'How are the corona-regulations for you'?
1. Missing contact with friends	'I miss my friends' 'Feeling alone, because I cannot see my friends anymore, it is different online'
2. Not allowed to go to school	'It is a pity that I cannot go to school' 'I miss my teacher and my class'
3. Missing freedom	'I am only allowed to play in and around the house' 'I have to stay at home, I am not allowed to go anywhere'
4. Not allowed to participate in sports	'I used to play soccer three times a week, I miss playing sports and being outside the most' 'I am not allowed to play field hockey anymore'
5. Joyful activities	'I want to party with my friends, to participate in my final exams and I want to go on a holiday but that is not possible now' 'It was my birthday and I was sad that nobody could visit me' 'It is not possible to go shopping or do fun things'
6. Difficulties with homeschooling	'I miss my daily routine and the boundary between school and home is completely gone' 'Schoolwork at home is not easy, I can concentrate better at school' 'I have the feeling that I do not learn anything, because homework is not discussed or revised'
7. Missing extended family	'I am not allowed to see or hug my grandparents' 'I miss my extended family a lot'
8. Boredom	'I am often bored, because we cannot do anything' 'It is boring to play alone all the time'

Discussion

This study compared the mental and social health of a representative sample of children and adolescents from the general population *during* the COVID-19 lockdown to a similar sample of children and adolescents *before* COVID-19. Children and adolescents reported poorer mental and social health during the COVID-19 lockdown on all six PROMIS domains. Substantial differences in percentages of children reporting severe anxiety and sleep-related impairment were observed. Fewer children and adolescents reported a poor global health during the COVID-19 lockdown, although the mean global health score was lower in this sample as compared to the sample before COVID-19. Significant associations with mental and social health complaints during the COVID-19 lockdown were found for family composition (growing up in a single-parent family or having three or more children in the family), a negative change in work situation of parents due to COVID-19 regulations, and an infected relative/friend with COVID-19. Children and adolescents reported a small decrease in the atmosphere at home during the lockdown. The majority of children and adolescents revealed a negative impact of the COVID-19 regulations on their daily life, that far outweigh the number of children who reported a positive effect. Especially missing contact with friends was considered important.

The results of this study confirm the suspicions of child and youth care professionals that the COVID-19 lockdown has negative effects on mental and social health of children and adolescents. In opinion papers, professionals elaborated on the vulnerability of this group and expected more feelings of loneliness, anxiety and depression, as well as a more

tense atmosphere at home [11-14]. Concerns were also expressed that the COVID-19 lockdown would lead to an increase in inequality and that children and families with lower socioeconomic status would be more susceptible to mental health issues [12, 15, 16]. Although this study could not definitely confirm these concerns, children from single parent families, from families with three or more children, and with parents who had a negative change in work situation reported more mental and social health problems during the COVID-19 lockdown.

While the Dutch partial lockdown was substantially different from the Chinese full lockdown, our results are in line with the three studies from China [17-19], who also reported higher anxiety and depressive symptoms during the COVID-19 lockdown. Likewise, one of the Chinese studies also found that having an infected relative/friend with COVID-19 was predictive of more anxiety [19]. Germany had comparable restrictions and also found worse mental health and higher levels of anxiety in children and adolescents during lockdown [20]. In addition to the effects on anxiety and depressive symptoms, our study results show negative effects of the COVID-19 lockdown on anger, sleep-related impairment and peer relationships.

Although the mean T-score on Global Health was lower (worse) in the sample during the lockdown as compared to before COVID-19, a lower percentage of children and adolescents reported poor Global Health during COVID-19. As data collection procedures were identical and the same measures were administered, methodological reasons are unlikely to cause these differences. There are a few possible explanations for this finding. It may be explained by the fact that the cut-offs are population-based and may not accurately represent clinically relevant cases as they have not been researched extensively. Secondly, cross-sectional data collection resulted in two independent samples, which may have had differences in the baseline distributions of clinical scores. Examining the item responses on the Global Health scale items indicated that less children reported "Poor" functioning on all items during COVID-19 (resulting in less clinical scores). However, the response category "Excellent" was also used less frequently (resulting in lower mean scores), which may have been a result of the limitations on daily life caused by the COVID-19 restrictions. Given the above possible explanations, this finding remains puzzling and prompts further study in a longitudinal design that is underway in our department.

Some limitations of this study need to be taken into account. First of all, self-reported responses may be influenced by social desirability. However, as the PROMIS data collection process was the same for the 2018 and 2020 sample we think it is unlikely that social desirability accounts for the differences observed between these samples. Secondly, although the aim was to obtain two representative samples that were comparable, significant differences with small effect sizes were found on age, parental educational level, and family composition. Parental country of birth did show a large risk ratio. As matching was not possible due to missing values in background characteristics in one of the samples, these differences between groups were corrected for by means of ANCOVAs. For comparing Anxiety and Depressive Symptoms, we were unable to correct for parental educational level in the ANCOVA, as this variable was not usable due to different categorization in the before COVID-19 sample. It is unlikely this influenced the results, as the effect size of this variable was small on other domains (Cramer's *V* below

0.1). In addition, the data collection during COVID-19 took place in April and May (2020), whereas the study data collection before COVID on anxiety and depression mainly took place in January and February (2018). Worse mental health is often reported during winter times [34]. This difference could have led to an underestimation of the actual impact of the COVID-19 lockdown.

We found that children and adolescents from families with certain risk factors (e.g., single-parent families) are more vulnerable to mental and social health problems. These children and adolescents should be in sight of health care professionals. However, in this study children and adolescents with existing mental or somatic problems were not included, while it is conceivable that these groups are even more vulnerable. More research is needed to study the mental and social health of these groups as well as to gain insight into the longitudinal effects, and to clarify if lower mental and social health scores are mainly due to the COVID-19 pandemic or the lockdown.

During the finalization of this paper, the Netherlands, and many other countries, are facing a second COVID-19 wave. This study showed that children and adolescents reported poorer mental and social health during the COVID-19 lockdown compared to before and exposed several risk factors for poor mental and social health. These risk factors and the effect of governmental regulations regarding lockdown on the mental and social health of children and adolescents should be taken into consideration when imposing new governmental regulations and should thus be brought to the forefront of political decision making and mental health care policy, intervention and prevention.

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Conflicts of interest

All authors declare that they have no conflict of interest.

Ethics approval

The Medical Ethical Committee of the Amsterdam UMC (location AMC and VUMC) approved the protocol and judged that the Dutch Medical Research Involving Human Subjects Act does not apply to this study. All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all individual participants and/or legal guardians included in this study.

Consent for publication

Not applicable.

Availability of data

Data are available upon reasonable request.

Code availability

Code is available upon reasonable request.

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CHAPTER 7

From statistics to clinics: the visual feedback of PROMIS® CATs

Maud M. van Muilekom, Michiel A. J. Luijten, Hedy A. van Oers, Caroline B. Terwee, Raphaële R. L. van Litsenburg, Leo D. Roorda, Martha A. Grootenhuis, Lotte Haverman

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Abstract

Background

To reduce the burden of completing Patient Reported Outcome Measures (PROMs), PROMIS® Computerized Adaptive Tests (CATs) are being implemented in pediatric clinical practice. We aimed to develop recommendations for visual feedback options for PROMIS CATs on individual item and domain score level as an evidence-based feedback recommendation for PROMIS CATs is lacking.

Methods

Focus groups were held with clinicians who use the KLIK PROM portal. Literature-based feedback options were provided to initiate group discussion. Data was analyzed using thematic coding method. Additionally, a questionnaire was sent out to assess patients' (12-18y) and parents' (child 0-18y) preference for individual item feedback. Data was analyzed using descriptive statistics.

Results

Six focus groups were held (*N* = 28 clinicians). Regarding individual item feedback, showing the complete item bank, with only responses to administered items in traffic light colors was preferred. For domain scores, line graphs were preferred, including numerical (T-) scores, reference and cut-off lines, and traffic light colors. Separate graphs per domain, ranked in order of importance and harmonization of directionality ('higher = better') were considered important. Questionnaire results (*N* = 31 patients/*N* = 131 parents) showed that viewing their own item responses was preferred above receiving no item feedback by 58.1% of the patients and 77.1% of the parents.

Conclusions

Based on the outcomes and after discussion with the Dutch-Flemish PROMIS National Center, recommendations for PROMIS CAT feedback options were developed. PROMIS CATs can now be used in clinical practice to help clinicians monitor patient outcomes, while reducing the burden of completing PROMs for patients significantly.

Key words

Visual feedback, Patient Reported Outcome Measures (PROMs), Patient-Reported Outcomes Measurement Information System (PROMIS®), Computerized Adaptive Testing (CAT), clinicians, pediatric patients and parents.

Background

With the systematic use of Patient Reported Outcome Measures (PROMs, questionnaires measuring the patients' view of their health status) in the consultation room, symptoms, physical and psychosocial functioning of patients can be monitored and discussed. When necessary, interventions can subsequently be offered timely [1, 2]. The use of PROMs in clinical practice has been shown beneficial as it resulted in increased discussion of patient outcomes and enhanced patient-clinician communication [3, 4], higher patient satisfaction [2], better Health Related Quality of Life (HRQOL) [5], and improved treatment outcomes including survival [5, 6].

Even though PROMs are increasingly used in clinical practice, several challenges with PROMs have been identified [7-10]. For example, available PROMs are often considered burdensome due to questionnaire length and irrelevancy and repetitiveness of questions. Additionally, when patients have multiple chronic conditions and thus have to complete PROMs for multiple diseases, scores of these PROMs cannot be compared due to different scoring methods.

To overcome these challenges and harmonize all existing PROMs into one assessment system, the Patient-Reported Outcomes Measurement Information System (PROMIS®) was developed by a consortium of US research centers, together with the National Institute of Health [11, 12]. PROMIS is a generic measurement system, consisting of various item banks, for adults and children, that measure separate domains representing physical, mental and social health (e.g., depression, pain interference) [13]. The item banks are based on Item Response Theory (IRT) modelling, where items are ordered by their difficulty and discriminative ability and scaled onto a single metric, which enables Computerized Adaptive Testing (CAT). With CAT, items are presented to patients based on responses to previously administered items. The computer estimates the domain score after each item, and when this score reaches a pre-defined precision, the CAT stops. Hence, patients only need to answer a small number of items (usually 5-7) per PROMIS item bank to get an accurate and reliable T-score [14]. Responses to remaining, non-administered items can be predicted (predicted responses) using the IRT model.

To facilitate the use of the PROMIS item banks in clinical practice in the Netherlands, a large number of PROMIS item banks were translated into Dutch-Flemish and validated [9, 15-17]. In 2019, the Dutch-Flemish pediatric PROMIS item banks were implemented in the Netherlands through the KLIK PROM portal [18-20], after linking KLIK to the Dutch-Flemish Assessment Center to enable CAT [21]. KLIK is an online portal (www.hetklikt.nu or www.klik-uk.org) where patients and/or caregivers complete PROMs regarding symptoms, HRQOL, physical and psychosocial functioning. Responses are visualized in the KLIK ePROfile, on individual item level (with traffic light colors: green – no problems, orange – some problems, red – many problems) and domain score level (with graphs including a reference line) [21] (Figure 1). It is essential that this visual feedback is easy-to-understand, as clinicians subsequently need to interpret the scores of different PROMs and discuss the feedback with the patients during consultation. However, for PROMIS CATs, new visual feedback options for the KLIK ePROfile are required, as an evidence-based feedback recommendation for PROMIS CATs is lacking.

Until now, several studies have investigated the visual feedback of PROMs in general, and current knowledge has been summarized [22, 23]. Two studies in an adult oncology and rheumatology setting showed that individual item feedback immediately attracts clinicians' attention to specific problems, especially when using colors [24, 25]. Regarding domain score feedback, line graphs were most preferred to show change over time [26-32]. However, bar charts, tables or textual reports might be good alternatives [31, 33-35]. Meaningful descriptive labeling of axes, harmonization of directionality (higher is better: upward trend indicates better functioning), highlighting deviating results with colors and inclusion of a reference population were all identified as important aspects of visual feedback [28-31, 36, 37]. Concerning feedback of PROMIS specifically, some studies have described how they visualized PROMIS domain score (T-score) feedback when using PROMIS item banks in adult orthopedic, oncology, cardiac and gastrointestinal clinical practice [22, 38-41], where line graphs including reference to a norm population [22], textual reports of T-scores [22, 39], symptom cards [40] and heat maps [38, 41] were used. Showing T-scores in order of importance, with the most deviating T-score first, was described to be helpful in two studies [40, 41]. Only one study in adult orthopedic care provided individual item feedback of PROMIS CATs to patients and clinicians, but they did not explore preferences of their participants regarding this feedback [38].

To conclude, several studies have investigated feedback of PROMs in general and some described how they provide feedback when using PROMIS item banks in clinical practice. However, to our knowledge no studies were performed that explored preferences for PROMIS CAT feedback specifically. Thus, more insight is needed into optimal PROMIS CAT feedback and, therefore, this study aimed to develop recommendations for individual item and domain score feedback for PROMIS CATs.

1a

Child

○ 03-11-2016 ✓ 03-06-2017 ○ 23-12-2017 ✓ 26-04-2018

Physical	03-06-2017	26-04-2018
It is hard for me to walk more than one block	Sometimes	Never
It is hard for me to run	Often	Almost always
It is hard for me to do sports activity or exercise	Often	Often
It is hard for me to lift something heavy	Sometimes	Almost always
It is hard for me to take a bath or shower by myself	Never	Never
It is hard for me to do chores around the house	Almost always	Often
I hurt or ache	Almost never	Sometimes
I have low energy	Often	Sometimes

Emotional	03-06-2017	26-04-2018
I feel afraid or scared	Never	Never
I feel sad or blue	Never	Almost never
I feel angry	Almost never	Sometimes
I have trouble sleeping	Never	Sometimes
I worry about what will happen to me	Never	Never

Social	03-06-2017	26-04-2018
I have trouble getting along with other kids	Never	Never
Other kids do not want to be my friend	Never	Never
Other kids tease me	Never	Almost never
I cannot do things that other kids my age can do	Sometimes	Often
It is hard to keep up when I play with other kids	Never	Never

School	03-06-2017	26-04-2018
It is hard to pay attention in class	Never	Never
I forget things	Almost never	Sometimes
I have trouble keeping up with my schoolwork	Sometimes	Never
I miss school because of not feeling well	Sometimes	Sometimes
I miss school to go to the doctor or hospital	Sometimes	Sometimes

1b

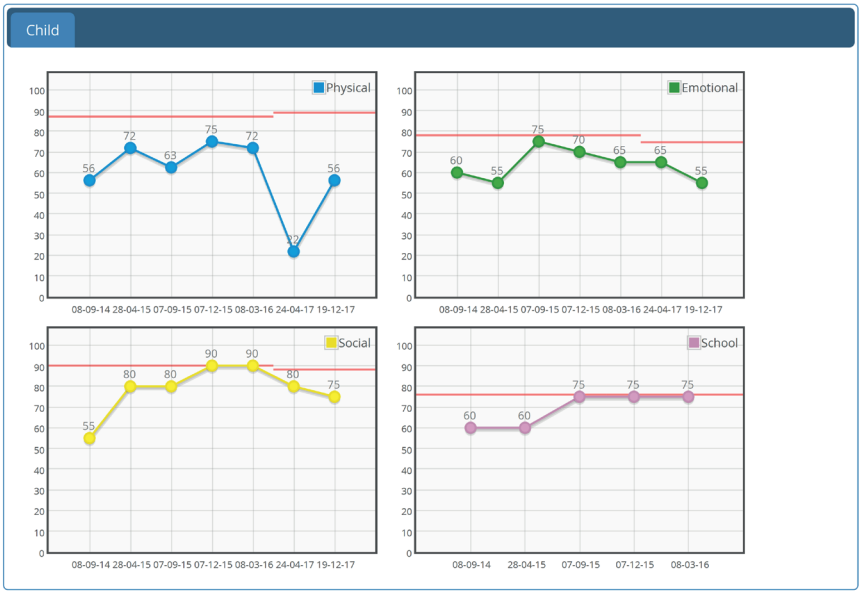


Figure 1. Current PROM individual item (1a) and domain score (1b) feedback in the KLIK ePROfile

Methods

Design

A mixed method design was used by combining qualitative and quantitative methodologies in two steps: 1) Focus groups with clinicians and 2) a questionnaire for pediatric patients and their parents. This study was approved by the Medical Ethics Committee of the Amsterdam University Medical Centers (Amsterdam UMC), location AMC. Informed consent was obtained from all participating clinicians and patients/parents.

Participants and procedure

Focus groups

Participants were recruited between September and November 2018 using a purposive sampling method. The aim was to include clinicians from diverse disciplines (e.g., physicians, psychologists, social workers) who use KLIK in the Emma Children's Hospital Amsterdam UMC or Princess Máxima Center. An invitation e-mail (explaining the goal of the study and including optional data for focus groups) was sent to all clinicians and a reminder e-mail was sent to clinicians who had not responded after 3 weeks. Interested clinicians could reply to the e-mail and sign up to participate. Thereafter, clinicians were allocated to one of the focus groups, where ideally three to six participants [42] and a mix of different disciplines was pursued. All applicants from the Princess Máxima Center were admitted to one focus group during their standard multidisciplinary meeting in their own center due to limited time.

Focus groups consisted of a group discussion guided by two moderators (MMvM and MAJL) using a topic guide in PowerPoint. Both moderators were trained in performing focus groups. First, a short recapitulation of KLIK and the current PROM feedback options was provided. Thereafter, PROMIS and the principles of CAT were explained, enabling clinicians to understand why new feedback was necessary. To obtain clinicians' input on PROMIS CAT feedback, four options for individual item and five options for domain score feedback were shown, based on or adapted from previous studies [40, 43-45]. Questions were provided to clinicians ('What appeals to you in this option?', 'What do you miss in this option?') to initiate the discussion about the feedback options (e.g., including predicted responses for non-administered items and providing reference lines). Furthermore, clinicians were asked to describe their optimal feedback option. The duration of each focus group was approximately 90 minutes. All focus groups were audio recorded.

Questionnaire

To receive patients' and parents' opinion on PROMIS CAT feedback, an online questionnaire was sent out between June and December 2019. All patients (12-18 years) and parents (of children 0-18 years) who use KLIK as standard part of care in the Emma Children's Hospital Amsterdam UMC, completed KLIK PROMs at least once, and were part of the KLIK panel (during registration on the KLIK PROM portal they could indicate they were willing to participate in research projects) were invited by email (Figure 2). Participants completed the questionnaire anonymously. Three reminder emails were sent over the course of six months to patients and parents who had not yet completed

the questionnaire. All patients and parents provided informed consent and received a gift card after participation.

The questionnaire (separate versions for patients and parents) was developed as part of a larger study that aimed to assess KLIK users' opinion about several aspects of the KLIK PROM portal [8]. Three questions were included in this study that focused on the feedback of PROMIS CATs. Only questions about individual item feedback could be asked, as patients and parents currently do not receive domain score feedback in their KLIK ePROfile. A short explanatory text about the working mechanism of PROMIS CATs was provided after which the following three questions were asked: 1) 'Would you like to see your responses in the KLIK ePROfile?' (yes/no), 2) 'Would you like to see all items of the item bank in the KLIK ePROfile?' (yes/no), and 3) 'Which of the two figures provided would you like to see in the KLIK ePROfile?' (option 1/option 2, Figure 3). For every question there was the possibility to add an explanation or provide additional remarks.

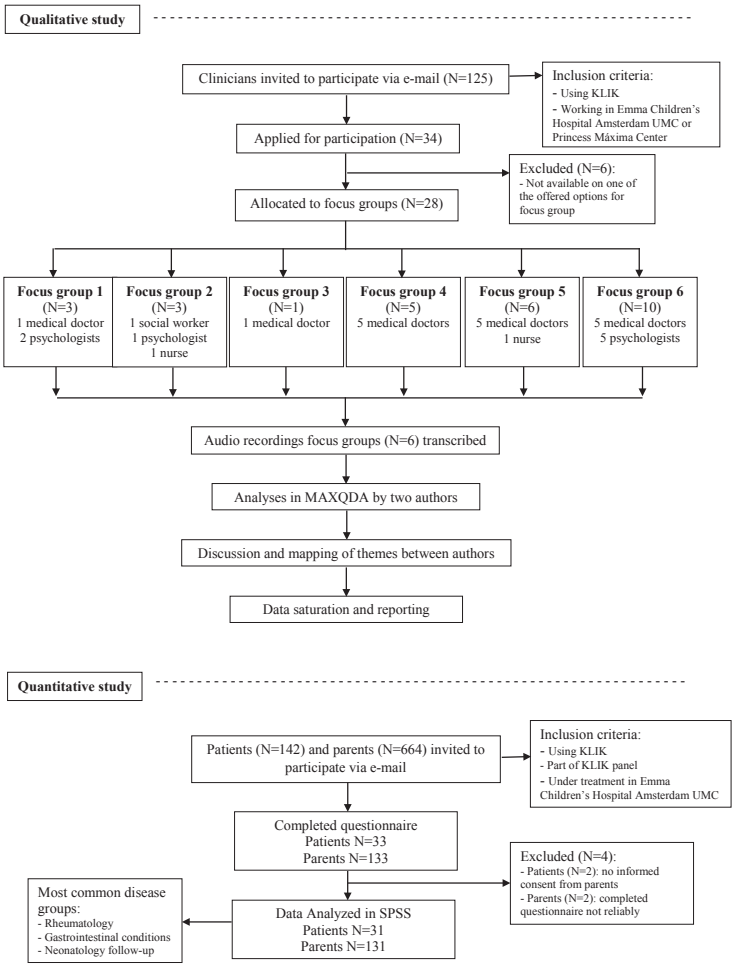


Figure 2. Study and participant flow chart of the qualitative (focus groups) and quantitative (questionnaire) study

Option 1

Physical functioning item bank		
The answers shown are answers you provided on the questionnaire.	**20-09-2018**	**11-12-2018**
Please answer about the past 7 days…		
I could walk 100m.		With a lot of trouble
I could run a marathon.		
I could stand on my own.	With some trouble	Without trouble
I could stand on my toes.	Without trouble	
I could move my legs.		
I could walk to the other side of the room.	With a lot of trouble	With some trouble
I could walk five miles.		
I could bend over.		

Option 2

Physical functioning item bank		
The answers with a black border are answers you provided on the questionnaire. The answers without black borders are estimates.	**20-09-2018**	**11-12-2018**
Please answer about the past 7 days…		
I could walk 100m.	With a lot of trouble	With a lot of trouble
I could run a marathon.	With a lot of trouble	With a lot of trouble
I could stand on my own.	With some trouble	Without trouble
I could stand on my toes.	Without trouble	Without trouble
I could move my legs.	Without trouble	Without trouble
I could walk to the other side of the room.	With a lot of trouble	With some trouble
I could walk five miles.	With a lot of trouble	With a lot of trouble
I could bend over.	Without trouble	Without trouble

Figure 3. Two options of individual item feedback shown to patients and parents in questionnaire
Note. Option 1 shows all items of the PROMIS item bank, with the responses in traffic light colors and blank spaces at non-administered items. Option 2 shows all items of the PROMIS item bank, with both provided and predicted responses in traffic light colors. Provided responses can be distinguished from predicted responses by the black border around the response.

Analyses

Focus groups

Audio recordings were transcribed verbatim (and data was anonymized) and two authors independently read and analyzed the transcripts with the qualitative data analysis tool MAXQDA (2018) using a thematic coding method [46]. Analyses included the following steps; 1) marking parts of the transcript related to the subject matter 2) generating initial codes to organize data into meaningful groups, 3) searching for themes and collating codes into the identified themes, 4) reviewing and refining themes into main themes and subthemes, 5) defining the final themes.

After analyzing all transcripts independently, analyses were discussed between two authors until consensus on the themes was reached. Data saturation was considered attained when, during analyses of the planned focus groups, no new themes emerged. If new themes did emerge, new focus groups would be planned until data saturation was reached.

Questionnaire

Descriptive analyses (percentages yes/no or option 1/option 2) were performed on the three questions to gain insight in participants' preference for feedback of PROMIS CATs by using the Statistical Package for Social Sciences (SPSS) version 25.0.

Development of recommended feedback options for PROMIS CATs

After analyzing the results of the focus groups and the questionnaire, a preliminary recommended individual item and domain score feedback option was developed. Thereafter, these feedback options were discussed with the Dutch-Flemish PROMIS National Center and an expert on data visualization was consulted, to develop a final recommendation for feeding back PROMIS CATs on individual item and domain score level.

Results

Focus groups

In the upper part of Figure 2 the study and participant flow chart of the focus groups is shown. In total, 28 clinicians participated in six focus groups (response rate: 22.4%). Characteristics of clinicians are shown in Table 1. On average, clinicians used KLIK for 5.2 years (range: 0.3-7.4). The majority of clinicians worked in the Emma Children's Hospital (64.3%) and most clinicians were employed as medical doctor (60.7%) or psychologist (28.6%). Data saturation was attained as no new themes emerged after analyzing the final planned focus group. Table 2 shows the most important themes and corresponding examples of statements expressed by clinicians about individual item and domain score feedback of PROMIS CATs.

Table 1. Characteristics of participating clinicians in six focus groups

	Participants (*N* = 28)	
	M	**Range**
KLIK user since (years)	5.2	0.3-7.4
	N (%)	
Hospital		
Emma Children's Hospital	18 (64.3)	
Princess Máxima Center[a]	10 (35.7)	
Discipline		
Medical doctor	17 (60.7)	
Psychologist	8 (28.6)	
Nurse	2 (7.1)	
Social worker	1 (3.6)	

Note. [a]Only 1 focus group (Focus group 6) was held in this hospital.

Individual item feedback

In all focus groups clinicians indicated that feedback of individual items is essential for the use of PROMs in clinical practice. Clinicians use the items to start a dialogue (as a conversation tool), to understand the domain scores that are provided and to discuss specific problems. Therefore, it was important for them to obtain individual item feedback for PROMIS CATs.

Even though with PROMIS CATs not all items are administered to patients, it was important for clinicians to have the possibility to see *all items* of the item bank in the feedback. According to the clinicians, the responses to the *completed items* in the CAT should be fed back, preferably in traffic light *colors*, where items on which no problems are reported are shown in green, items on which some problems are reported are shown in orange and items on which many problems are reported are shown in red. In this way clinicians can quickly see if the patient has problems with certain symptoms or aspects of their daily functioning. The option to include *predicted responses* in the feedback (which is possible using the IRT model) for non-administered items, was unanimously rejected. Reasons were that predicted responses are not recognizable for patients and can be confronting and confusing. A suggestion provided by clinicians was to leave blank spaces at items that were not administered. Over time, clinicians can then easily see which items were administered with every CAT completion.

Table 2. Themes and examples found in focus groups

Feedback	Themes	Focus group number	Examples
Individual item	All items	3	*"I would like to see all items in the feedback, as then there is the possibility to discuss also not completed items."*
		1	*"For non-experienced clinicians who do not know the questionnaires it is nice to be able to see all items."*
		6	*"Seeing all the items of the questionnaire provides the opportunity to use them as a conversation tool."*
	Completed items	2	*"Only the responses to the items that the patient has completed should be fed back."*
		5	*"Feedback of the responses to the completed items provides the opportunity to start a conversation with the patient."*
	Colors	4	*"The use of traffic light colors helps me in focusing quickly on what is important."*
		6	*"Seeing the traffic light colors is essential as it makes interpreting easy and simple."*
	Predicted responses	1	*"The predicted responses provide too much information. If predicted responses are shown I would still want to check them and adjust them if needed, which would cost me more time!"*
		2	*"Feeding back predicted responses is very confusing for use in clinical practice, especially to discuss them with the patient. Perhaps in research predicted responses might be useful."*
Domain score	Dots or lines	5	*"I think viewing lines between the dots that represent the domain scores for that time point is clearer and interpretation is easier."*
	Numerical information	4	*"If the numerical domain (T-)scores are provided in the graph, this is very useful. Especially, as you can also use these scores in the report about the patient in the electronic health record."*
	Reference line (and cut-offs)	3	*"A norm line makes the graph more insightful and clear."*
		1	*"It is relevant to see the cut-off lines as well, as with these lines you can judge if a patient has a subclinical or clinical score."*
	Colors	3	*"The use of traffic light colors makes the graph easier interpretable and provides a quick overview of how the patient is functioning."*
		6	*"When the domain scores or cut-off lines are shown in traffic light colors you can see how good or bad the score of the patient is."*
		2	*"Another option is to show the background of the graph in traffic light colors, in accordance with the cut-off lines, whilst showing the domain scores in a neutral color. In this way I can quickly see on what level the patient is functioning."*
	Combined or separate graphs	1	*"Separate graphs per domain are better, as the domains are so different from each other. Putting them together in one graph would result in oversimplification of the findings."*
		4	*"It is more difficult to discuss the outcomes if they are all put in one graph."*
	Order of importance	2	*"It would be very helpful if the graph where the most deviating domain score in the clinical direction is found and thus needs most attention, is ranked in order of importance and is shown first."*
	Directionality	4	*"For me it is important that if several graphs are shown on one page that all lines are going in the same direction."*
		5	*"I would prefer to see norm lines go up when functioning is better and go down when functioning is worse. In other words, higher is better."*

Domain score feedback

Regarding the domain score feedback of PROMIS CATs it became clear, by discussing the several options provided, that clinicians had a preference for graphical over textual options. Graphs were seen as clearer and easier to interpret, and the option to show domain scores longitudinally in one graph was desired.

A large majority of clinicians preferred to see the domain scores over time in graphs as *dots* connected with *lines,* though for a few clinicians this connection did not matter, as long as there was a graphical feedback option. According to the clinicians, the *numerical domain (T-)score* should be shown with each dot, as these scores help improve the interpretation of scores and can be easily included in the health record. In addition to the individual patient's domain scores, inclusion of a *reference line* was valued by all clinicians, in order to make a comparison with a reference group. To be able to judge the severity of scores deviating from the reference line, several options were discussed, for example showing the dots in traffic light *colors* or adding *cut-off lines* in traffic light *colors* indicating subclinical (moderate deviation from norm) or clinical (severe deviation from norm) scores. An additional suggestion provided by clinicians, was to give areas in the background of the graph traffic light *colors* (similar to a heat map), in accordance with the cut-off lines, and the dots of the domain scores in neutral colors. Although at first participating psychologists thought that the use of colors was confronting for patients, they later agreed that it is useful to quickly assess if a patients deviates from the reference group.

As PROMIS measures domains on similar scales (T-score metric), it is possible to display multiple domain scores in one graph. However, this was considered unclear and difficult to interpret. Clinicians preferred *separate graphs* per domain, all shown on one page, and if possible ranked in *order of importance*. They indicated that graphs where the most deviating scores were found on a domain should be presented first, by which clinicians can easily see which domains need most attention. The last topic that came up was the *directionality* of lines. A large majority of clinicians indicated that it is important for them to harmonize the directionality in all graphs. They preferred to see lines where an upwards trend represents an improvement in functioning (higher is better). To do this, they suggested to reverse the scale on the y-axis for some domains (e.g., for anxiety, where higher scores indicate higher anxiety levels).

Questionnaire

In the lower part of Figure 2 the study and participant flow chart of the questionnaire is presented. In total, completed questionnaires of 31 patients (response rate: 21.8%) and 131 parents (response rate: 19.7%) were analyzed. Since participants completed the questionnaire anonymously, no information on sociodemographic characteristics of participants was available, nor information about the non-participants. Table 3 shows the results of the questionnaire for both patients and parents.

Table 3. Questionnaire results for patients and parents

	Patients			Parents		
Question	***N***	**Yes (%)**	**No (%)**	***N***	**Yes (%)**	**No (%)**
Would you like to see your responses?	31	18 (58.1)	13 (41.9)	131	101 (77.1)	30 (22.9)
Would you like to see all items of the item bank?	31	13 (41.9)	18 (58.1)	131	55 (42.0)	76 (58.0)
		Option 1 (%)	**Option 2 (%)**		**Option 1 (%)**	**Option 2 (%)**
Which of the two figures provided would you like to see?	31	16 (51.6)	15 (48.4)	129[a]	96 (74.4)	33 (25.6)

Note. [a] Two parents were excluded as they indicated in the explanation box that they did not understand the figures at all.

Patients (12-18 years)

The majority of patients (58.1%) indicated they would like to see their item responses fed back in the KLIK ePROfile, as they provide clarity and insight into their functioning. Less than half of the patients (41.9%) would like to see all items of the item bank. In their opinion the not completed items were unnecessary to show. Finally, 51.6% of the patients preferred not to see predicted responses (option 1). As an explanation for this choice, patients mentioned that option 2 was very unclear and contained too many details.

Parents

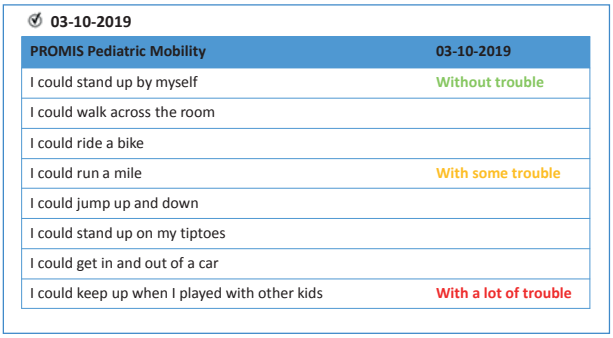
Most parents (77.1%) preferred to see their responses to the items. An explanation for this preference was that these provide insight into the functioning of their child, especially when the responses of several measurement occasions are shown. In accordance with patients, less than half of the parents (42.0%) would like to see all items of the item bank, as they think that viewing the not completed items is not of added value. The majority of parents (74.4%) preferred not to see predicted responses (option 1). Explanations were that option 2 was too complicated to read and contained too many details which makes the option unclear.

Recommended feedback options for PROMIS CATs

Based on the outcomes of the focus groups and questionnaire a preliminary recommended individual item and domain score feedback option was developed (Figure 4). Regarding *individual item feedback*, all items of the item bank are shown (based on the preference of clinicians), with the responses of patients shown in traffic light colors and blank spaces at items that were not administered. Regarding *domain score feedback* separate graphs per domain are shown on one page. The graphs include dots (with numerical domain (T-) scores) connected by a blue line with a background in traffic light colors (heat map), showing the deviation of the reference line in orange (moderate) and red (severe). In addition, on the y-axis the scales are reversely presented for some domains in order to harmonize the directionality of the lines in all graphs (higher is less symptoms or better functioning).

After discussion with the Dutch-Flemish PROMIS National Center and consultation of a data visualization expert, some adjustments were made and a final recommendation was developed (Figure 5). The most important adaptation is that a wider color-palette is used, which was adjusted for people with color-blindness [47]. Additionally, for individual item feedback, colors are now applied to the items based on the item location (difficulty) in the underlying IRT model. For domain score feedback, 95% confidence error bars (included with the scores), an extra cut-off line and y-axis labels (mild, moderate, severe, based on deviation of the reference line) were added.

4a



4b

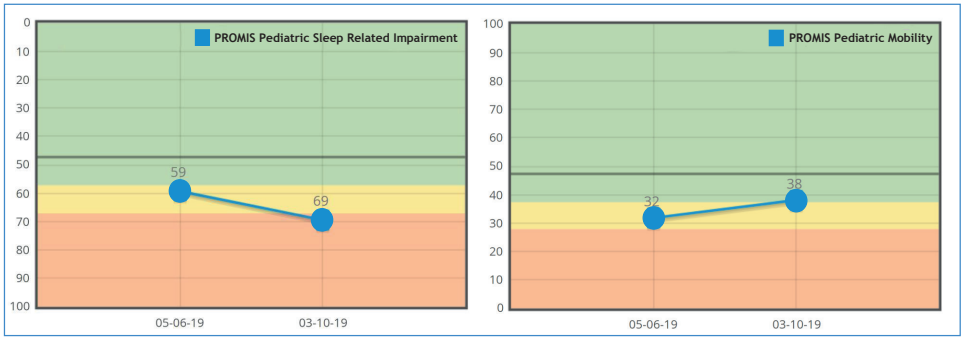


Figure 4. Preliminary recommended individual item (4a) and domain score (4b) feedback of PROMIS CATs
Note. In 4a not all items of the PROMIS Pediatric Mobility item bank are shown.

5a

PROMIS Pediatric Mobility	06-08-2020
I could stand up by myself	Without trouble
I could walk across the room	With some trouble
I could ride a bike	
I could run a mile	With some trouble
I could jump up and down	
I could stand up on my tiptoes	
I could get in and out of a car	
I could keep up when I played with other kids	With a lot of trouble

5c

Individual item feedback recommendations

- All items of the item bank are shown
- Only item responses to administered items are presented
- Colors (adjusted for color-blindness) are applied to item responses
- When applying colors, item location (difficulty) in de underlying IRT model is taken into account
- Item feedback of the final measurement occasion is shown

Domain score feedback recommendations

- PROMIS domain scores are presented in separate graphs but on the same page
- A graph shows all measured scores over time, presented as blue dots connected with lines
- Numerical T-scores are presented with the dots, including (95%) confidence intervals (1.96*SE(T-score)), shown as thin lines.
- Y-axes have different scales, but with the same meaning: higher=better. T-scores are not reversed numerically, as they should be kept on their original scale [48]
- A reference line is shown, representing the average of the general Dutch population per item bank
- Cut-off lines are included to distinguish between mild, moderate and severe complaints per PROMIS item bank (0.5*SD, 1*SD and 2*SD respectively of the general Dutch population scores)
- Background colors change from red to green (heat-map), adjusted for color-blindness
- Background remains the same (reference line is always in the middle), numbers on the y-axis can change

5b

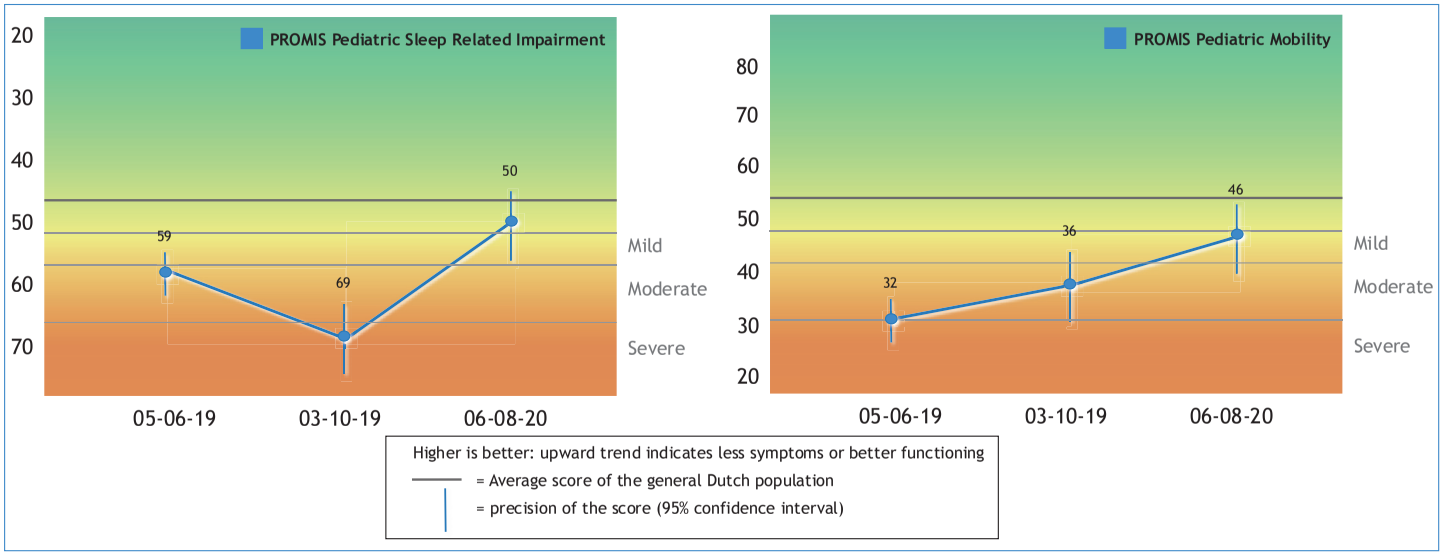


Figure 5. Final recommended individual item (5a) and domain score (5b) feedback of PROMIS CATs including recommendation boxes (5c) [48]

Discussion

To facilitate the use of PROMIS item banks in clinical practice, this study developed preliminary recommendations to feed back PROMIS CATs, on individual item and domain score level. Regarding individual item feedback, results displayed clinicians' preference for showing all items of the item bank. Both clinicians and patients/parents agreed that only responses to administered items (in traffic light colors) and no predicted responses for non-administered items should be shown. Graphs were preferred for domain score feedback, which should include dots connected by lines, numerical domain (T-)scores, and a reference line. Deviating scores should be distinguishable by the use of cut-off lines, dots or the background of the graph in traffic light colors. Separate graphs per domain, ranked in order of importance and harmonization of directionality ('higher is better') were also preferred. To our knowledge, this was the first study that developed feedback options of PROMIS CATs, which is an important step for implementation in clinical practice. Based on the results and after discussion with the Dutch-Flemish PROMIS National Center, a final recommended individual item and domain score feedback option for PROMIS CATs were developed, which was also implemented in the KLIK PROM portal. In this final version color-blindness was taken into account for both individual item and domain score feedback.

Individual item feedback was regarded as essential by clinicians to discuss PROMs in clinical practice as items can be used as a conversation tool and immediately attract clinicians' attention to problems, especially when using traffic light colors. Patients and parents also preferred to see their responses on individual items in the KLIK ePROfile. This finding is in accordance with previous studies on feeding back individual items of PROMs in clinical practice [24, 25, 38].

There are two challenges regarding feeding back individual items of PROMIS CATs. First, clinicians indicated that they preferred the option to see all items of the item bank, where both administered and non-administered items are shown. Even though this option was appropriate for pediatric item banks (maximum of 34 items per item bank), which was the focus of this study, a challenge arises when individual items of adult PROMIS item banks are to be fed back, as these item banks sometimes consist of more than hundred items. A solution could be to only present the responses in traffic light colors of the items that have been administered over time, and not all items of the item bank. This might also be an option for patients and parents, as they indicated they do not necessarily want to see all items of the item bank. For them there is the possibility in for example the KLIK PROM portal to show an adjusted individual item feedback option. The second challenge is the use of traffic light colors for item responses. In the preliminary individual item feedback option developed in this study, colors were applied to item responses based on the response category (i.e. responses "without trouble" are always shown in green and responses "with a lot of trouble" are always shown in red). An alternative – implemented in the final recommendation – is to take the item location (difficulty) of the underlying IRT model into account. For example, the response "with a lot of trouble" of a very 'difficult' item (e.g., "I could run a mile") may not necessarily indicate a problem and would not be presented in red.

Regarding domain score feedback, a strong preference of clinicians was found for graphs, as graphs can easily display longitudinal data, which was reported in previous

studies as well [22, 26-32]. All other options like tables, textual reports or symptom cards were immediately discarded, which is in contrast with earlier research [22, 31, 33-35, 38-41]. Reasons reported in the focus groups were that these alternatives take more time to interpret, are more difficult to discuss with the patient and cannot present more than two measurement occasions without losing overview. All other features that were reported as important, e.g., reference to a norm group, highlighting deviating results, harmonization of directionality and ranking graphs in order of importance, are in accordance with previous literature on PROM feedback [22, 28-31, 36, 37].

There are three challenges regarding domain score feedback. First, clinicians indicated they preferred to see a reference line in the graph, including cut-off points to judge the severity of deviation. However, which reference line and cut-off values should be fed back is a point of discussion. They can be based on the US metric (reference score of 50 and SD of 10) or based on the average scores of the country-specific general population (reference score and SD differ a little bit per item bank). Additionally, how many cut-off points should be shown? And what labels should be included? In the final recommended domain score feedback option we chose to include the average and SD of the general Dutch population. Three cut-off points with labels 'mild', 'moderate' and 'severe' were chosen (based on 0.5*SD, 1*SD, and 2*SD) in accordance with the suggested score interpretations on the Healthmeasures website (www.healthmeasures.net). However, these cut-offs could be adapted once, for example, bookmarking study results (cut-offs based on patient input) are available. Second, for the ranking of graphs in order of importance, it should be further explored whether ranking should be based on deviation of scores from the reference group, on relevance of the domain for the patient or clinician, or based on recent changes in scores. Third, no consensus was reached in the focus groups on how to indicate deviating scores (either dots, cut-off lines or background in traffic light colors). The background coloring (heat map) with cut-off lines was chosen as final recommendation, as this is easiest to comprehend and takes least time to interpret. This point however, needs to be discussed and evaluated again in the future.

There are some limitations to this study that should be mentioned. First, the sample could be biased as both clinicians and patients/parents were KLIK users and they were thus already used to the feedback that is currently provided for other PROMs. This might have influenced their opinion about their optimal feedback option, which is visible in the similarities between the recommended feedback options and the feedback options used in KLIK. However, as the findings are in accordance with previous literature and as clinicians also came up with new important features that are currently not available in KLIK, it can be assumed that the developed feedback option represents the opinion of a wider audience. Second, the clinician sample was somewhat skewed and consisted mainly of medical doctors. However, this is representative of the disciplines that use KLIK in clinical practice, where medical doctors are also the main user group. Only nurses were relatively underrepresented. Third, response rates for the questionnaire were low and only a small number of pediatric patients participated. Even though reminder emails were sent, future studies could consider to approach patients by telephone or emphasize the importance of their participation more to increase the response rates. Fourth, patients' and parents' perspectives were not optimally taken into account by using a questionnaire

only. For example, it was difficult to explain the working mechanism of PROMIS CATs to patients and parents in a questionnaire and to verify their understanding of the concept. Especially from the responses of patients in the explanation boxes this lack of understanding was noticed, and this might explain the non-conclusive results regarding the questions about not answered items and predicted responses. In addition, they could only provide their opinion about individual item feedback, as domain score feedback is currently not shown to patients and parents in KLIK. Since several studies have shown patients' and parents' preference for viewing domain score feedback for other PROMs [22, 26, 29, 30, 32, 33], we decided to include domain score feedback (without reference lines) for patients and parents in KLIK in the near future. In future, preferably qualitative studies, the developed recommendations (especially the domain score feedback) should then be discussed with patients and parents as well.

Conclusions

In conclusion, this study developed recommendations for feedback options for PROMIS CATs. Based on the preferences of clinicians and patients/parents and discussion with the Dutch-Flemish PROMIS National Center, an individual item and domain score feedback option were developed. In future studies, the current recommendations should be investigated with clinicians, patients and parents on interpretation accuracy and effectiveness in clinical practice. The availability of these feedback options facilitates using PROMIS CATs in clinical practice. With CAT, patients only have to complete a small number of items per domain that are applicable to their situation, which reduces the burden of completing PROMs significantly. For clinicians the developed simple and clear feedback of PROMIS CATs might help in monitoring and discussing patient outcomes, which contributes to optimal care for patients.

List of abbreviations

PROMs; Patient Reported Outcome Measures
HRQOL; Health Related Quality of Life
PROMIS®; Patient-Reported Outcomes Measurement Information System
IRT; Item Response Theory
CAT; Computerized Adaptive Testing
Amsterdam UMC; Amsterdam University Medical Centers
SPSS; Statistical Package for Social Sciences
SD; Standard Deviation

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Competing interests

The authors declare that they have no competing interests.

Ethical approval and Consent to participate

All procedures performed in this study were in accordance with the ethical standards of the international and/or national research committee (Medical Ethics Committee of the Amsterdam UMC, location AMC – reference number W18_023 # 18.034 and W19_272 # 19.324) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication

Informed consent was obtained from all individual participants included in this study.

Availability of supporting datadata and supporting materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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CHAPTER 9

General discussion

Several barriers for using and implementing PROMs in clinical practice were identified in literature and during the implementation process of the KLIK PROM portal. The aim of this thesis was to overcome several of these barriers, with the ultimate goal to optimize the use of PROMs in clinical practice. This was done by gaining insight into the implementation of PROMs in clinical practice from the clinicians' and patients/parents' perspective (Part 1), and optimizing PROM use in clinical practice by dashboard improvement, PROM improvement, and empowering patients and parents (Part 2).

This chapter includes a reflection on the main findings, the clinical implications, methodological considerations, and the current implementation of the optimized KLIK PROM portal. Additionally, further steps and remaining barriers for PROM implementation are discussed, and directions for future PROM implementation and research are provided.

Main findings

Part 1: Stakeholders' perspective on PROM use in clinical practice

To overcome the barrier of not systematically involving clinicians and patients, the first part of this thesis provided insight into the experiences of clinicians, patients and parents with the use of the KLIK PROM portal in daily clinical practice (Table 1). **Chapter 2** focused on clinicians; they were generally satisfied with discussing PROMs in clinical practice using the KLIK PROM portal. However, several barriers were also mentioned: no integration of KLIK with the EHR, irrelevant and long PROMs, low response rate of patients and parents, and using and discussing PROMs takes time. In **Chapter 3** the perspective of patients and parents was shown; they were satisfied with the use of KLIK, but the following barriers were mentioned: long, repetitive and irrelevant PROMs, no discussion of PROMs by the clinician, no integration with the EHR, no KLIK app available, suboptimal lay-out of the KLIK website, and not daring to start the discussion about PROMs themselves when the clinician does not discuss PROMs.

Table 1. Overview of studies and main findings of this thesis in part 1.

Chapter	Aim	Sample	Measures/content	Main findings/conclusions
2	To gain insight into clinicians' perspective on the use of PROMs using the KLIK PROM portal in clinical practice.	Users of the KLIK PROM portal: - N=148 clinicians from 14 hospitals in the Netherlands completed the evaluation questionnaire	- Online evaluation questionnaire (24 questions) regarding: 1) overall satisfaction, 2) feeling competent to discuss PROMs, 3) use of KLIK during the consultation, 4) influence of KLIK on the consultation, 5) usability of the KLIK PROM portal, 6) satisfaction with PROMs and feedback, 7) support of the KLIK expert team. Open questions about barriers for using PROMs in KLIK.	1. Clinicians are generally satisfied with KLIK. 2. A large percentage (85.8%) of clinicians feel competent to discuss the KLIK ePROfile. 3. 70.3% (almost) always discuss the KLIK ePROfile. 4. KLIK improves the consultation according to 70.3%. 5. 71.6% of clinicians think KLIK is easy to use. 6. Most clinicians (80.4%) are satisfied with the feedback in the KLIK ePROfile. 7. Clinicians (71.6%) experience enough support of the KLIK team. Barriers for using PROMs were no integration of KLIK with the EHR, irrelevant and long PROMs, low response rate, and takes time.
3	To gain insight into patients' and parents' perspective on the use of PROMs using the KLIK PROM portal in pediatric clinical practice.	Users of the KLIK PROM portal: - Patients (12-19y): N=8 participated in focus groups, N=31 completed the questionnaire - Parents (of children 0-19y): N=17 participated in focus groups, N=130 completed the questionnaire	- Focus groups to obtain patients' and parents' opinion about KLIK. - Online evaluation questionnaire (19 questions) regarding: 1) overall satisfaction, 2) completion of PROMs in the KLIK PROM portal, 3) discussing PROMs with the clinician, 4) influence of KLIK on (preparation of) the consultation, 5) usability of the KLIK PROM portal, 6) content of PROMs. Open questions about barriers for using PROMs in the KLIK PROM portal.	- Focus groups: Patients and parents are generally satisfied with the use of PROMs using the KLIK PROM portal Patients mentioned that KLIK has an attractive lay-out and parents valued that KLIK provides insight into their child's functioning. - Questionnaire: 1. Patients and parents report a satisfaction score of 7.9/10 and 7.3/10. 2. 90% of patients and 95% of parents (almost) always complete PROMs. 3. The KLIK ePROfile is (almost) always discussed by the clinician according to 52% of patients and 45% of parents. 4. KLIK is of added value for the conversation with the clinician according to 58% of patients and 59% of parents. 5. 81% of patients and 74% of parents indicate that KLIK is easy to use. 6. Most patients (80%) and parents (74%) are satisfied with the PROMs they complete. Barriers for using PROMs reported in focus groups and questionnaire: PROMs sometimes long, irrelevant and repetitive, no discussion of PROMs by clinician, no integration with the EHR, no KLIK app available, suboptimal lay-out website, not daring to start discussion about PROMs themselves.

In part 1 several barriers for using PROMs were identified based on input of clinicians, patients, and parents (Table 2). In part 2 several of the these identified barriers (long and irrelevant PROMs, not daring to start discussion about PROMs) as well as barriers identified in the literature and during KLIK PROM implementation (suboptimal PROM visualization, burdensome PROMs and missing supportive tools) were addressed, resulting in *dashboard improvement*, *PROM improvement*, and *patient/parent empowerment*. Remaining barriers are discussed later in this chapter.

Table 2. Barrier levels and identified barriers for using and implementing PROMs in clinical practice in literature and the KLIK implementation process, and based on clinicians' and patients/parents' perspective

Barrier level	Barriers identified in literature	Barriers identified during KLIK implementation process	Barriers identified based on clinicians' perspective	Barriers identified based on patients/ parents' perspective
Clinicians	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training	**- Not systematically involved in implementation of PROMs** - No information on available psychosocial interventions	- Takes time	- No discussion of PROMs by clinician
Patients/ parents	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training - Lack of focus on patients with lower health literacy or language proficiency	**- Not systematically involved in implementation of PROMs** - Supportive tools/ training for discussing PROs missing - No information on available psychosocial interventions	- Low response rate	- Not daring to start discussion about PROMs
PROM system	- Non-automated PROM data collection system - No integration of PROM data collection system in EHR - Suboptimal and complex PROM visualization in dashboard	- No integration with EHR - Suboptimal PROM visualization in dashboard - Suboptimal use on mobile phone or tablet	- No integration with EHR	- No integration with EHR - No KLIK app available - Suboptimal lay-out
PROMs	- Burdensome PROMs - PROM scores not comparable due to different scoring methods	- Burdensome PROMs	- Irrelevant and long PROMs	- Long, irrelevant and repetitive PROMs

Note. Barriers in **bold** were addressed in part 1.

Part 2: Optimization of PROM use in clinical practice

Dashboard improvement

To overcome the barrier of suboptimal PROM visualization in dashboards (KLIK ePROfile), new reference lines were necessary in the KLIK ePROfile to aid interpretation for clinicians. In **Chapter 4** normative data of a HRQOL PROM was therefore collected for the Dutch general population and a pediatric population, which became available for

use as reference lines. Furthermore, by analyzing and comparing the two samples, it was shown that pediatric patients reported worse HRQOL than the general population, and factors associated with worse HRQOL were school absence, female gender and younger age (Table 3).

PROM improvement

To overcome the barrier of burdensome PROMs due to questionnaire length and irrelevancy and repetitiveness of questions, the PROMIS pediatric measures can be used, preferably as computerized adaptive test (CAT). These measures were previously translated into Dutch-Flemish [1] and validated in a Dutch clinical sample [2]. However, validation in a general population sample was necessary to provide reference data for research studies and clinical practice. Therefore, in 2018 our research group started the validation process of 8 Dutch PROMIS pediatric measures. This thesis investigated the validity and reliability of the PROMIS pediatric Anger scale (**Chapter 5).** This measure displayed sufficient psychometric properties within the Dutch population, and we provided reference data. **Chapter 6** subsequently focused on the use of the PROMIS pediatric measures and its reference data in research. In our COVID-19 study, children completed 6 PROMIS measures, including the Anger scale. Children reported worse mental and social health during the COVID-19 lockdown compared to before. Single-parent families, having three or more children in the family, a negative change in work situation of parents, and having a relative/friend infected with COVID-19 were factors associated with worse mental and social health. Thereafter, to be able to use the PROMIS CATs in clinical practice, **Chapter 7** described the development of new visualization options of PROMIS CATs. New visualizations were necessary as with CAT not all items are administered, domain scores are calculated differently and an evidence-based visualization was missing. On individual item level, showing all items of the item bank, with only responses to administered items in traffic light colors was preferred. On domain score level, line graphs including numerical T scores, reference and cut-off lines, and traffic light colors were preferred.

Patient/parent empowerment

Although PROMs facilitate the discussion of PROs in clinical practice, patients and parents still reported to find it difficult to discuss certain PROs and initiate discussion about PROM outcomes themselves. To overcome this barrier, **Chapter 8** provided insight into difficult yet important PROs to discuss for patients and parents (e.g., future perspectives, mental functioning, sexuality) and into perceived barriers (presence of parents/child, forgetting to discuss PROs, time pressure) and facilitators (talking to the clinician in private and preparation of the consultation) for discussing these PROs. The outcomes informed the development of two tools (educational video and topic list), that aim to support and empower patients and parents in discussing difficult yet important PROs during consultation.

Table 3. Overview of studies and main findings of this thesis in part 2.

Chapter	Barrier / Optimization	Aim	Sample	Measures/content	Main findings/conclusions
4	**Suboptimal PROM visualization** **Dashboard improvement**	To collect new normative data of a HRQOL PROM of the Dutch general population and a pediatric population to add as reference lines to the KLIK ePROfile, and: 1. Compare HRQOL of pediatric patients with the Dutch general population. 2. Explore responses to individual HRQOL items. 3. Investigate variables associated with HRQOL.	Samples of children (8-12y) and adolescents (13-17y): - Representative of the Dutch general population: N=966 - Emma Children's Hospital: N=1209	- Sociodemographic questionnaire - Pediatric Quality of Life Inventory (PedsQL™)	1. Pediatric patients reported significantly worse HRQOL than the general population on all PedsQL™ scales, except social functioning. 2. A high proportion of pediatric patients reported problems on PedsQL™ items. 3. Younger age, female gender and school absence were negatively associated with HRQOL. As a result, normative PedsQL™ data has become available for the Dutch general population and a pediatric population, which were implemented in the KLIK PROM portal as reference lines in the PedsQL™ graphs.
5	**Burdensome PROMs** **PROM improvement**	To investigate psychometric properties of the PROMIS pediatric v2.0 Anger scale in the Dutch general population and provide reference data.	Sample of children and adolescents (8-18y) representative of the Dutch general population: - N=527	- Sociodemographic questionnaire - Patient-Reported Outcomes Measurement Information System (PROMIS®) pediatric v2.0 Anger scale - Pediatric Quality of Life Inventory (PedsQL™)	1. Structural validity of the PROMIS pediatric Anger scale was sufficient, as no items displayed misfit. Regarding construct validity, a moderate correlation was found between the Anger scale and the PedsQL emotional functioning subscale score. 2. A Dutch mean T-score of 44.2 (SD=11.39) was found, with cut-offs of >52.2 for moderate and ≥62.3 for severe symptoms. 3. Reliable measurements were obtained at the population mean and >2SD in the clinically relevant direction, and CAT outperformed all other measures in efficiency. As a result, reference data became available, which can be used in research and clinical practice.

Chapter	Barrier / Optimization	Aim	Sample	Measures/content	Main findings/conclusions
6	**Burdensome PROMs** **PROM improvement**	To apply PROMIS CATs and reference data in a COVID-19 study by: 1. Comparing mental/social health between two samples before and during COVID-19 lockdown on six PROMIS domains. 2. Comparing the proportion of severe scores on PROMIS domains between the before and during COVID-19 sample. 3. Exploring variables associated with worse mental/social health during COVID-19. Assessing the impact of COVID-19 regulations on daily life of children qualitatively.	Samples of children and adolescents (8-18y) representative of the Dutch general population: - Before COVID-19 lockdown: N=2401 - During COVID-19 lockdown (April 2020): N=844	- Sociodemographic questionnaire - Patient-Reported Outcomes Measurement Information System (PROMIS®) pediatric item banks/scales: V1.0 Global Health (7+2) Scale, V2.0 Anger Scale, V2.0 Peer Relationships CAT, V1.0 Sleep-Related Impairment CAT, V2.0 Anxiety CAT, and V2.0 Depressive Symptoms CAT - Three COVID-19-related additional questions	1. Participants reported worse PROMIS T-scores on all PROMIS domains during COVID-19 lockdown compared to before. 2. During COVID-19 lockdown, more children reported severe anxiety and sleep-related impairment, and fewer children reported poor global health. 3. Associated factors with worse mental/social health during COVID-19 were single-parent families, having three or more children in the family, a negative change in work situation of parents due to COVID-19 regulations, and having a relative/friend infected with COVID-19. 4. A large majority of children/adolescents reported a negative impact of the COVID-19 regulations on daily life.
7	**Burdensome PROMs** **PROM & Dashboard improvement**	To develop recommendations for visualization options for PROMIS CATs on individual item and domain score level.	Users of the KLIK PROM portal: - N=28 clinicians - N=31 patients (12-18y) - N=131 parents (child 0-18y)	- Focus groups to obtain clinicians' input on PROMIS CAT feedback by showing four options for individual item and five options for domain score feedback. - Online questionnaire (3 questions) to assess patients' and parents' preference for individual item feedback.	- Focus groups: Regarding individual item visualization, clinicians preferred showing the complete item bank, with only responses to administered items in traffic light colors. For domain scores, line graphs were preferred, including numerical T-scores, reference and cut-off lines, and traffic light colors. Separate graphs per domain, ranked in order of importance and harmonization of directionality (higher=better) were considered important. - Questionnaire: The majority of patients and parents preferred to view their own item responses above receiving no item feedback. Based on the outcomes and after discussion with the Dutch-Flemish PROMIS National Center, recommendations for PROMIS CAT visualization options were developed, which were also implemented in the KLIK PROM portal.

Chapter	Barrier / Optimization	Aim	Sample	Measures/content	Main findings/conclusions
8	**Supportive tools for discussing PROs missing** **Patient/parent empowerment**	1. To gain insight into difficult yet important PROs to discuss for pediatric patients and parents, and into perceived barriers and facilitators 2. To subsequently inform the development of supportive tools for discussing PROs during consultation.	Users of the KLIK PROM portal: - Patients (12-19y): N=8 participated in focus groups, N=31 completed the questionnaire - Parents (of children 0-19y): N=17 participated in focus groups, N=130 completed the questionnaire Stakeholders (patients, parents, patient associations, researchers, psychologists, medical communication expert, developers tools): - N=21 evaluated the drafts of the educational videos - N=7 evaluated first version educational videos - N=8 evaluated first version topic lists	A two-step mixed-method design: 1. Identification difficult yet important PROs, barriers and facilitators and input on supportive tools using: a. Focus groups b. Online questionnaire (8 questions) 2. Development supportive tools by: a. Drafting and evaluating with stakeholders first versions supportive tools b. Developing supportive tools	1. Difficult yet important PROs, barriers and facilitators, input supportive tools (focus groups/questionnaire): - Most difficult yet important PROs to discuss for pediatric patients and parents were: future perspectives, home situation/family, sexuality and body perception, mental functioning, and medication use/treatment of the condition. - Perceived barriers were presence of parents/child, time pressure, forgetting to discuss PROs, feelings of shame, and ignoring attitude of clinicians. - Perceived facilitators were talking to the clinician in private and preparation of consultation. - Regarding the content of the tools, communication tips, information on consultation preparation, indicating which PROs could be difficult, statement one can say everything to clinician should be provided. Regarding the type of tool, online short videos and topic lists were mentioned. 2. a. It was decided to develop online educational animation videos and topic lists as supportive tools. Drafts were developed and evaluated with stakeholders, and minor changes were made regarding language use. b. Final versions of the educational videos and topic lists were developed and are available online.

Reflection on the findings & clinical implications

Stakeholders' perspective on PROM use

Clinicians as well as patients/parents were in general quite satisfied with using the KLIK PROM portal and reported the following advantages: the PROMs provide insight into the patients' functioning, improve patient-clinician communication, more topics are discussed and problems are earlier detected. The use of KLIK is easy and helps in preparing for the consultation. However both groups also mentioned several barriers (Table 2). Interestingly, clinicians reported a low response rate of completing PROMs by patients/parents, while patients and parents mentioned a low PROM discussion rate of clinicians. These two points probably influence each other, as it was shown that patients and parents saw no added value of using the KLIK PROM portal when clinicians do not discuss the PROM outcomes, which subsequently may result in low response rates.

The identified advantages of using the KLIK PROM portal in clinical practice are in accordance with other studies on the use of PROMs performed both in clinician and adult patient populations, especially regarding the insight that is provided into patients' functioning and improved patient-clinician communication [3-11]. The identified barriers were also reported in previous studies focusing on identifying barriers for using PROMs [12-18] and studies taking into account the perspectives of clinicians and adult patients [3-7, 11, 19, 20].

Our study was one of the first that took the perspective of pediatric patients and parents regarding PROM use in clinical practice into account. Only recently, some studies focused on the perspective of pediatric patients and their parents on the use of PROMs in clinical practice for specific conditions (solid organ transplantation and diabetes) [21, 22]. Improved patient/parent-clinician communication and better insight into patients' functioning were also mentioned as positive aspects of using PROMs, while the fixed structure of PROMs and long PROMs were reported as barriers.

Involving all stakeholders, especially patients, is thus essential for successful implementation of PROMs in clinical practice, and therefore we will in the future continuously evaluate the use of PROMs using the KLIK PROM portal with all stakeholders to match their needs and make improvements where necessary.

Dashboard optimization

The visualization of PROM outcomes in the KLIK dashboard was originally developed based on input of clinicians and consisted of literal representations of individual items (using traffic light colors) and graphs including a reference line of the healthy population [23, 24]. Over the years, it evolved into a broader spectrum of visualization options where summary scores and more graphical options such as cut-off threshold lines and pictures are also used [25]. All developments in PROM visualization in the KLIK dashboard were performed in accordance with existing literature. For example, research showed that line graphs are the preferred and best interpreted visualization formats [26], and that the inclusion of cut-off threshold lines or reference lines aids interpretation of concerning scores [27, 28]. Additionally, clear labeling of the graph axes, using (traffic light) colors and harmonization of directionality (higher is better) are all important aspects [5, 29, 30]. Our study showed that clinicians prefer to use the visualization of individual items.

Although the visualization of individual items is less studied in literature, the few studies conducted indicated that it immediately attracts clinicians' attention to specific problems, especially when using colors [31, 32].

Regarding the use of reference lines in graphs, it was recognized that this needed to be optimized for the most often used generic HRQOL PROM (PedsQL™) in the KLIK dashboard. Normative data of this PROM was outdated and representativeness for the general population was lacking, and there was a wish for reference information of a pediatric population. Therefore, new normative data of the PedsQL was collected of a general population that was representative on key demographics and HRQOL data of a pediatric population was analyzed. These new normative PedsQL data were thereafter implemented as gender and age-specific reference lines in the KLIK dashboard. Additionally, an option to switch on or switch off reference lines was built into the KLIK dashboard, so clinicians can choose themselves with which group they want to compare the individual patient. In line with this optimization, the training for clinicians was updated with more information on these visualizations and meaning of outcomes. This is very important, as a recent study showed that clinicians had the highest preference for more information on interpretation of PROM data in a training [33]. These improvements will aid in interpretation of PROM outcomes for clinicians, which subsequently leads to more optimal use of PROMs in clinical practice.

PROM improvement

To overcome the barrier of burdensome PROMs, the generic PROMIS CATs and scales, measuring physical, mental and social health domains were introduced in part 2. First, a validation study of one of the PROMIS measures, the PROMIS pediatric Anger scale, was performed, where it was shown that this scale performed very well in the Dutch general population. Results were in line with the results of the validation study in the clinical sample [2] and in the development study of this scale in the U.S. [34]. Viewing these outcomes in light of the broader validation studies of the Dutch-Flemish PROMIS pediatric measures, results are also comparable [35, 36]; the PROMIS pediatric item banks and scales show sufficient validity and reliability, and are most efficient when applied as CAT.

As a result of these validation studies, reference data became available and the PROMIS pediatric measures were implemented in the KLIK PROM portal. This was done by linking the KLIK PROM portal with an application programming interface (API) to the Dutch-Flemish Assessment Center (www.dutchflemishpromis.nl), by which the two systems can communicate with each other and CAT was facilitated. From then on, the PROMIS measures in KLIK could be used for pediatric research, which we did in our COVID-19 study. Here it was shown that the PROMIS measures can be efficiently used when you want to gain insight into several PROs in a short period of time, while not burdening respondents too much. Therefore, PROMIS CATs are now completed on the KLIK PROM portal in many other research projects (e.g., COVID-19 follow-up studies, hemophilia research study, diabetes study, pediatric oncology study).

Finally, new visualization options for PROMIS CATs were developed based on input of clinicians and pediatric patients and parents. The findings were in line with existing literature [5, 23-30]. Clinicians and patients/parents preferred to see individual item

visualization using traffic light colors. For domain score visualization, line graphs including reference lines and cut-off thresholds, where directionality is harmonized into 'higher is better' were preferred. These visualizations were implemented in the KLIK PROM portal, and thereafter, the PROMIS measures could also be used in clinical practice. Currently, more than 10 patient groups (e.g., neonatology, vascular malformations, sickle cell disease) in several hospitals use the PROMIS CATs through the KLIK PROM portal in clinical practice, and this number is only increasing.

The use of the PROMIS measures in both research and clinical practice fits in well with the shift towards using generic PROMs, that is present in the Netherlands (within Uitkomstgerichte Zorg, www.platformuitkomstgerichtezorg.nl), and internationally as well. It was shown in a study that there is currently considerable overlap in PROs across condition-specific Standard Sets developed by the International Consortium for Health Outcomes Measurement (ICHOM) and that many different PROMs are recommended to measure the same PROs [37]. Additionally, they found that all PROs, 307 in total, could be categorized into 22 unique PRO concepts, of which 17 could be measured with PROMIS measures. The authors thus recommend a more universal and standardized 'generic unless' approach to the selection of PROs and PROMs, where the PROMIS measures could be used as a core generic set, which can be supplemented with disease-specific PROMs where necessary. This subsequently will facilitate the uptake and use of PROMs in clinical practice. We therefore also see great promise in PROMIS.

Patient/parent empowerment

During the implementation process of the KLIK PROM portal, we recognized that when the clinician does not discuss the KLIK ePROfile during consultation, pediatric patients and parents do not bring up important PROs themselves. This finding was confirmed in our study on the perspectives of patients and parents, where it was shown that quite a large percentage of patients and parents did not dare to bring up for them important PROs when the clinician did not discuss PROM outcomes. This is worrisome, as then using PROMs with the KLIK PROM portal does not facilitate communication, while patient-clinician communication is suggested to be an important mediator in the effects PROMs can have [38].

For clinicians and adult patients several programs and tools were therefore already developed that train and support them in discussing PROs and to improve patient-clinician communication [39-46]. However, tools that can support pediatric patients and their parents in communicating with the clinician and in initiating PRO discussion during consultation were missing. We therefore first investigated what PROs are difficult yet important to discuss for patients and parents, and what factors negatively or positively influence the discussion of these PROs, which would be the basis for the development of supportive tools. The participants were already experienced users of the KLIK PROM portal, and we were therefore interested if they would report different PROs and barriers and facilitators than previous studies, as they might already have been adjusted to discussing certain PROs with the clinician. However outcomes were similar to the few previously performed studies; future perspectives, sexuality, home situation/family functioning, and mental functioning were reported to be important and difficult to discuss [47-50], and perceived barriers were presence of parents/child, time pressure,

forgetting to discuss PROs, and a closed attitude of the clinician [48, 51, 52].

We developed two supportive tools; educational videos and topic lists, which are freely available online. The supportive tools were shared on websites that are often visited by pediatric patients and parents, such as the Cyberpoli (www.cyberpoli.nl), Kind&Ziekenhuis (www.kindenziekenhuis.nl) and (Sch)ouders (www.schouders.nl) to create visibility. When the supportive tools are used by patients and parents, they hopefully empower and support them during consultation to discuss PROs they find difficult and important and to bring up PROs in case the clinician does not discuss PROM outcomes with them. This might subsequently contribute to optimal patient/parent-clinician communication in which PROM outcomes and PROs are discussed and shared-decision making is facilitated, and the PROM completion rate is increased. For the clinician, there are also some implications; they should realize that there are difficult PROs for patients/parents and that it is essential that they give the chance to ask questions, and provide support in discussing PROs. This should therefore be included and underlined in the training we provide to clinicians.

Educating and involving patients and parents is thus essential for optimal implementation of PROMs. Other options that may help in increasing PROM completion rates, already taken care of for the KLIK PROM portal, are information letters that are sent to patients and parents explaining the rationale and method for completing PROMs, having a clear and informative patient-facing website with specific information for patients and parents, and providing printed brochures or folders (www.healthmeasures.net).

Additional findings

Patient Reported Outcomes

In addition to optimizing the use of PROMs in clinical practice, two studies also provided insight into HRQOL of a pediatric population and mental and social health of the general Dutch population during COVID-19. It was shown that pediatric patients who complete PROMs in clinical practice using the KLIK PROM portal, reported worse HRQOL than the general population, which was in line with previous studies [53, 54]. Furthermore, we found that during the first COVID-19 lockdown (April 2020), children reported worse mental and social health, and that more children reported severe anxiety and sleep problems. As we were one of the first research groups that measured mental and social health in children and adolescents just after the first COVID-19 lockdown was implemented in the Netherlands, not many comparable studies were available then. Our results were however in line with the few studies that were already performed [55-58]. Over the course of the pandemic, more studies were published, which all pointed in the same direction; mental and social health of children and adolescents is affected [59, 60]. Interestingly, a similar COVID-19 study from our research group among pediatric patients that use KLIK in clinical practice, showed that they reported less problems on mental and social health during the COVID-19 lockdown compared to a psychiatric and general population sample [61]. Similar results were found in a COVID-19 study among pediatric oncology patients [62]. This might be explained by the fact that they may already have developed more adaptive coping strategies due to previous confrontation with stressful

events and restraints in daily life, or because the lockdown regulations might have been less invasive for them as they already are used to living with restrictions.

In both studies associated variables were investigated. For pediatric patients, variables associated with worse HRQOL were younger age, female gender and school absence. For children during the COVID-19 lockdown, family composition (single parent families and having three or more children in the family), loss of work of parents due to COVID-19, a COVID-19 infection in the family, and younger age were associated with worse mental/social health. Similar associations have been found in previous HRQOL studies among pediatric patients and in other mental/social health studies during COVID-19 [57, 63, 64], although there were mixed findings on the association with age [53, 57, 59, 64].

Living with a chronic condition or in a situation where a pandemic dominates society was thus shown to have a substantive impact on outcomes of pediatric patients and children of the general population. These results underline the importance to structurally pay attention to these problems, for example by monitoring pediatric patients using PROMs to detect problems and provide immediate support or refer to the appropriate resources when necessary. Or by taking the outcomes for children during the COVID-19 pandemic into consideration in political decision making and future policy regarding pandemics or lockdowns to 1) determine regulations for children specifically, and 2) to properly organize mental health care, also regarding intervention and prevention, at an early stage.

Methodological considerations

Some overall limitations should be taken into account when looking at the findings described in this thesis.

Representative samples of clinicians and patients

In many of the chapters in this thesis, patients, parents or clinicians were included as participants to gain insight into their perspective or to measure their functioning. Although we aimed to include a wide variety of participants in every study, it should be noted that there might have been question of bias in the samples. Not all clinicians who use KLIK wanted to participate in the evaluation meetings and focus groups resulting in a skewed sample with more doctors participating than other disciplines (e.g., nurses, psychologists). However, this is representative of the disciplines that use KLIK in clinical practice, where medical doctors are also the main user group. Moreover, regarding patients that were included, no purposive sampling method could be used due to practical reasons, by which spread in for example age, gender, region, and chronic condition could not be ensured. Additionally, the fact that in two studies participants (both patients/parents and clinicians) were all KLIK users, might have influenced the input they provided on the visual feedback options and the difficult PROs and experienced barriers they mentioned respectively. As this thesis and research focused on pediatric patients and their parents, as well as on PROM implementation in pediatric clinical practice, it is hard to generalize these outcomes to adult care. However, our results were in line with previous literature on dashboards, discussing PROs, and barriers experienced for implementation of PROMs in adult care, which suggests that being a child, parent and/or KLIK user did not influence the outcomes substantively.

Representative samples of the Dutch population

In three studies, data of very large general population samples was collected or used. Although we tried to get as representative as possible samples by using a two-step stratified sampling technique, taking into account key demographics, it remains difficult to reach everybody. Examples are people with low language proficiency or that have no access to a computer or internet. This is a common issue in PROM research and real-world implementation as well.

Patient participation

Although we tried to include patients' and parents' perspectives optimally by using a mixed-method design, it is always difficult to motivate patients and parents to complete questionnaires or to participate in the focus groups only for research purposes. Second, patients needed some guidance in the focus groups to express and formulate their opinion, especially the younger patients, which might have led to a bias in the results. Therefore also questionnaires were used in these studies to see if focus group outcomes were confirmed, which was the case. Finally, patients' and parents' perspectives might not have been optimally taken into account regarding PROMIS CAT visualization using a questionnaire only, and in the development process of the supportive tools by asking feedback through e-mail.

Comparing samples

In the two large cross-sectional studies, two samples were compared on HRQOL and mental/social health outcomes respectively. However, in both studies, the data collection of the two samples took place on different time scales and seasons. Seasonal variations might thus partly have accounted for the differences that were found between the samples, as it is known that worse mental health is reported during winter times [65]. However, for our studies this could only have led to an underestimation of the difference in HRQOL or mental/social health between the samples, as in both studies only the comparison group was measured during winter time. Additionally, significant differences were detected between samples on sociodemographic characteristics. However, these differences were very small and corrected for in the analyses.

Further implementation of the KLIK PROM portal in clinical practice

The optimized KLIK PROM portal

Since 2017, after the start of the project funded by the Dutch National Healthcare Institute and this thesis, the KLIK PROM portal has developed further and enormous steps have been taken in four years (Table 4). The goal to optimize and further implement PROMs in clinical practice can thus be considered attained. Probably the barriers that have been overcome in this thesis, have contributed to this.

Table 4. Development of usage of the KLIK PROM portal from 2017 to 2021

	2017	2021
Patients using KLIK	>7000	>27500
Patient groups using KLIK	>35	>70
Clinicians trained in using KLIK	>500	>1700
Hospitals using KLIK	17	37

Next to the optimizations that were performed and described in this thesis (Table 5), other identified barriers were also addressed by the KLIK team. First, **a front-end (hybrid) integration with EHRs** has been realized between the KLIK PROM portal and two often used EHRs in the Netherlands; Epic© and Hix© in three hospitals. Clinicians can now view the KLIK dashboard in the EHR, and do not need to open two separate systems.

Second, a **mobile phone version of the KLIK PROM portal** was developed, by which patients and parents can complete PROMs on their tablet or smartphone.

Third, an **upgrade of the lay-out of the KLIK PROM portal** was performed, by changing the design of the website (using more visuals and creating a more professional look), and specific information pages were developed for all KLIK users (pediatric patients, parents, adult patients and clinicians).

Fourth, an **intervention report with all available psychosocial interventions** for pediatric patients, their siblings and parents was developed, and made available on the KLIK website. This may help clinicians in referring to the right help or interventions when problems are detected. Additionally, links to the informative websites of these interventions were integrated in the information pages for patients and parents.

Finally, the KLIK PROM expertise team was previously set up to support the implementation and use of PROMs in clinical practice. By giving webinars and contributing to conferences, our **knowledge on PROM implementation is spread** and shared with other people interested in using PROMs in clinical practice. Since recently, we are also involved as experts in the PROM expertise center of the Amsterdam UMC, to support the implementation of PROMs in the entire Amsterdam UMC. Furthermore, on a national level, as part of Uitkomstgerichte Zorg (www.uitkomstgerichtezorg.nl), we support the development of the generic PROM set and we act as coaches to implement PROMs in other hospitals. On an international level, we are affiliated with ISOQOL (www.isoqol.org) and the PROTEUS initiative (www.proteus.uk) to share our experience and knowledge on PROM implementation and developed tools with others.

Table 5. Barrier levels and identified barriers for using and implementing PROMs in clinical practice in literature and the KLIK implementation process, and based on clinicians' and patients/parents' perspective

Barrier level	Barriers identified in literature	Barriers identified during KLIK implementation process	Barriers identified based on clinicians' perspective	Barriers identified based on patients/ parents' perspective
Clinicians	- Lack of knowledge on how to utilize and interpret PROMs - Insufficient training	**- Not systematically involved in implementation of PROMs** *- No information on available psychosocial interventions*	- Takes time	- No discussion of PROMs by clinician
Patients/ parents	- Lack of knowledge on how to utilize and interpret PROMs **- Insufficient training** - Lack of focus on patients with lower health literacy or language proficiency	**- Not systematically involved in implementation of PROMs** **- Supportive tools/ training for discussing PROs missing** *- No information on available psychosocial interventions*	- Low response rate	**- Not daring to start discussion about PROMs**
PROM system	*- Non-automated PROM data collection system* *- No integration of PROM data collection system in EHR* **- Suboptimal and complex PROM visualization in dashboard**	*- No integration with EHR* **- Suboptimal PROM visualization in dashboard** *- Suboptimal use on mobile phone or tablet*	*- No integration with EHR*	*- No integration with EHR* *- No KLIK app available* *- Suboptimal lay-out*
PROMs	**- Burdensome PROMs** **- PROM scores not comparable due to different scoring methods**	**- Burdensome PROMs**	**- Irrelevant and long PROMs**	**- Long, irrelevant and repetitive PROMs**

Note. Barriers in **bold** were addressed in part 1 and 2 of this thesis. Barriers in *italic* were addressed outside this thesis. Barriers underlined are remaining points of attention.

Some of the barriers reported by clinicians and patients/parents regarding the KLIK PROM portal, such as takes time, low response rate, and no discussion of PROMs by clinician, remain continuous points of attention. Further optimizations are thus necessary, which are described below. Additionally, from the barriers identified in literature, some were also not yet addressed. For these barriers, directions for future research are provided at the end of this thesis.

Future optimizations of the KLIK PROM portal

There are still some points that could be improved for the KLIK PROM portal specifically, which include the following on several levels:

Clinicians and patients

- Updating the KLIK training for clinicians. For example by including more recommendations for responding to problems that are reported by patients and parents [66]. Additionally, we should stress even more in the training and during

evaluation meetings the importance to discuss PROM outcomes when patients have completed PROMs, by which we can increase the response rate.
- Gaining insight into adult patients' perspective on the KLIK PROM portal, as adult patients are increasingly using KLIK as well.

PROM system
- Realizing a full data integration between KLIK and all available EHRs. In this way, patients and parents only have to use one system for their care, and can complete PROMs in the user-friendly KLIK portal through the EHR. Additionally, appointments registered in the EHR can be linked to KLIK, by which PROMs are automatically sent out. This will all save time for both patients and clinicians.
- Optimizing the visualization of PROMs in the KLIK dashboard further. First, domain score visualization (without reference lines) should be added for patients and parents in the KLIK dashboard, as currently only individual item visualization is shown. Second, a solution should be found for individual item visualization of PROMIS CATs for adult patients, as PROMIS item banks for adults often consist of many more items (over one hundred) than the pediatric item banks. Third, the possibilities for reference lines in the graphs should be expanded, as clinicians have indicated the preference to see condition-specific and longitudinal reference lines as well. Fourth, in all graphs in the KLIK dashboard, directionality should be harmonized into 'higher is better', to improve interpretability. Additionally, providing clear descriptive texts and labels with the graph, indicating the direction of scoring and the meaning of the score (e.g., mild/moderate/severe) if available, should be provided. Finally, all graphs should be ranked in order of importance, where the graphs with the most deviating scores on a domain should be presented first. This can help clinicians to see which domains need most attention during consultation.
- Creating an aggregated KLIK dashboard, where aggregated PROM data that is already collected, can be shown to be able to benchmark between hospitals or clinicians, or to compare PROM data between different patient groups or diagnoses.
- Making the KLIK PROM portal available as app. Through this app, real-time monitoring of patients would be possible, by which direct actions can be taken by clinicians. Currently, the feasibility and effectiveness of a KLIK app for pain monitoring in pediatric cancer care is being investigated [67]. When this study shows positive results, the KLIK app could be developed and implemented for more patient groups and monitor other symptoms as well.

PROMs
- Maintaining a stricter policy when new multidisciplinary teams want to use PROMs using the KLIK PROM portal, in line with the shift towards 'generic unless'. A generic core set should be advised, for example consisting of PROMIS CATs, and when necessary condition-specific PROMs can be added.

On the higher levels, it is important that the governments as well as hospitals keep supporting the use of PROMs in clinical practice. For KLIK and through our experience

with implementing PROMs in the Amsterdam UMC with the PROM expertise center, we recognized that support from the board of directors is essential to provide time and resources. Still, it remains difficult to automate the complete PROM implementation process and implementation support practitioners are necessary to support the process and provide help when needed.

Initiatives and implementation science to support further PROM implementation

Implementing PROMs in clinical practice remains a challenging process. Initiatives such as the ISOQOL user's guide and the PROM cycle can help, by taking into account the important steps that are necessary for PROM implementation. The optimizations performed in this thesis therefore corresponded to several of the essential steps as described by these initiatives. Additionally, frameworks and theories derived from implementation science can be used. Implementation science is the scientific study of methods to make the implementation process more systematic, which increases the chance that health innovations, such as PROMs, are adopted in clinical practice [68]. For PROM implementation, determinant frameworks, such as the Consolidated Framework for Implementation Research (CFIR) [69] are currently most often used [70], which are useful to understand and explain what determinants (both barriers and facilitating factors) influence implementation outcomes and that provide implementation strategies as potential solutions to barriers [68]. If these frameworks are used before starting with the implementation of PROMs in a setting, this may help in identifying factors that need to be taken into account, which can lead to a more successful implementation.

Directions for future research

Effects of PROMs in clinical practice and underlying mechanisms

PROM effect studies, combined in the recent systematic review of Gibbons et al. 2021 [71], and for pediatric patients specifically in the systematic reviews of Bele et al. 2020 [72] and Cheng et al. 2020 [73] showed positive effects of PROMs on processes of care and to a smaller extent on outcomes of and experiences with care. A downside of most systematic reviews that were published on PROM effects in clinical practice, especially in adult care, is that mostly randomized controlled trials (RCTs) were included and studies using other good designs such as sequential cohort designs were excluded. It would be interesting for future research to also include these types of studies in systematic reviews to see if the outcomes will be different. In the systematic reviews focusing on pediatric clinical practice, other designs were namely included and here stronger effects on e.g., outcomes of care were found. Additionally, in the systematic review of Gibbons et al. 2021, many studies focusing on mental health settings were included, which is substantively different from the medical setting. PROMs were previously shown to be less effective in this setting [74] and it would therefore be interesting to investigate if other outcomes would be found when focusing on the medical setting only.

Additionally, there is growing interest into the mechanisms (e.g., training clinicians

in PROM use and communication skills, type of PROMs and PROM visualization used) that can play a role in the effect of PROMs. The realist synthesis of Greenhalgh et al. provided a first impression of possible mechanisms [75], however, a more systematic analysis on available PROM effect studies such as meta-analysis and meta-regression is necessary to be able to draw conclusions on important mechanisms. Therefore, a study using these methods is currently underway at our department.

Testing interpretation accuracy of PROM visualization

Although studies focusing on PROM visualization are increasing, including the study in this thesis on PROMIS CAT visualization, most studies investigated preferences for PROM visualization of clinicians and did not investigate interpretation accuracy of different PROM visualizations by both clinicians and patients. Only the studies performed by the research group of professor Snyder also focused on interpretation accuracy. However, in these studies only a few visualization options were shown to clinicians and patients, only adult patients from one disease group (oncology) were included, and the study was performed in the United States, by which cultural differences in interpreting visualizations could have played a role [26, 30]. At our department, we are therefore working on a study where a broad range of patients (including children and patients with low health literacy) with different conditions are included, using both qualitative (e.g., interviews) and quantitative (e.g., online test using a survey) research methods to come to the optimal PROM visualization option. Only when visualizations of PROM outcomes are understood and correctly interpreted, PROMs can be discussed and of use in the consultation room.

Effectiveness studies of supportive tools and training patients

In one study in this thesis the development process of supportive tools was described. However, the final versions of the tools were not tested for effectiveness and usability in clinical practice with end users. Therefore a study is necessary to test if using the supportive tools results in increased discussion of PROs and improved patient-clinician communication. Furthermore, an implementation study should be performed to test if the tools are used and found by patients and parents, and if necessary, implementation strategies should be used to improve implementation.

Additionally, there are currently mixed results regarding the effect of training patients in PROM use. It should therefore be investigated if training patients (e.g., on how to interpret PROM outcomes in a dashboard, how to use a PROM data collection system, how to use PROM outcomes in communication with the clinician) helps to successfully implement PROMs in clinical practice.

Involving patients with low health literacy and language proficiency

Almost one in three people in the Netherlands has low health literacy skills, meaning that they have difficulty with finding, understanding and applying information about their health [76]. Additionally, there are many patients that have low proficiency in the language of the country they live in. Currently, these patients are not enough involved in PROM use and implementation in clinical practice by which they cannot take advantage

of using PROMs. This was also identified as an important barrier in literature [12, 14, 77], which is not yet overcome. In research and during the implementation process of PROMs in clinical practice, more attention should thus be paid to patients with low health literacy and low language proficiency. For example by involving them in the selection of PROs and PROMs, by using PROMs that are available in multiple languages (e.g., PROMIS measures) or easy to understand, by taking their views into account regarding access to PROMs (how to complete PROMs in a portal or EHR), by asking for their opinion about PROM visualization preferences and testing their interpretation accuracy, by developing specific PROM communication training tools or PROM information brochures, and by evaluating the PROM implementation process with them as well.

Training on PROMs and shared decision making

PROM use and shared-decision making are two important practices to achieve Value Based Health Care (VBHC) [78], which is increasingly endorsed in hospitals all over the world. When PROMs are properly used and discussed during consultation, patient-clinician communication is enhanced, which subsequently can contribute to and facilitate the shared-decision making process [38]. Patient-clinician communication is thus suggested to be an important mediator in this effect [38, 79], but most currently available PROM training programs do not teach clinicians extensive enough how to communicate about PROMs [39]. Additionally, training programs currently do not focus on when and how PROM outcomes can be used for shared-decision making and which parts of shared-decision making (team talk, option talk, choice talk, and decision talk) PROMs can facilitate [78]. Training programs should thus be developed for clinicians where more information on PROM communication is included and where the practices of PROM use and shared-decision making are integrated. Using the theoretical framework of patient-centered communication of Epstein and Street might provide a good basis [79], as recently described in the development study of a PROmunication tool [39].

Conclusion

Implementation of PROMs in clinical practice is a challenging process, where several barriers can be identified. With this thesis we have contributed to the optimization of this process by overcoming several barriers. The way PROMs are used and implemented in clinical practice is of utmost importance for their effect on processes, outcomes and experiences with care. Therefore, a continuous improvement cycle is necessary, where evaluations are performed, identified barriers are addressed and subsequent adjustments are made. Working together on this in multidisciplinary teams, consisting of patients, clinicians, PROM experts and IT experts is crucial.

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ADDENDUM

Summary

Approximately twenty-five percent of the Dutch population under the age of 26 grow up with a chronic condition. Due to medical developments, more children survive previously terminal medical childhood conditions, resulting in a continuing increase of the prevalence of chronic conditions. Growing up and living with a chronic condition has substantive effects on patients and their families. To gain insight into these effects, we can focus on Patient Reported Outcomes (PROs), which are direct reports by the patient on aspects of their health status (e.g., physical, mental, and social health), without interference of another person. PROs can be measured with standardized questionnaires, also called Patient Reported Outcome Measures (PROMs). PROMs can be used for several purposes; in scientific research, for quality registration of care, or on the individual patient level in medical clinical practice. This thesis focuses on the latter.

The use of PROMs on the individual patient level in clinical practice encompasses several aspects; 1) patients complete PROMs at home before the consultation with the clinician, 2) responses are visualized in a dashboard, and shown to the clinician before consultation, 3) the clinician discusses the PROM outcomes with patients during consultation. In this way, they can discuss important outcomes for the patient, monitor functioning over time, identify problems and subsequently provide tailored advice and interventions, or refer to the appropriate help. Using PROMs in clinical practice has been shown effective, especially in improving processes of care (e.g., patient-clinician communication), but less consistently in outcomes of care (e.g., mental functioning) and experiences with care (e.g., patient satisfaction).

The KLIK PROM portal (www.hetklikt.nu) is a tool that facilitates the use of PROMs in clinical practice for already over 10 years. However, over the years, it became clear that implementation of PROMs is an ongoing challenge. In the literature, as well as based on implementation experience, several barriers have been identified that reduce optimal use and implementation of PROMs in clinical practice. Barriers can be distinguished on different levels, for example on the level of clinicians, patients/parents, the PROM system, and PROMs.

The aim of this thesis is to overcome several identified barriers, with the ultimate goal to optimize the use of PROMs in clinical practice. In **Chapter 1**, the general introduction, the context of this research is described and the barriers for PROM use in clinical practice are introduced. The identified barriers are subsequently addressed in two parts in this thesis. The first part addresses the stakeholders' perspective on using PROMs in clinical practice. The second part focusses on optimization of PROM use in clinical practice, by dashboard improvement, PROM improvement, and empowering patients/parents.

Part 1: Stakeholders' perspective on PROM use in clinical practice

The most important stakeholders in the development and implementation process of PROMs are the users; the clinicians, patients and parents. Their perspective on the barriers and facilitators is therefore crucial, which was not systematically taken into account previously. **Chapter 2** focused on clinicians. In general, they (N=148) reported on a questionnaire to be satisfied with discussing PROMs in clinical practice using the

KLIK PROM portal. However several barriers were identified: no integration of KLIK with the electronic health record (EHR), irrelevant and long PROMs, low response rate of patients and parents, and using and discussing PROMs takes time. Patients' and parents' perspective on PROM use in pediatric clinical practice was subsequently described in **Chapter 3**, which showed with focus groups and questionnaires that patients (N=8 and N=31) and parents (N=17 and N=130) were satisfied with using PROMs through KLIK. However, the following barriers were mentioned; long, repetitive and irrelevant PROMs, no discussion of PROMs by the clinician, no integration of KLIK with the EHR, no KLIK app available, suboptimal lay-out of the KLIK website, and not daring to start the discussion about PROs themselves.

Part 2: Optimization of PROM use in clinical practice

In part 2 barriers identified in the literature and during the KLIK implementation process as well as barriers identified by users in part 1 are addressed.

Dashboard improvement

A barrier of PROM use is suboptimal visualization of PROM outcomes in a dashboard. Clear visualization of PROMs is essential for clinicians to correctly interpret PROM outcomes and subsequently detect problems and provide the appropriate help to patients. In previous research, line graphs including reference lines were often shown to be best interpreted and preferred visualization formats and are therefore used in the KLIK dashboard (KLIK ePROfile). However, new reference lines were necessary for the graphs in the KLIK ePROfile because reference data was outdated and not representative, and information on pediatric patients was lacking. In **Chapter 4** normative data of an often used Health-Related Quality of Life (HRQOL) PROM was collected for the Dutch general population (N=966) and a pediatric population (N=1209).

Furthermore, by analyzing and comparing the two samples, it was shown that pediatric patients reported worse HRQOL than the general population, and factors associated with worse HRQOL were school absence, female gender and younger age. The new normative data could thereafter be used as gender and age-specific reference lines, and were implemented in the KLIK ePROfile.

PROM improvement

PROMs are often experienced as burdensome due to questionnaire length and irrelevancy, and repetitiveness of questions. To overcome this barrier, computerized adaptive tests (CATs) of the Patient-Reported Outcomes Measurement Information System (PROMIS) measures can be used. With CAT, items are selected based on responses to previously completed items by a patient, resulting in a selection of relevant questions and a reduction of questionnaire length. The PROMIS measures were previously translated into Dutch-Flemish and validated in a Dutch clinical sample. However, validation in a general population sample was necessary to provide reference data for research studies and clinical practice. Therefore, as part of a larger PROMIS measures validation study from

our research group, **Chapter 5** showed that the PROMIS pediatric Anger scale displayed sufficient psychometric properties within the Dutch population (N=527), and reference data were provided. In **Chapter 6**, six validated PROMIS pediatric measures, including the Anger scale, were used for our COVID-19 study, showing that children reported worse mental and social health during the COVID-19 lockdown (N=844) compared to before (N=2401). Single-parent families, having three or more children in the family, a negative change in work situation of parents, and having a relative/friend infected with COVID-19 were factors associated with worse mental and social health. Finally, to be able to use the PROMIS CATs in clinical practice, new visualizations were necessary as with CATs not all items are administered and domain scores are calculated differently. In **Chapter 7**, preferences for PROMIS CAT visualization options were studied in focus groups with clinicians (N=28) and a questionnaire for patients (N=31) and parents (N=131). On individual item level, showing all items of the item bank, with only responses to administered items and the use of traffic light colors were preferred. On domain score level, graphs including numerical T-scores, reference and cut-off lines, and traffic light colors were preferred. Based on the results, recommendations for PROMIS CAT visualization were developed and implemented in the KLIK dashboard.

Patient/parent empowerment

Although PROMs facilitate the discussion of PROs in clinical practice, we recognized the barrier that patients and parents still find it difficult to discuss certain PROs and initiate discussion about PROM outcomes themselves. To overcome this barrier, in **Chapter 8**, using focus groups and questionnaires, insight was gained into difficult yet important PROs to discuss for patients (N=8 and N=31) and parents (N=17 and N=130). The most often mentioned difficult yet important PROs were future perspectives, family functioning, sexuality, and mental functioning. Perceived barriers to discuss these PROs were presence of parents/child during consultation, forgetting to discuss PROs, time pressure and an ignoring attitude of the clinician. Perceived facilitators were talking to the clinician in private and preparation of consultation by patients/parents. These outcomes informed the development of two tools; an educational video and topic list. Both are now available online and aim to support and empower pediatric patients and parents in discussing PROs with their clinician.

This thesis ends with **Chapter 9**, the general discussion, which includes a reflection on the main findings, clinical implications, methodological considerations, and the current implementation of the KLIK PROM portal. Additionally, further steps and remaining barriers for PROM implementation, and directions for future PROM implementation and research are provided.

In conclusion, implementation of PROMs in clinical practice is challenging with barriers on multiple levels. This thesis contributes to the optimization of the use of PROMs in clinical practice by overcoming several of these barriers. Stakeholders were involved and improvements were performed 1) by optimizing PROM visualization in a dashboard, 2) by making PROMIS CATs available for use in research and clinical practice, and 3) by

developing tools to support patients/parents in discussing PROs during consultation.

The way PROMs are implemented in clinical practice is of utmost importance for optimal use. Therefore, a continuous improvement cycle is necessary where evaluations with users are performed and subsequent adjustments are made by working together with important stakeholders such as clinicians, patients, PROM experts and IT experts.

Key messages

- Implementation of PROMs in clinical practice is a challenging process with barriers on multiple levels.
- Involving important stakeholders, e.g. clinicians, patients and parents, is essential for optimal PROM implementation in clinical practice.
- Clinicians, patients and parents are generally satisfied with using PROMs in clinical practice, but report barriers about suboptimal PROM visualization, long and irrelevant PROMs, and discussing PROM outcomes.
- Clear visualization of PROM outcomes is necessary for correct interpretation and subsequent discussion of PROM outcomes. Therefore dashboards should include individual item feedback, domain score feedback using line graphs with representative reference lines, and the use of traffic light colors.
- The PROMIS pediatric measures have excellent psychometric properties and can be efficiently used in research and clinical practice to replace burdensome PROMs.
- Although PROMs help in discussing PROs during consultation, pediatric patients and parents still find it difficult to initiate discussion about e.g., future perspectives, mental functioning, and sexuality. Supportive tools could help and empower pediatric patients and parents in discussing these PROs during consultation.
- The PROM implementation process remains challenging and to lower the barriers, stakeholder involvement, a multidisciplinary implementation team, as well as scientific knowledge and clinical experience is crucial.

Summary in Dutch - Nederlandse samenvatting

Ongeveer 25 procent van de Nederlandse kinderen en jongeren onder de 26 jaar groeit op met een chronische aandoening. Kinderen die eerder overleden aan dodelijke aandoeningen, overleven nu door de vooruitging in de medische wereld. Hierdoor is er een toename van het aantal kinderen met een chronische aandoening. Opgroeien en leven met een chronische aandoening heeft een enorm effect op deze kinderen en hun families. Om te weten hoe het met deze kinderen gaat, kunnen we ons richten op 'Patient Reported Outcomes' (PROs, oftewel patiënt-gerapporteerde uitkomsten). PROs zijn een directe weergave van de mening van de patiënt over zijn/haar gezondheidsstatus (bijv. fysieke, mentale, en sociale gezondheid), zonder tussenkomst van een ander persoon. PROs kunnen gemeten worden met gestandaardiseerde vragenlijsten, ook wel Patient Reported Outcome Measures (PROMS, oftewel patiënt-gerapporteerde uitkomsten vragenlijsten). PROMs kunnen voor verschillende doelen worden gebruikt; in wetenschappelijk onderzoek, voor kwaliteitsregistratie in de zorg, of op individueel patiënt niveau in de medisch klinische praktijk. Dit proefschrift focust op dit laatste doel.

Het gebruik van PROMs op individueel patiënt niveau kan bestaan uit de volgende stappen: 1) patiënten vullen thuis PROMs in voor het consult met de zorgverlener, 2) antwoorden worden gevisualiseerd in een dashboard voor de patiënt en zorgverlener, 3) de zorgverlener bespreekt de PROM uitkomsten met patiënten tijdens het consult. Het doel is om voor de patiënt belangrijke uitkomsten te bespreken, het functioneren van de patiënt over tijd te monitoren, problemen te identificeren en vervolgens advies te geven en juiste interventies of hulp aan te bieden. Het gebruik van PROMs in de klinische praktijk blijkt effectief, vooral in het verbeteren van processen van zorg (bijv. patiënt-zorgverlener communicatie), maar minder duidelijk in uitkomsten van zorg (bijv. mentaal functioneren) en ervaringen met zorg (bijv. patiënttevredenheid).

Het KLIK PROM portaal (www.hetklikt.nu) faciliteert het gebruik van PROMs in de klinische praktijk. Al meer dan 10 jaar worden PROMs geïmplementeerd, en het is duidelijk dat dit een voortdurende uitdaging is. In de literatuur, en op basis van implementatie ervaring, zijn verschillende barrières geïdentificeerd die het optimale gebruik van PROMs in de klinische praktijk verminderen. Barrières kunnen worden onderscheiden op verschillende niveaus, bijvoorbeeld op het niveau van de zorgverleners, patiënten/ouders, het PROM systeem, en de PROMs.

Dit proefschrift focust op het overwinnen van de geïdentificeerde barrières, met als uiteindelijk doel het gebruik van PROMs in de klinische praktijk te optimaliseren. In de algemene inleiding in **Hoofdstuk 1** wordt de context van dit onderzoek geschetst en worden de barrières voor PROM gebruik in de klinische praktijk geïntroduceerd. De geïdentificeerde barrières worden vervolgens aangepakt in twee delen in dit proefschrift. Het eerste deel richt zich op het perspectief van gebruikers van het KLIK PROM portaal. Het tweede deel focust op de optimalisatie van PROM gebruik in de klinische praktijk door dashboard verbetering, PROM verbetering en het mondiger maken van patiënten/ouders.

Deel 1: Perspectief van patiënten en zorgverleners op PROM gebruik in de klinische praktijk

Het is cruciaal om de gebruikers (zorgverleners, kinderen en ouders) te vragen naar hun perspectief op barrières en faciliterende factoren als het gaat om het gebruik van PROMs. Dit was nog niet eerder gedaan. **Hoofdstuk 2** richtte zich op zorgverleners (N=148), zij rapporteerden op de vragenlijst dat ze tevreden zijn met het bespreken van PROMs in de klinische praktijk middels het KLIK PROM portaal. Zij noemden echter ook verschillende barrières: geen integratie van KLIK met het elektronisch patiëntendossier (EPD), irrelevante en lange PROMs, een laag responspercentage van patiënten en ouders en het gebruiken en bespreken van PROMs kost tijd. Het perspectief van patiënten en ouders op PROM gebruik in de pediatrische klinische praktijk werd vervolgens besproken in **Hoofdstuk 3**. Hier werd met focusgroepen en vragenlijsten gevonden dat patiënten (N=8 en N=31) en ouders (N=17 en N=130) tevreden zijn met het gebruik van het KLIK PROM portaal. De volgende barrières werden genoemd: lange, zich herhalende en irrelevante PROMs, PROMs worden vaak niet besproken door de zorgverlener, geen integratie van KLIK met het EPD, geen KLIK app, een suboptimale lay-out van de KLIK website en patiënten en ouders durven zelf niet het gesprek aan te gaan over PROs.

Deel 2: Optimalisatie van PROM gebruik in de klinische praktijk

In deel 2 worden de eerder geïdentificeerde barrières en de barrières gerapporteerd in deel 1 aangepakt.

Dashboard verbetering

Een duidelijke visualisatie van PROMs is essentieel om PROM uitkomsten juist te interpreteren en vervolgens te bespreken. In eerder onderzoek is aangetoond dat lijngrafieken met normlijnen het best geïnterpreteerd worden door zorgverleners en de voorkeur hebben boven andere opties. Daarom vormt dat de basis van het KLIK dashboard (KLIK ePROfiel). De normlijnen in de grafieken waren echter gebaseerd op verouderde en niet representatieve data. Bovendien miste een normlijn van een pediatrische populatie. Daarom werden in **Hoofdstuk 4** normdata van de meest gebruikte kwaliteit van leven PROM, de PedsQL™, verzameld van de algemene Nederlandse bevolking (N=966) en een pediatrische populatie (N=1209).

Daarnaast werd aangetoond, door het analyseren en vergelijken van de twee groepen, dat kinderen met een chronische aandoening een slechtere kwaliteit van leven rapporteerden dan de algemene populatie. Als kinderen vaker school missen, meisje zijn en jonger zijn, bleek dat samen te hangen met een slechtere kwaliteit van leven. De nieuwe geslachts- en leeftijdsspecifieke normdata zijn gebruikt voor nieuwe normlijnen en deze zijn inmiddels geïmplementeerd in het KLIK ePROfiel.

PROM verbetering

PROMs kunnen door patiënten als belastend worden ervaren door de lengte van de vragenlijst en de irrelevante en overlappende vragen. Computer adaptieve tests (CATs) van

de Patient-Reported Outcomes Measurement Information System (PROMIS) vragenlijsten kunnen een oplossing bieden. Met CATs worden vragen geselecteerd op basis van eerder gegeven antwoorden, waardoor alleen relevante vragen worden geselecteerd en de vragenlijst korter wordt. De PROMIS vragenlijsten werden eerder al vertaald naar het Nederlands, maar validatie in de Nederlandse populatie was nog nodig voor gebruik in onderzoek en de klinische praktijk. Daarom werd in **Hoofdstuk 5**, als onderdeel van een grotere PROMIS validatiestudie, de PROMIS Boosheid schaal gevalideerd. Deze bleek goede psychometrische kwaliteiten te hebben (N=527) en normdata kwamen beschikbaar. In **Hoofdstuk 6** werden vervolgens zes pediatrische PROMIS vragenlijsten, waaronder de Boosheid schaal, gebruikt in onze COVID-19 studie. Hierin werd aangetoond dat kinderen een slechtere mentale en sociale gezondheid rapporteerden tijdens de COVID-19 lockdown (N=844) in vergelijking met daarvoor (N=2401). Eenoudergezinnen, gezinnen met drie of meer kinderen, een negatieve verandering in werksituatie van ouders en het hebben van een familielid/vriend met COVID-19 waren factoren die samenhingen met een slechtere mentale en sociale gezondheid. Tot slot was een nieuwe visualisatie nodig om PROMIS CATs in de klinische praktijk te gebruiken. Met CAT worden namelijk niet alle vragen afgenomen en domeinscores worden anders berekend. In **Hoofdstuk 7** werden patiënten (vragenlijst, N=31), ouders (vragenlijst, N=131) en zorgverleners (focusgroep, N =28) daarom gevraagd wat hun voorkeuren waren voor de PROMIS CAT visualisatie. Zij gaven aan dat ze graag alle vragen van de vragenlijst zien, waarbij de antwoorden van de afgenomen vragen worden getoond met stoplichtkleuren. De domeinscores zagen ze graag terug in grafieken met scores, waarbij normlijnen worden getoond en afkapwaardes in stoplichtkleuren. Op basis van deze resultaten werden aanbevelingen voor PROMIS CAT visualisaties ontwikkeld en geïmplementeerd in het KLIK dashboard.

Mondiger maken van patiënten/ouders

PROMs faciliteren het bespreken van PROs in de klinische praktijk. Toch geven kinderen en ouders aan dat ze het moeilijk vinden om zelf het gesprek te starten over de PROM uitkomsten. Om deze barrière te overwinnen, wilden we eerst inzicht krijgen in de moeilijke, maar belangrijke PROs om te bespreken en in de barrières en faciliterende factoren voor het bespreken van deze PROs. In **Hoofdstuk 8** vroegen we in focusgroepen en met vragenlijsten patiënten (N=8 en N=31) en ouders (N=17 en N=130) hiernaar. De meest genoemde moeilijke, maar belangrijke PROs waren toekomstperspectieven, familie functioneren, seksualiteit en mentaal functioneren. Barrières waren de aanwezigheid van ouders/kind tijdens het consult, vergeten om PROs te bespreken, tijdsdruk en een gesloten houding van de zorgverlener. Faciliterende factoren waren privé praten met de zorgverlener en het voorbereiden van het consult door patiënten en ouders. Deze informatie werd vervolgens gebruikt voor het ontwikkelen van twee hulpmiddelen; een educatieve video en een themalijst. Beide zijn online beschikbaar en hebben als doel om kinderen en ouders te ondersteunen en mondiger te maken in het bespreken van PROs met de zorgverlener.

Dit proefschrift eindigt met **Hoofdstuk 9**, de algemene discussie, waarin een reflectie wordt gegeven op de belangrijkste bevindingen, klinische implicaties, methodologische overwegingen en de huidige implementatie van het KLIK PROM portaal. Daarnaast

worden vervolgstappen en resterende barrières voor PROM implementatie beschreven en worden aanwijzingen voor toekomstige PROM implementatie en onderzoek gegeven.

Concluderend, het implementeren van PROMs in de klinische praktijk is uitdagend, met barrières op verschillende niveaus. Dit proefschrift draagt bij aan de optimalisatie van PROM gebruik in de klinische praktijk door verschillende van deze barrières te overwinnen. Kinderen, ouders en zorgverleners werden betrokken en verbeteringen werden uitgevoerd: 1) door PROM visualisatie in een dashboard te optimaliseren, 2) door PROMIS CATs beschikbaar te stellen voor het gebruik in onderzoek en de klinische praktijk, en 3) door het ontwikkelen van hulpmiddelen die patiënten en ouders kunnen ondersteunen in het bespreken van PROs tijdens het consult.

De manier waarop PROMs worden geïmplementeerd in de klinische praktijk is dus cruciaal. Een continue verbetercyclus is nodig waarin het gebruik wordt geëvalueerd met gebruikers en vervolgens aanpassingen worden gedaan door samen te werken met belangrijke betrokkenen, zoals zorgverleners, patiënten, PROM experts en IT experts.

Kernboodschappen

- Het implementeren van PROMs in de klinische praktijk is een uitdaging met barrières op verschillende niveaus.
- Het betrekken van zorgverleners, patiënten en ouders is essentieel voor optimale PROM implementatie in de klinische praktijk.
- Zorgverleners, patiënten en ouders zijn over het algemeen tevreden met het gebruik van PROMs in de klinische praktijk. Ze noemen echter ook barrières zoals een onduidelijke PROM visualisatie, lange en irrelevante PROMs en de moeite die ze hebben met het bespreken van PROM uitkomsten.
- Duidelijke visualisatie van PROMs is nodig voor juiste interpretatie van de uitkomsten. Daarom zouden dashboards moeten bestaan uit: individuele item feedback, domeinscores in lijngrafieken met representatieve normlijnen en stoplichtkleuren.
- De PROMIS vragenlijsten hebben excellente psychometrische eigenschappen en kunnen efficiënt gebruikt worden in onderzoek en de klinische praktijk om andere, belastende PROMs te vervangen.
- Ook al helpen PROMs in het bespreken van PROs tijdens het consult, kinderen en ouders vinden het toch moeilijk om een gesprek te starten over bijvoorbeeld toekomstperspectieven, mentaal functioneren en seksualiteit. Video's en een themalijst zouden kinderen en ouders kunnen ondersteunen in het bespreken van PROs tijdens het consult.
- Het PROM implementatieproces blijft uitdagend. Om de barrières te overwinnen is het betrekken van zorgverleners, kinderen en ouders als ook het inzetten van een multidisciplinair implementatie team, wetenschappelijke kennis en klinische ervaring cruciaal.

List of publications

This thesis

Lorynn Teela, **Maud M. van Muilekom**, Lieke H. Kooij, Anouk W. Gathier, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman, Hedy A. van Oers (2021). Clinicians' perspective on the implemented KLIK PROM portal in clinical practice. *Quality of Life Research*, 30(11), 3267-3277.

Maud M. van Muilekom & Lorynn Teela, Hedy A. van Oers, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman (2021). Patients' and parents' perspective on the implementation of Patient Reported Outcome Measures in pediatric clinical practice using the KLIK PROM portal. *Quality of Life Research*, 1-14.

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Maud M. van Muilekom, Michiel A.J. Luijten, Raphaele R. L. van Litsenburg, Martha A. Grootenhuis, Caroline B. Terwee, Lotte Haverman (2021). Psychometric properties of the Patient-Reported Outcomes Measurement Information System (PROMIS®) Pediatric Anger Scale in the Dutch general population. *Psychological Assessment,* 1-6.

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Maud M. van Muilekom, Michiel A. J. Luijten, Hedy A. van Oers, Caroline B. Terwee, Raphaele R. L. van Litsenburg, Leo D. Roorda, Martha A. Grootenhuis, Lotte Haverman (2021). From statistics to clinics: the visual feedback of PROMIS® CATs. *Journal of Patient-Reported Outcomes*, 5(1): 1-14.

Maud M. van Muilekom, Hedy A. van Oers, Ellen M. Smets, Lorynn Teela, Martha A. Grootenhuis, Lotte Haverman. Supporting pediatric patients and parents in discussing Patient Reported Outcomes with their clinician in clinical practice: the development of online tools. *Submitted.*

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Lotte Haverman & Hedy A. van Oers, **Maud M. van Muilekom**, Martha A. Grootenhuis (2020). Options for the Interpretation of and Recommendations for Acting on Different PROMs in Daily Clinical Practice Using KLIK. *Medical Care,* 57: S52-S58.

Maite E. Houwing, Madieke J. Muntendam, **Maud M. van Muilekom**, Lorynn Teela, Karin Fijnvandraat, Anne P. J. de Pagter, Henriette Heijboer, Hedy A. van Oers, Marion H. Cnossen, Lotte Haverman (2021). Health-related quality of life in infants, toddlers and young children with sickle cell disease. *Pediatric Blood & Cancer,* e29358.

Josjan Zijlmans & Lorynn Teela, Hanneke van Ewijk, Helen Klip, Malindi van der Mheen, Hyun Ruisch, Michiel A. J. Luijten, **Maud M. van Muilekom,** Kim J. Oostrom, Jan Buitelaar, Pieter J. Hoekstra, Ramon Lindauer, Arne Popma, Wouter Staal, Robert Vermeiren, Hedy A. van Oers, Lotte Haverman, Tinca J. C. Polderman (2021). Mental and social health of children and adolescents with pre-existing mental or somatic problems during the COVID-19 pandemic lockdown. *Frontiers in Psychiatry,* 12: 692853.

Karen Fischer, Jacintha M. Tieskens, Michiel A.J. Luijten, Josjan Zijlmans, Hedy A. van Oers, Rowdy de Groot, Daniël van der Doelen, Hanneke van Ewijk, Helen Klip, Rikkert M. van der Lans, Ronald de Meyer, Malindi van der Mheen, **Maud M. van Muilekom**, I. Hyun Ruisch, Lorynn Teela, Germie van den Berg, Hilgo Bruining, Rachel van der Rijken, Jan Buitelaar, Pieter J. Hoekstra, Ramón Lindauer, Kim J. Oostrom, Wouter Staal, Robert Vermeiren, Ronald Cornet, Lotte Haverman, Meike Bartels, Tinca J. C. Polderman, Arne Popma. Internalizing problems before and during the COVID-19 pandemic in Dutch children and adolescents with and without pre-existing mental health problems. *Submitted.*

Publications in Dutch

Maud M. van Muilekom & Michiel A. J. Luijten, Lorynn Teela, Tinca J. C. Polderman, Caroline B. Terwee, Josjan Zijlmans, Leonie Klaufus, Arne Popma, Kim J. Oostrom, Hedy A. van Oers, Lotte Haverman (2021). Impact van covid-19-maatregelen op de mentale en sociale gezondheid van kinderen. *Nederlands Tijdschrift voor Geneeskunde,* 165: D6296.

List of contributing authors

Thirsa Conijn
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Amsterdam Lysosome Center "Sphinx", Pediatric Metabolic Diseases, Amsterdam, the Netherlands.

Anouk W. Gathier
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Johannes B. van Goudoever
Amsterdam University Medical Centers, University of Amsterdam, Vrije Universiteit Amsterdam, Emma Children's Hospital, Department of Pediatrics, Amsterdam, the Netherlands.

Martha A. Grootenhuis
Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands.

Lotte Haverman
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Leonie Klaufus
Amsterdam University Medical Centers, Vrije Universiteit, Department of Public and Occupational Health, Amsterdam, the Netherlands.

Public Health Service Amsterdam, Department of Epidemiology, Health Promotion, and Health Care Innovation, Amsterdam, the Netherlands.

Lieke H. Kooij
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Raphaele R. L. van Litsenburg
Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands.

Amsterdam University Medical Centers, Vrije Universiteit, Emma Children's Hospital, Pediatric Oncology, Cancer Center Amsterdam, Amsterdam, the Netherlands.

Michiel A. J. Luijten
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Amsterdam University Medical Centers, Vrije Universiteit, Epidemiology and Data Science, Amsterdam, The Netherlands.

Heleen Maurice-Stam
Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands.

Hedy A. van Oers
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Kim J. Oostrom
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Tinca J. C. Polderman
Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Public Health, Amsterdam, the Netherlands.

Arne Popma
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Public Health, Amsterdam, the Netherlands

Leo D. Roorda
Amsterdam Rehabilitation Research Center | Reade, Amsterdam, the Netherlands.

Ellen M. Smets
Amsterdam University Medical Centers, University of Amsterdam, Department of Medical Psychology, Amsterdam Public Health, Amsterdam, the Netherlands.

Lorynn Teela
Amsterdam University Medical Centers, University of Amsterdam, Emma Children's Hospital, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Reproduction and Development, Amsterdam Public Health, Amsterdam, the Netherlands.

Caroline B. Terwee
Amsterdam University Medical Centers, Vrije Universiteit, Epidemiology and Data Science, Amsterdam, The Netherlands.

Josjan Zijlmans
Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Child and Adolescent Psychiatry & Psychosocial Care, Amsterdam Public Health, Amsterdam, the Netherlands.

Authors' contributions per chapter

Chapter 2: Clinicians' perspective on the implemented KLIK PROM portal in clinical practice.
Authors: Lorynn Teela, Maud M. van Muilekom, Lieke H. Kooij, Anouk W. Gathier, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman, Hedy A. van Oers.

LH conceived the study. LT, MMvM, LH and HAvO developed the evaluation questionnaire. LT, AG and HAvO carried out the data collection. LT, LK and HAvO performed the statistical analysis. The first draft of the manuscript was written by LT. JBvG, MAG, LH and HAvO handled the supervision. All authors critically revised the manuscript for intellectual content and approved the final version of the manuscript.

Chapter 3: Patients' and parents' perspective on the implementation of Patient Reported Outcome Measures in pediatric clinical practice using the KLIK PROM portal.
Authors: Maud M. van Muilekom, Lorynn Teela, Hedy A. van Oers, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman.

LH conceived the study. MMvM, LT, HAvO, and LH conceptualized and designed the study, performed the focus groups, and developed the evaluation questionnaire. MMvM and LT performed the qualitative and statistical analyses and wrote the first draft of the manuscript. JBvG, MAG, LH and HAvO handled the supervision. All authors critically revised the manuscript for intellectual content and approved the final version of the manuscript.

Chapter 4: Pediatric patients report lower health-related quality of life in daily clinical practice compared to new normative PedsQL™ data.
Authors: Maud M. van Muilekom, Michiel A.J. Luijten, Hedy A. van Oers, Thirsa Conijn, Heleen Maurice-Stam, Johannes B. van Goudoever, Martha A. Grootenhuis, Lotte Haverman.

LH and HAvO conceived the study. MMvM, HAvO, MAG, JBvG and LH conceptualized and designed the study. MMvM, MAJL, and TC collected and prepared the data. MMvM carried out the data analyses and wrote the first draft of the manuscript. MAJL, HAvO, HMS and LH supervised the data analyses and HAvO, MAG, JBvG and LH handled the supervision of the process. All authors critically reviewed and revised the manuscript and approved the final version of the manuscript.

Chapter 5: Psychometric properties of the Patient-Reported Outcomes Measurement Information System (PROMIS®) pediatric Anger scale in the Dutch general population.
Authors: Maud M. van Muilekom. Michiel A.J. Luijten, Raphaele R.L. van Litsenburg, Martha A. Grootenhuis, Caroline B. Terwee, Lotte Haverman.

LH, MAG, and CBT conceived the study. MMvM, MAJL, LH and CBT conceptualized and designed the study. MMvM and MAJL prepared the data and performed the statistical analyses in R. CBT and LH supervised the analyses. The first draft of the manuscript was written by MMvM and all authors commented on previous versions of the manuscript. LH and CBT supervised the process. All authors critically revised the manuscript for intellectual content and approved the final version.

Chapter 6: The impact of lockdown during the COVID-19 pandemic on mental and social health of children and adolescents.
Authors: Maud M. van Muilekom, Michiel A.J. Luijten, Lorynn Teela, Tinca J.C. Polderman, Caroline B. Terwee, Josjan Zijlmans, Leonie Klaufus, Arne Popma, Kim J. Oostrom, Hedy A. van Oers, Lotte Haverman.

LH conceived the study. MAJL, MMvM, LT, HAvO, and LH conceptualized and designed the study. MAJL, MMvM, LT, HAvO, CBT and LH developed the sociodemographic questionnaire and MAJL, MMvM and LT carried out the data collection. MMvM, MAJL, LT and JZ performed the statistical analyses and HAvO and LT performed the qualitative analyses. CBT supervised the statistical analyses. The first draft of the manuscript was written by MMvM, MAJL and LH, and all authors commented on previous versions of the manuscript. LH, HAvO, TJCP, AP, KJO and CBT supervised the process. All authors critically revised the manuscript for intellectual content and approved the final version. MAJL and MMvM contributed equally as co-first authors.

Chapter 7: From statistics to clinics: the visual feedback of PROMIS® CATs.
Authors: Maud M. van Muilekom, Michiel A.J. Luijten, Hedy A. van Oers, Caroline B. Terwee, Raphaele R.L. van Litsenburg, Leo D. Roorda, Martha A. Grootenhuis, Lotte Haverman.

LH, CBT, and MAG conceived the study. MMvM, MAJL, HAvO and LH conceptualized and designed the study. MMvM and MAJL prepared and performed the focus groups, and MMvM, MAJL, HAvO and LH developed the questionnaire. MMvM and MAJL carried out the data collection and performed the qualitative and statistical analyses. MMvM wrote the first draft of the manuscript. HAvO, CBT and LH supervised the process. All authors critically read and revised the manuscript for intellectual content and approved the submitted version.

Chapter 8: Supporting pediatric patients and parents in discussing Patient Reported Outcomes with their clinician in clinical practice: the development of online tools
Authors: Maud M. van Muilekom, Hedy A. van Oers, Ellen M. Smets, Lorynn Teela, Martha A. Grootenhuis, Lotte Haverman.

LH and MAG conceived the study. MMvM, HAvO, and LH conceptualized and designed the study. MMvM and LT prepared the focus groups and MMvM, LT, HAvO and LH performed the focus groups. MMvM, LT, HAvO and LH developed the questionnaire and MMvM and LT carried out the data collection. MMvM and LT performed the qualitative

and statistical analyses. LH, HAvO, EMS, and MAG provided input on the development process of the aiding tools. The first draft of the manuscript was written by MMvM and all authors commented on previous versions of the manuscript. LH, HAvO, EMS and MAG supervised the process. All authors critically revised the manuscript for intellectual content and approved the final version.

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PhD Portfolio

Name: Maud van Muilekom
PhD period: October 2017 - December 2021
Promotor: Prof. dr. M.A. Grootenhuis
Co-promotores: dr. L. Haverman, dr. H. A. van Oers
Department: Child and Adolescent Psychiatry & Psychosocial Care, Emma Children's Hospital, Amsterdam UMC

1. PhD training	Year	Workload (ECTS)
Courses		
Course 'Focus groups'	2017	0.6
Basic Course Legislation and Organization for Clinical Researchers (BROK)	2018	0.9
Practical Biostatistics	2018	1.1
Endnote	2018	0.1
Computing in R	2019	0.4
Scientific Writing in English for Publication	2020	1.5
Seminars, workshops and master classes		
Two-weekly research meeting (researchers), Psychosocial Department, Emma Children's Hospital Amsterdam	2017-2021	3
One-monthly research meeting (researchers and psychologists), Psychosocial Department, Emma Children's Hospital, Amsterdam	2017-2020	1.5
Workshop APH Mental health junior board: 'Self-care in Science' (organized)	2019	0.2
Workshop APH Mental Health junior board: 'Transferrable skills' (organized)	2020	0.2
Masterclass of the Amsterdam Pediatrics Symposium	2021	0.25
Selected for the TULIPS PhD curriculum, including Grant Writing Weekend	2019-2021	4
Workshop ISOQOL 28th Annual Conference: 'PROM data visualization in the clinical setting: what do clinicians need to see?'	2021	0.2
One-monthly research seminar VKC psyche, online	2021	0.5
One-monthly PROMIS researchers network meeting, online	2021	0.5

Oral Presentations		
Health-Related Quality of Life of Dutch children and adolescents with a chronic health condition aged 8-17 years. ISOQOL 25th Annual Conference in Dublin, Ireland	2018	0.5
Feedback options for using PROMs in daily pediatric clinical practice using KLIK, Amsterdam Pediatrics Symposium.	2019	0.2
Empowering patients: developing educational videos about discussing PROs. Amsterdam Pediatrics Symposium	2020	0.2
Psychometric properties of the PROMIS® pediatric Anger scale in the general Dutch population. ISOQOL 27th Annual Conference, online	2020	0.5
The impact of lockdown during the COVID-19 pandemic on mental and social health of children and adolescents. Amsterdam Pediatrics Symposium – Masterclass	2021	0.5
De impact van COVID-19 (maatregelen) op de mentale en sociale gezondheid van kinderen. Oorthuys overleg	2021	0.5
Systematische review: PROMs in de dagelijkse zorg – de PROMs black-box. Linnean initiatief werkgroep Evaluatie	2021	0.5
Empowering patients and parents: the development of educational videos about discussing PROs. European Paediatric Psychology Conference, online	2021	0.5
Poster Presentations		
Health-Related Quality of Life of Dutch children and adolescents with a chronic health condition aged 8-17 years. European Pediatric Psychology Conference, Ghent, Belgium	2018	0.5
Health-Related Quality of Life of Dutch children and adolescents with a chronic health condition aged 8-17 years. Amsterdam Public Health annual meeting, Amsterdam, the Netherlands	2018	0.5
Health-Related Quality of Life of Dutch children and adolescents with a chronic health condition aged 8-17 years. Science Exchange Day, Amsterdam, the Netherlands	2019	0.9
Empowering patients: a first step in developing educational videos about discussing PROs. ISOQOL 26th annual conference, San Diego, United States of America	2019	0.5
Empowering patients: a first step in developing educational videos about discussing PROs. Amsterdam Public Health annual meeting, Amsterdam, the Netherlands	2019	0.5

(Inter)national conferences		
Medical Psychology Research meeting, Amsterdam, the Netherlands	2017, 2019, 2021	0.75
TULIPS Young Investigators day (Culemborg, Utrecht, online), the Netherlands	2017-2021	1.2
Amsterdam Pediatrics Symposium, Amsterdam, the Netherlands	2018-2021	1
TULIPS Child Health symposium/weekend (Noordwijk, Rotterdam, Utrecht, Egmond), the Netherlands	2018-2021	2
Transition Care conference, Utrecht, the Netherlands	2018	0.2
European Pediatric Psychology conference, Ghent, Belgium	2018	0.5
ISOQOL 25th annual conference, Dublin, Ireland	2018	1
ISOQOL-NL symposium, Utrecht, the Netherlands	2018	0.25
APH annual meeting, Amsterdam, the Netherlands	2018, 2019	0.5
Implementation Science conference, Utrecht, the Netherlands	2019	0.25
CARE days, Eindhoven, the Netherlands	2019	0.5
APH spring meeting, Amsterdam, the Netherlands	2019	0.2
ISOQOL-NL/KLIK symposium, Amsterdam, the Netherlands	2019	0.25
Science Exchange Day, Amsterdam, the Netherlands	2019	0.2
ISOQOL 26th annual conference, San Diego, United States of America	2019	1
Dutch-Flemish PROMIS symposium, Amsterdam, the Netherlands	2020	0.25
ISOQOL 27th annual conference, online	2020	1
APH Junified meeting, Amsterdam, the Netherlands	2021	0.25
European Pediatric Psychology conference, online	2021	0.5
ISOQOL 28th annual conference, online	2021	1
APH networking afternoon, Amsterdam, the Netherlands	2021	0.2

2. Teaching	**Year**	**Workload (ECTS)**
Lecturing		
PROMs in Epic training for clinicians (Amsterdam UMC)	2021	1
Supervising		
Co-supervisor Master Thesis Psychology – Marjolein Smit	2020-2021	0.5

3. Parameters of Esteem	Year	Workload (ECTS)
Grants		
Amsterdam Reproduction and Development – Travel grant (€1000) for visiting the ISOQOL conference in San Diego, United States of America	2019	
Amsterdam Universiteitsfonds – Travel grant (€700) for visiting the ISOQOL conference in San Diego, United States of America	2019	
Stichting Steun Emma Kinderziekenhuis - Kwaliteit van leven bij kinderen en adolescenten ten tijde van de Corona crisis (€38000). Applicant: dr. L. Haverman, Co-applicants: dr. Kim Oostrom, prof. dr. Arne Popma, KLIK research team (i.a. drs. Maud van Muilekom	2020	
Awards and Prizes		
Abstract "From statistician to clinician: the feedback of PROMIS CATs in KLIK" selected for 'Cutting Edge Research Plenary' at ISOQOL conference, San Diego, United States of America	2019	
Selected among best 6 abstracts at the Amsterdam Pediatrics Symposium	2020	
Other		
Assistant for organizing the monthly Research meeting of the Psychosocial Department of the Emma Children's Hospital, Amsterdam UMC	2017-2020	1
ISOQOL-NL board assistant	2018-2021	3
Member of the organizing committee for the Young Investigators Day of TULIPS in November 2019 and 2020	2019-2020	2
Member of the APH Mental Health Junior Council	2019-2021	3

Curriculum Vitae

Maud Meta van Muilekom werd geboren op 11 september 1993 te Utrecht, als dochter van Jan van Muilekom en Aletta Wietsma. Zij groeide op met haar zus Milou en behaalde in 2011 haar gymnasium diploma aan het Christelijk Gymnasium Utrecht.

Vervolgens verhuisde ze naar Amsterdam en startte ze met de bachelor Psychologie aan de Universiteit van Amsterdam. Aan het begin van 2015 kreeg ze de kans om, als onderdeel van de bachelor, een uitwisseling te doen met Hunter College New York. Voor een half jaar woonde ze in New York en volgde ze verschillende vakken in de psychologie. Na terugkomst in Nederland werd ze toegelaten tot de tweejarige master Medische Psychologie aan de Universiteit van Tilburg. In het eerste jaar volgde ze hiervoor verschillende vakken op het raakvlak van de psychologie en geneeskunde. Het tweede jaar liep zij twaalf maanden stage op de medische psychologie afdeling van het Admiraal de Ruyterziekenhuis in Vlissingen, waarvoor zij naar Zeeland verhuisde, en schreef ze haar masterscriptie. In 2017 behaalde ze haar master cum laude en keerde weer terug naar Amsterdam. Naast haar studie heeft Maud altijd bijbaantjes gehad als oppas en bijlesdocent, en was ze tevens langere tijd tandartsassistente in de Tandartsspoedpraktijk in het OLVG te Amsterdam.

Vanaf oktober 2017 startte Maud met haar promotieonderzoek gericht op het optimaliseren van PROM gebruik in de klinische praktijk bij de afdeling Kinder- en Jeugdpsychiatrie & Psychosociale Zorg in het Emma Kinderziekenhuis Amsterdam UMC. Ze werd hierin begeleid door prof. dr. Martha Grootenhuis, dr. Lotte Haverman en dr. Hedy van Oers. Het resultaat is het proefschrift dat nu voor u ligt.

In de afgelopen jaren heeft Maud haar promotieonderzoek gecombineerd met verschillende andere taken en projecten. Zo heeft ze zich bezig gehouden met de KLIK implementatie en publiciteit, heeft ze presentaties gegeven op verschillende (inter)nationale congressen, is zij betrokken (geweest) bij verschillende sikkelcelziekte projecten, voert ze een systematische review uit naar onderliggende mechanismen van het effect van PROMs, en is ze als adviseur PROM implementatie betrokken bij het PROM Expertisepunt in het Amsterdam UMC. Daarnaast nam ze deel aan het TULIPS PhD curriculum en organiseerde ze als lid van verschillende commissies, zoals ISOQOL-NL, het APH mental health junior council en de TULIPS jonge onderzoekersdag commissie, verschillende congressen en workshops.

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