Patient Reported Outcome Measures in clinical practice

From implementation to optimization

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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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