Implementation and use of patient-reported outcome measures in routine nephrology care

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Summary and general discussion

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This dissertation aimed to provide insight into and practical knowledge of the implementation and use of patient-reported outcome measures (PROMs) in routine nephrology care. We performed research within the different steps for implementation of PROMs into routine care, including the selection of PROMs, pilot testing PROMs, and nationwide implementation and use of PROMs, using a broad variety of quantitative and qualitative research methods. We investigated the use of PROMs both at individual patient level and at population level, with the potential to facilitate personalised treatment and evaluation of healthcare quality. In this chapter, we summarize our main findings, discuss the implications of our main findings, and provide suggestions for future research, and for further implementation of PROMs into routine care.

Summary of main findings

Implementation of PROMs into routine nephrology care

SELECTION OF PROMS

Based on existing literature and in collaboration with patient representatives and healthcare professionals, we identified generic health-related quality of life (HRQOL) and disease-specific symptom burden as important outcomes to measure at individual and population level in routine nephrology care **(Chapter 1)**. The next step was to select PROMs to assess these patient-reported outcomes (PROs). In **Chapter 2**, we described the selection of the best suitable existing PROM to assess disease-specific symptom burden for routine assessment in nephrology care. We conducted this study in four phases. In the first two phases, we searched and build on the existing literature, from which we identified 28 potentially suitable symptom questionnaires and 10 symptom clusters. During the third phase, the questionnaires were evaluated based on predefined criteria regarding the relevance (e.g., applicable to CKD population), completeness (e.g., 90% cluster coverage) and comprehensibility (e.g., appropriate length, and straightforward and clear questions). Two questionnaires met the criteria: the Dialysis Symptom Index (DSI) and Palliative Care Outcome Scale-Renal Version (IPOS-Renal). In the fourth phase, these questionnaires were reviewed by 2 panels of in total 151 patients who were randomly assigned to a questionnaire, and 1 panel of 6 experts (i.e., experienced questionnaire assessors) who compared both questionnaires. Patients reported more symptoms using the DSI compared to the IPOS-Renal (12 and 8 symptoms, respectively), and needed less time to complete the DSI (5.4 and 7.5 minutes to complete the DSI and IPOS-Renal, respectively). Both the patients and

experts panels assessed the DSI as the most complete, specific and comprehensible symptom questionnaire. Therefore, the DSI was selected as PROM to assess disease-specific symptom burden in routine nephrology care.
The 12-item Short-Form Health Survey (SF-12) is a validated and commonly used PROM to assess generic HRQOL, and was recommended by an European expert consensus group for use in routine nephrology care.[1] In addition, the SF-12 was – similarly to the DSI – selected by our patients and experts panels as suitable PROM to assess generic HRQOL in routine nephrology care. Later in time, the Patient-Reported Outcomes Measurement Information System (PROMIS) was selected as one of the recommended PROMs to measure generic HRQOL in patients with CKD by a consensus group of the International Consortium of Health Outcomes Measurement (ICHOM).[2] PROMIS instruments can also be administered as computerized adaptive tests (CATs), that are expected to deliver similar or even more precise measurements with fewer questions compared with fixed (i.e., non-adaptive) PROMs.[3] To explore this relatively novel method in healthcare, we examined and compared the psychometric properties of seven PROMIS CATs compared with the SF-12 in patients with advanced chronic kidney disease (CKD) in **Chapter 3**. We performed a content comparison between the seven PROMIS CATs (assessing physical function, pain interference, fatigue, sleep disturbance, anxiety, depression, and the ability to participate in social roles and activities) and the SF-12, and examined the construct validity and test-retest reliability. We found evidence for sufficient construct validity of all seven PROMIS CATs. Furthermore, the PROMIS CATs, the SF-12 summary scores and most SF-12 domains, and the DSI showed sufficient test-retest reliability. Overall, PROMIS CATs showed better reliability, resulting in a lower minimal detectable change (MDC), compared with the SF-12. However, seven PROMIS CATs required 45 items (10 minutes), which is 3 to 4 times the length of the SF-12 (12 items; 3 minutes). These results show evidence for sufficient construct validity and a better test-retest reliability of seven PROMIS CATs, but requiring more items, compared with the SF-12. Moreover, these results do not address the suitability and feasibility of PROMIS CATs in routine nephrology care and therefore, the SF-12 is retained for now.

PILOT TESTING AND NATIONWIDE IMPLEMENTATION OF PROMS

Chapter 4 described the experiences and results of the first introduction of PROMs into Dutch routine nephrology care, in the form of a pilot study in 16 dialysis centres across the Netherlands. We used quantitative and qualitative research methods to explore these first experiences. In total, 512 patients receiving dialysis treatment completed 908 PROMs across three time points. The quantitative

part showed that there is room for improvement in patients' PROM-scores: patients receiving dialysis treatment experienced a substantially decreased physical HRQOL and a high symptom burden, with on average 11 different symptoms of moderate burden. The variation between the symptom frequency and burden suggests that the most common symptoms are not necessarily the most burdensome for patients. Furthermore, this first introduction of PROMs in routine dialysis care showed a low average response rate of 36%, which varied from 6% to 70% among centres. The high variability across centres underlines that achieving high response rates is feasible, but challenging and may require extra encouragement of patients and healthcare professionals. In the qualitative part, we explored patients' and healthcare professionals' experiences and preferences regarding the use of PROMs in clinical practice. Patients appreciated the content, length and structure of the PROMs (DSI and SF-12) and the online completion of PROMs. Individual feedback should be presented in a relevant context (e.g., with reference scores of similar patients) and can contribute to and in preparation for a consultation. Furthermore, some patients already discussed individual PROM-results with their healthcare professional. Patients and healthcare professionals indicated that discussing HRQOL and symptom burden scores was highly insightful and valuable, and individual feedback on PROM-scores was considered crucial. These first experiences with discussing PROM-results were promising.

Building on the findings from the pilot study, the PROMs infrastructure was further optimized for nationwide implementation and use of PROMs in routine dialysis care. For example, improvements were made to broaden the applicability (e.g., PROMs came available in four languages), to support implementation (e.g., a webpage about PROMs with information and hand-outs with tips and tricks to guide implementation), and to facilitate the use of PROMs (e.g., reports with individual PROM-results were provided to patients and their healthcare professionals directly after completing the PROMs). The PROMs became available to all dialysis centres in the Netherlands through Nefrovisie (as part of the renal registry Renine), and centres were invited to implement using PROMs into routine dialysis care.

Use of PROMs in routine nephrology care

USE OF PROMS AT POPULATION LEVEL

At aggregated population level, PROM-results can be used to evaluate healthcare quality and to inform patients and healthcare professionals about the effects and course of disease or treatment. Funnel plots can be used to evaluate healthcare quality by comparing hospital performances on certain outcomes. In **Chapter 5**, we explained the use and interpretation of funnel plots by presenting an overview

of the basic principles, pitfalls and considerations when applied to PROs, using examples from Dutch routine dialysis care. A funnel plot is a graphical method to evaluate healthcare quality and has several advantages, including clearly visualized precision, detection of volume-effects, discouragement of ranking hospitals and easy interpretation of results. However, without sufficient knowledge of underlying methods, it is easy to stumble into pitfalls, such as overinterpretation of standardized scores, incorrect direct comparisons of hospitals and assuming a hospital to be in-control (i.e., to perform as expected) based on underpowered comparisons. Furthermore, application of funnel plots to PROs is accompanied by additional challenges related to the multidimensional nature of PROs and difficulties with measuring PROs. To enable relevant and fair comparisons of PROs, high and consistent response rates, adequate case mix correction and high-quality PRO measures are required. These challenges need to be addressed before using PRO data for healthcare quality evaluations, for instance by using funnel plots. In **Chapter 6,** we showed an example of aggregated PROM-results that can be used to inform patients and healthcare professionals about the course and effects of disease and outcomes. In this chapter, we investigated the impact of itching on HRQOL and interactions with sleep problems and psychological symptoms in patients receiving dialysis treatment. We performed cross-sectional and longitudinal analyses in 2978 patients who completed the PROMs between 2018 and 2020. Our results showed that half of the patients experienced itching and in 70% of them, itching was persistent over time. Patients with itching experienced a 3 to 4 points lower physical and mental HRQOL compared with patients without itching, which remained stable during 2 years of follow-up. Furthermore, we found that sleep problems (70% versus 52%) and psychological symptoms (36% versus 19%) were more common in patients with itching. These symptoms had an additional negative effect on physical and mental HRQOL but did not interact with itching (i.e., the combination of both symptoms did not result in a significantly lower or higher HRQOL than the sum of individual effects). The high prevalence and persistence of itching, its impact on HRQOL over time and the additional effect on HRQOL of the often co-occurring sleep problems and psychological symptoms emphasize the need for recognition and effective treatment of itching to reduce symptom burden and improve HRQOL in patients receiving dialysis treatment.

USE OF PROMS IN INDIVIDUAL PATIENTS

For optimal use of PROMs in individual patients, knowledge on how to interpret and discuss PROM-results is needed. In **Chapter 7**, we explained the different types and characteristics of PROMs and provide guidance on how to interpret

individual PROM-scores and changes in PROM-scores over time. In this chapter, we introduced types and characteristics such as generic and specific PROMs, and scoring systems of PROMs. We explained that intuitive measures such as information about the average and distribution of PROM-scores in a reference population or in comparison to more familiar outcomes (e.g., laboratory measures) are indispensable to interpret and get used to PROM-scores. Furthermore, methodological concepts such as the MDC and minimal important change (MIC) are important to inform us about statistically and clinically relevant changes, respectively. Besides, one must be aware that response shift may occur, which refers to a change in the meaning of the patient's evaluation of the PRO over time (e.g., a change in one's perception on HRQOL). A response shift may explain unexpectedly small (or large) changes in PROM-scores. Finally, having a conversation with the patient is important to interpret individual PROM-scores. The best manner to interpret individual PROM-scores and changes in PROM-scores is through a discussion between the patient and the healthcare professional, in which measures like MDC, MIC and response shift may have a facilitating role. For example: the MIC provides an indication of which changes in PROs are likely considered relevant at group level and the discussion of individual results reveals what changes are important to this specific patient, to what extent, and in which manner.

In **Chapter 8**, we investigated how to optimally discuss PROM-results by conducting semi-structured interviews with 22 patients receiving dialysis treatment and healthcare professionals about their experiences with and perspectives on discussing PROM-results in routine dialysis care. Interviews focused on general situations and specific situations (e.g., addressing sensitive topics or when no medical treatment is available). Patients and healthcare professionals (nephrologists and nurses) highly appreciated the use of PROMs, as it provides insight and overview of how the patient is doing and feeling, and contributes to patient-professional communication. Furthermore, patients and healthcare professionals provided practical guidance for optimal discussion about PROM-results. First, patients and healthcare professionals emphasised that PROM-results should always be discussed and indicated how to create a suitable setting, adequately prepare, deal with time constraints and use PROMs as a tool for personalised holistic consultations. Second, patients should actively participate and healthcare professionals should take a guiding role. A trusting patient-professional relationship was considered a prerequisite and patient-professional interaction was described as a collaboration in which both contribute their knowledge, experiences and ideas. Third, follow-up after discussing PROM-results was considered important, including evaluations and actions (e.g., symptom management) structurally embedded

into the multidisciplinary treatment process. These general themes also applied to the specific situations, for example: results should also be discussed when no medical treatment is available. Interesting to note is that healthcare professionals were expected to take more initiative and a leading role when discussing sensitive topics. This study provided in-depth knowledge and practical guidance on how to organise and conduct conversations about PROM-results in routine nephrology care.

General discussion

The findings of this dissertation provide insights into and practical knowledge of the implementation and use of PROMs in routine nephrology care. Specific considerations and implications regarding each study have been discussed in the corresponding chapters (Chapter 2-8). In this part, we discuss the implications for clinical practice, and future directions for research and further implementation of PROMs, based on our overall findings and experiences with PROMs in routine nephrology care.

Implications for clinical practice

IMPLEMENTATION IS AN ITERATIVE PROCESS THAT TAKES COLLABORATION, TIME, AND EFFORT

The added value of PROMs is to a great extent determined by how well the PROMs are integrated into healthcare.[4, 5] Therefore, a structured and carefully prepared approach to implement PROMs into routine care is necessary.[6-8] Based on our experiences with implementing PROMs into routine nephrology care, we would like to highlight several important aspects to facilitate optimal implementation of PROMs into a routine care setting.

Firstly, collaborate with all stakeholders in all phases: from designing the project to implementing PROMs into routine care. Literature shows that patients are often not or only partly involved, even when new PROMs are being developed.[9, 10] We believe that here is great room for improvement. For example: in our project, a patient representative was one of the initiators and part of our research team, and was involved in all phases of the project. Furthermore, patients played an indispensable role in the implementation of PROMs into routine dialysis care, for instance by making sure that the PROMs, setting, timing, interpretation and feedback fits the patients' needs (Chapter 2, 4 and 8). Based on our experience, collaboration with patients and patient representatives supports both research and practice, and we hope that our inclusive approach will encourage more initiatives

to collaborate with patients and patient representatives. Furthermore, healthcare professionals play an important role in all phases to ensure that the use of PROMs fits the workflow (e.g., which timing, setting and healthcare professionals' roles are suitable) and that PROMs also provide added value for the healthcare professionals themself (e.g., when and how PROMs can provide insights and serve as a tool to conduct the conversation). Indeed, our results showed that engagement of healthcare professionals is an important facilitator both to implement PROMs (e.g., a coordinator on-site resulted in higher response rates) and to get the most benefits out of using PROMs (e.g., optimal discussion about individual PROM-results) (Chapter 4 and 8). A passionate professional may be a role model and important motivator for colleagues to optimally use PROMs.[11, 12] Besides, the healthcare quality institute of nephrology care (Nefrovisie Foundation) was an important facilitator and shows that implementation of PROMs at a national level is feasible, for example through use of the existing network and ICT infrastructure of the national registry.[8, 11, 13]

Secondly, carefully design and prepare the implementation of PROMs.[6] Designing includes defining the steps to be taken and which studies should be performed to inform the next steps, exploring the setting and purposes, and selecting the PROs and PROMs. Our research showed that the psychometric quality of the PROM but also factors related to the feasibility and suitability given the setting and purposes are important, for instance: the questionnaire length (i.e., number of items and time to complete), completeness and comprehensibility (Chapter 2). These factors should be examined for each PROM, setting, purpose and population that is considered. For example, PROMIS CATs showed good psychometric properties in patients with advanced CKD, but the feasibility and suitability in routine nephrology care remains to be explored before the next steps towards implementation of PROMIS CATs can be taken (Chapter 3).[14]

Preparation involves developing an electronic system to invite patients, collect PROMs and obtain individual feedback, and providing instructions and guidance to centres and healthcare professionals on why and how to use PROMs.[6, 15, 16] A great advantage of organising this nationally is that it is structured and similar across all centres, and not dependent on resources of individual centres. However, the manner in which PROMs are collected and used must fit within the workflow of the centres, and therefore, pilot testing is essential (Chapter 4).

Thirdly, treat the implementation as an iterative process of learning and improving, and invest time and effort. As with any other new approach in healthcare, it takes practice to adjust and become familiar with it. For PROMs, both the instrument itself and its use by patients and healthcare professionals are relatively new

in routine healthcare, and thus both the interpretation of PROM-scores and how to use it for personalised treatment takes practice (Chapter 7 and 8). Moreover, the iterative process involves adjusting expectations and assumptions. Barriers that are often reported in the literature[7, 15, 17] – such as 'PROMs take too much time' or 'PROMs create too high expectations in patients' – were nuanced in our studies by patients and healthcare professionals that had some experience with using PROMs, for example: healthcare professionals indicated that time was actually spent more efficiently by focussing on what is important to patients, and patients pointed out that they do not expect their healthcare professional to solve all complaints, only that it is discussed and that they are informed about potential causes, prognoses and treatment options (Chapter 8). Nevertheless, these nuances do not discard that it remains challenging to successfully implement PROMs into routine care. In this dissertation, the first steps taken are described, but the iterative process of optimal implementation of PROMs into routine nephrology care is still ongoing. Continuous evaluation of experiences with using PROMs in routine care, further research, training and guidance is needed to keep learning and improving.

IMPROVE RESPONSE RATES TO ENHANCE THE USE OF PROMS AT POPULATION LEVEL

The low average response rate of 36% with high variability across centres at first introduction of PROMs in routine dialysis care (Chapter 4) is an important finding of our pilot study, but also one of the main limitations when using PROMs at population level (Chapter 5 and 6). Although PROMs are now used in all Dutch dialysis centres and response rates are still increasing (45% in 2021)[18], the response rate remains an important point of attention. High and consistent response rates are needed to ensure that information at population level (i.e., in each centre and at national level) is of sufficient quality. Consistency in PROMs response is needed for multiple aspects, for example (unmeasured) characteristics of responders should not differ from non-responders; responders should be representative of the entire population of interest. In addition, the reason and timing of collecting PROs should be consistent. Patients should have an equal chance of being invited and being able to complete PROMs. Even though at individual level it may be reasonable to complete PROMs at indication (e.g., when someone has many symptoms), this should not be the main recruitment strategy, as this likely results in a biased or incomplete picture at population level (and also risk of under-recognition at individual level).[19, 20] Moreover, deciding on the right timing to collect PROs in nephrology care may be challenging since there is often no clear starting point in chronic care (e.g., prevalent dialysis patients). However, different timing in the

trajectory of the disease or treatment may demonstrate different PROM-results[21, 22], for example: it may matter whether someone has just started dialysis treatment or is already receiving dialysis treatment for a year (Chapter 7). The timing should thus be taken into account and preferably, comparable timepoints of PROMs completion over the entire disease and treatment trajectory are used for all patients.
Thus, recruitment strategies that yield high and consistent response rates are needed to enhance the use of PROMs at population level. Although the validity of the data strongly depends on the randomness of the (non-)response (i.e., representativeness of the responders), thresholds of 60-80% have been proposed in the literature as adequate response rates.[20, 23, 24] Patients and healthcare professionals considered discussing individual PROM-results essential in using PROMs in routine care (Chapter 4 and 8), and we believe this may be the most important facilitator in reaching high response rates. Furthermore, additional training of healthcare professionals (e.g., preparing healthcare professionals on how to invite and inform patients, and how to use PROMs) and support of patients (e.g., availability of tablets onsite or help with completing PROMs online) may improve response rates.[6, 25, 26] In addition, further development of the ICT infrastructure could improve response rates, for instance incorporation of PROMs into the electronic health record including automated invitations (e.g. 2-6 weeks prior to patients' upcoming annual consultation) and reminders to complete PROMs.[6, 27]

START WITH USING PROMS WHERE THEY DIRECTLY PROVIDE ADDED VALUE: AT INDIVIDUAL LEVEL

Our results show that already at first introduction of PROMs into routine dialysis care, the use of PROMs could facilitate the conversation about symptom burden and HRQOL between patients and healthcare professionals (Chapter 4 and 8). These findings confirm that using PROMs can improve patient-professional communication and support shared decision making by providing a tool to start and conduct a conversation and by providing a more complete picture and awareness of patient-relevant outcomes. These benefits of using PROMs contribute to a more person-centred healthcare and are directly achievable at individual patient level. Discussing individual PROM-results is already possible as soon as the patient has completed the PROMs, and is not dependent on population-level factors like high response rates or full integration into the electronic health record. However, these factors can further improve the use of PROMs at individual level; high quality information of similar patients – also known as 'patients-like-me' information – can facilitate the interpretation of individual PROM-results and shared decision making, and integration into the electronic health record provides insight into individual

results over time and comparison with clinical measures.[28, 29] Hence, our results imply that PROMs should directly be used at individual patient level and at the same time be further implemented at population level, so that the added value of completing and using PROMs is directly experienced by patients and healthcare professionals and will further improve over time.

Despite the fact that there are still steps to be taken, there are already some examples in the literature showing that PROs can be of added value in healthcare quality evaluation.[30-32] Future research should demonstrate whether this also applies to nephrology care. Our findings show that patients and healthcare professionals particularly consider the individual use of PROs of great added value, and individual use may therefore be the primary purpose of collecting PROs in routine nephrology care. However, we should keep in mind that individual and aggregated use often go together and may strengthen each other, for example, aggregated PROM-results can inform patients and healthcare professionals about prognosis, treatment and factors influencing PROs.[33, 34] Use at individual level is expected to improve response rates, which in turn results in better quality of aggregated information. Finally, the ultimate aim of collecting PROs is to improve patient-relevant outcomes and healthcare quality, and in order to evaluate whether the use of PROMs at individual level indeed results in these improvements, data on an aggregated level is required.

IMPROVE PATIENT-RELEVANT OUTCOMES

Our findings confirm the high symptom burden and decreased HRQOL that patients receiving dialysis treatment experience.[35-38] The high average number of 11 symptoms, the broad range of physical and psychosocial symptoms experienced by patients, and the fact that the most common symptoms are not necessarily the most burdensome (Chapter 4), may partly explain why symptoms were missed in routine nephrology care when not systematically assessed and discussed.[37, 39] Furthermore, by further investigating a common symptom in dialysis patients (i.e., itching) we found that this symptom is persistent in many patients, often co-occurs with other burdensome symptoms (i.e., sleep problems and psychological symptoms) and has a high impact on HRQOL (Chapter 6). These findings highlight the need for recognition, discussion and effective treatment to reduce symptom burden and improve HRQOL. Literature suggests that the use of PROMs may contribute to better symptom management, and that this in turn might result in improved patient-relevant outcomes such as a better HRQOL, less hospitalizations and lower mortality.[40-45] By implementing the PROMs into routine dialysis care, the first steps have been taken to provide insight into and facilitate discussion about

patients' symptoms and needs. However, to actually improve patient-relevant outcomes, follow-up actions in response to PROM-results are needed. The need for guidance to adequately respond to and act upon patients' symptoms and needs was also emphasized by healthcare professionals who already use and discuss individual PROM-results (Chapter 8).

In addition, using PROMs during consultations can help to focus on what is important to patients (Chapter 8). This may be of added value in decision making about starting, stopping or fine-tuning a treatment, for example: to what extent should anaemia be treated when the patient does not experience fatigue or other burdensome anaemia-related symptoms?[46] Until when is dialysis treatment beneficial, given the impact on someone's daily life?[47] Or to what extent is it beneficial to increase the prescription of phosphate binders when the patient experiences a high pill burden?[48] The patient's perspective is important in answering such questions and should be taken into account, just like clinical and biomedical values routinely are. The use of PROMs can already contribute to this more person-centred approach, and a personalised and holistic treatment. This may require a different approach from healthcare professionals and takes time and learning in practice to become familiar with.

Future directions for research

This dissertation provides grounds for further research into improving PROs and how to optimally use PROMs. Based on our findings, we would like to highlight some suggestions for further research.

FEASIBILITY AND SUITABILITY OF PROMIS CATS IN ROUTINE NEPHROLOGY CARE

Recently, PROMIS instruments have been recommended as generic PROMs for all medical specialist care in the Netherlands.[49] Our research showed sufficient validity and good test-retest reliability of PROMIS CATs (Chapter 3). However, in contrast to the SF-12 (and DSI), we did not investigate the suitability of PROMIS CATs within the setting and purpose of using PROMs in routine nephrology care. Therefore, further research is needed to explore the feasibility and suitability in routine nephrology care. In addition to characteristics such as questionnaire length (i.e., number of items and time to complete), comprehensibility and completeness, some additional factors specific for PROMIS CATs should be further examined: first, as the PROM is adapted to the patient's ability, questions will vary across patients and over time. Our research showed that particularly the specific items and not the overall scores are being used in clinical practice when discussing individ-

ual PROM-results (Chapter 8). Therefore, research is needed to explore whether and how PROMIS CATs can be used and provide (similar) added value during consultations in routine nephrology care. Second, PROMIS CATs can only be completed digitally. Currently, some dialysis centres are (also) using paper-based versions to reach the entire population and enable completion by the patient himself (without help). Further research could provide insight into whether it is feasible and desirable to shift towards only digital completion of PROMs (e.g., regarding accessibility to all patients and response rates, and digital resources and availability of help). Research findings regarding the feasibility and suitability of PROMIS CATs in routine nephrology care may help in determining the next steps in the iterative process of implementation and continuing to improve the use of PROMs.

RESEARCH TO ENABLE HEALTHCARE QUALITY EVALUATIONS BASED ON PROS

Using PROMs to evaluate healthcare quality requires not only further implementation at population level (e.g. higher and more consistent response rates), but also further research on the association between healthcare quality and PROs, and relevant case mix factors (Chapter 5). A PRO that is important to patients is not necessarily a suitable PRO for healthcare quality evaluation.[50, 51] To evaluate healthcare quality, an association between the PRO and healthcare quality must be plausible or established. To make relevant comparisons, there should also be room for improvement (i.e., variation across hospitals) and actionable care plans must exist.[50, 52] For most PROs, these associations have not yet been investigated. In addition, adequate case mix correction is required to enable fair comparisons and to draw conclusions about differences in healthcare quality. PROs and clinical outcomes may have different underlying mechanisms and also different case mix factors playing a role.[53] Identifying a sufficient set of case mix factors may be more challenging for PROs given the complexity and multidimensional character of PROs such as HRQOL.[54, 55] More research on which factors and through which mechanisms PROs are influenced may contribute to the selection of an adequate set of case mix factors.

FURTHER RESEARCH ON HOW TO IMPROVE PROS

The ultimate aim of using PROMs is to improve patient-relevant outcomes and healthcare quality. Building on our findings, future research should focus on investigating to what extent and how PROMs can be successfully incorporated and used in routine care to actually achieve these improvements. As part of this, our results emphasize the importance to explore how common and highly burdensome

symptoms (e.g., itching) can be improved, and suggest that better symptom management may also improve HRQOL. Our findings regarding the impact of itching, and the often co-occurring sleep problems and psychological symptoms, on HRQOL also highlighted the need for effective (para)medical treatment options (Chapter 6). Healthcare professionals also expressed the research priority that actionable care plans must be identified or developed to respond to individual PROM-results (Chapter 8). In Dutch nephrology care, the first steps towards such actionable care plans have been taken with the recently started research project 'Integrating Patient-Reported Outcome (PRO) measures into Dutch dialysis care: Toward a PRO Treatment Guide to achieve optimal multidisciplinary and personalized dialysis care' (PRO-GUIDE), in which a communication and treatment guide (and a supplementary generic toolbox for using PROMs in clinical practice) will be developed, in order to reduce the symptom burden and improve HRQOL.[56]

Future directions for further implementation of PROMs

TRAINING AND SUPPORT TO IMPROVE IMPLEMENTATION AND USE OF PROMS

Our research shows that there is a need for guidance and training for the implementation and use of PROMs in routine care. This applies to all steps: from getting the centres ready and inviting patients, to discussing individual PROM-results and taking and monitoring follow-up actions. Our results already provide a part of the necessary guidance and form the foundation for development of training and tools, including for instance practical implementation guidelines, training tools to support the interpretation of PROM-scores and to improve patient-professional communication about individual PROM-results.[15, 26, 56, 57] Training and tools can be of added value to both healthcare professionals and patients, especially when it comes to patient-professional communication. Guidance and training can help to optimize the use of PROMs and integrate it as a standard approach into healthcare.[26, 57] This will increase the added value and will help to reach the potential effects of using PROMs, contributing to person-centred care. In addition, to stimulate and facilitate improvements in using PROMs, a platform to easily share experiences and facilitating factors among centres may be of added value, to readily learn from each other.

Moreover, this dissertation comprises the implementation and use of PROMs in routine care until the discussion about individual PROM-results between patients and healthcare professionals. Although discussing individual PROM-results was regarded as an essential part in using PROMs and the main aim of completing PROMs, it does not stop after this step; using PROMs is an ongoing process and

also includes follow-up actions and monitoring. Guidelines are needed to adequately take this next step after discussing the results, and are yet to be developed as part of the PRO-GUIDE project.[56]

IMPROVE ACCESSIBILITY OF PROMS AND PROM-RESULTS

PROMs and PROM-results should be easily accessible for all patients and their healthcare professionals. Despite our efforts to optimize the implementation process (e.g., individual PROM-results were directly provided and PROMs were available in four languages), some challenges regarding technical issues and inclusivity remain. For example, an important and often mentioned barrier is that PROMs and PROM-results are not yet integrated into the electronic health record.[58] Patients and healthcare professionals need to work with a separate electronic system and PROM-results are therefore not easily combined with clinical measures and monitored over time. We expect a higher added value of PROMs in personalised and holistic treatment when fully incorporated into the standard workflow, and therefore, PROMs should be integrated into the electronic health record. Preferably as part of a clinical dashboard and in such a way that all steps are included: PROMs invitations and reminders are send (automatically) and results are collected and visualised within the electronic health record. Visualisation (for example through dynamic dashboards) should enable monitoring of individual PROM-scores over time in comparison to relevant clinical measures and PROM-results from similar patients (i.e., 'patients-like-me' information). Moreover, additional information (e.g., MIC and MDC) and explanations (e.g., colour-indications and meaning of scores) can support the interpretation of PROM-results, and may help both patients and healthcare professionals to identify outcomes that may require attention and discussion during consultations.

Furthermore, the PROMs and the methods of using PROMs in routine care setting must be further developed to improve the accessibility for all patients, including those with low (health) literacy, poor digital skills and language barriers. PROMs can help to start conversations about experiences and needs that may otherwise remain undiscussed, and this is perhaps of most added value for people who have difficulties with expressing themselves and with self-management.[59] However, these people might be those who also experience difficulties to complete PROMs.[60] This should be taken into account when taking the next steps in the implementation of PROMs into routine care. For example: simplify the language and layout with help of experts in this field[61], on short term where possible (e.g., PROM instructions and feedback) and after validation where necessary (e.g., PROM itself). In addition, when integrating PROMs into the electronic health record, one

should think of alternatives or extra help for people with poor digital skills. Explore for instance the possibilities to complete PROMs onsite (e.g., provide tablets and offer help to open the PROM), use of image answer options (e.g., smileys), and build-in read-aloud functions or video-instructions. Ideally, completing PROMs is facilitated in such a way that all patients can answer the questions by themselves, to ensure the results reflect their own perspective without any interpretation of others.[37, 39, 62]

BROADENING THE IMPLEMENTATION OF PROMS TO TOTAL NEPHROLOGY CARE AND BEYOND

During this research project, the PROMs were implemented into routine dialysis care. In addition, it laid the foundation for implementation of PROMs into the entire population in nephrology care. First steps have been taken to introduce PROMs for kidney transplant recipients (e.g., the 'PROs: Input of Valuable Endpoints' [POSITIVE] study[63]) and patients with CKD prior to kidney failure (e.g., the 'Patient-Relevant Outcomes in CKD' [PRO-CKD] project and the Dutch Outcome-based Healthcare program[64]), and will be included into the infrastructure of the Dutch renal registry Renine in the near future. This enables monitoring and individual follow-up of PROs – in addition to the already available clinical measures – over the entire disease and treatment trajectory (i.e., from advanced CKD to kidney failure and including different types of kidney replacement therapy and comprehensive conservative care). This will provide a more complete picture of disease patterns and can inform treatment decisions.

Literature shows that PROMs are also of added value in other fields, such as oncology, neurology and orthopaedics.[16, 41, 45, 65] Currently, different PROMs and separate workflows are often applied across the medical specialties. We hope that in the future, generic PROMs are no longer integrated into each medical specialty separately, but really organised around the patient, corresponding to the person-centred approach. This is especially of great added value in multimorbid populations, like patients with CKD in which comorbidities like diabetes and cardiovascular disease are common. Using the same PROM across medical specialties can lower the questionnaire burden and facilitate multidisciplinary use of the information, since the same PROM-results can be used by multiple specialists (i.e., reuse of information; there is no need to complete a PROM for each medical specialty separately). Particularly generic PROMs (e.g., SF-12 or PROMIS) are suitable for this broad application. First steps have already been taken to agree on suitable generic PROMs (e.g., PROMIS instruments) and crosswalks are being developed to enable transition between PROMs without losing historical PROM-data.[49, 66] Furthermore, the integration of PROMs into the electronic health record – although one of the biggest challenges – would bring

the person-centred collection of PROMs one step closer. Nevertheless, we expect that a certain generic approach will provide a good standard, but will not always be sufficient. Our results show that especially the Dialysis Symptom Index (DSI) – a disease specific PROM – provided valuable and additive insights, and was considered highly important by patients and healthcare professionals for the discussion and actionability of individual PROM-results (i.e., improvement of symptom management). PROMs specific for a certain disease or treatment may thus remain of great importance and an valuable addition to a generic PROM in routine care.

Conclusions

This dissertation provides insight into and practical knowledge of the implementation and use of PROMs in Dutch routine nephrology care. The introduction of PROMs into routine dialysis care corroborates the importance of a structured approach involving all relevant stakeholders (especially patients) and careful preparation (e.g., selection of PROMs and facilitate infrastructure to collect and use PROMs). Although further improvements in the implementation are required to enable valuable use of PROMs at aggregated level – for instance high and consistent response rates must be achieved – our results also show that PROMs are directly suitable and of added value for use at individual patient level. The high symptom burden (e.g., itching, sleep problems and psychological symptoms) and its impact on HRQOL in patients receiving dialysis treatment, highlights the need for recognition, discussion and effective treatment of PROs. Discussing individual PROM-results between patients and healthcare professionals is an essential part of using PROMs and facilitates patient-professional communication and shared decision making. Our results form the foundation for training and guidance for healthcare professionals and patients, and for further development (e.g., regarding ICT facilities and inclusivity) to optimize the use of PROMs in routine care. The ultimate aim of using PROMs is to improve patient-relevant outcomes, and to achieve this follow-up actions (i.e., monitoring over time and improve symptom management) in response to PROM-results are required. Finally, based on our highly positive and valuable experiences with PROMs in routine dialysis care, we continue optimizing the implementation of PROMs and expand on it by also including care for patients with advanced CKD and kidney transplant recipients. The presented approach can serve as an example and we hope that our results and lessons learned provide guidance to other researchers, policy makers, healthcare professionals and patients, within and beyond (inter)national nephrology care, regarding the implementation and use of PROMs in routine care.

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