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

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Routinely measuring symptom burden and health-related quality of life in dialysis patients: first results from the Dutch registry of patient-reported outcome measures (PROMs)

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Abstract

Background: The use of patient-reported outcome measures (PROMs) is becoming increasingly important in healthcare. However, incorporation of PROMs into routine nephrological care is challenging. This study describes the first experience with PROMs in Dutch routine dialysis care.

Methods: A pilot study was conducted in dialysis patients in 16 centres. Patients were invited to complete PROMs at baseline, 3 and 6 months. PROMs consisted of the 12-item Short-Form (SF-12) and Dialysis Symptom Index (DSI) to assess health-related quality of life (HRQOL) and symptom burden. Response rates, HRQOL and symptom burden scores were analysed. Qualitative research methods were used to gain insight into patients' view on using PROMs in clinical practice.

Results: In total, 512 patients (36%) completed 908 PROMs (24%) across three time-points. Response rates varied from 6-70% among centres. Mean (SD) scores for physical and mental HRQOL were 35.6 (10.2) and 47.7 (10.6), respectively. Patients experienced on average 10.8 (6.1) symptoms with a symptom burden score of 30.7 (22.0). Only 1-3% of the variation in PROM-scores can be explained by differences between centres. Patients perceived discussing their HRQOL and symptom scores as insightful and valuable. Individual feedback on results was considered crucial.

Conclusions: First results show low average response rates with high variability among centres. Dialysis patients experienced a high symptom burden and poor HRQOL. Using PROMs at individual patient level is suitable and may improve patient-professional communication and shared decision-making. Further research is needed to investigate how collection and use of PROMs can be successfully integrated into routine care in order to improve healthcare quality and outcomes.

Introduction

Patients with advanced chronic kidney disease (CKD) experience numerous physical and emotional disease-related symptoms and a poor health-related quality of life (HRQOL).[1-3] In daily healthcare, these patient-reported outcomes (PROs) are frequently underrecognized and underestimated [2, 4], and consequently, may remain unattended.[5] The under-identification may be partly explained by patients not sharing their symptoms and needs easily [6, 7], and by difficulties for clinicians to identify the full spectrum and severity of patients' symptoms and needs.[4, 7, 8]

The use of patient-reported outcome measures (PROMs) may facilitate communication about symptoms and needs, and may provide insight into PROs both at individual and at centre or national level.[9-13] Although the importance of PROs is recognized [14-16] and the use of PROMs in routine care is highly supported [9, 16], PROMs are often not yet part of standard nephrological care.[9, 13, 17] In Europe, few renal registries have initiated routine collection of PROMs [18-20]. The Scottish Renal Registry recently described their first experience with collecting PROMs and encountered challenges including a low response rate, selective response, organizational struggles and low commitment from centres.[18] Literature also corroborates that it is challenging to incorporate PROMs into routine care.[9-11, 17, 20-22] A major challenge is to incorporate PROMs in such a way that it can be used for different purposes at different levels; to evaluate healthcare quality at aggregated level, and, perhaps even more important for patients, to support patient-professional communication and decision-making at individual patient level.[9-11, 13] Using PROMs for different purposes requires engagement at all levels, high response rates and feedback on outcomes tailored to the context and the purpose.[9-13]

Currently, PROMs are being implemented into Dutch nephrological care to provide insight into PROs of individual patients and at centre and national level. PROMs will be collected in Renine, the Dutch Renal Registry (www.nefrovisie.nl/renine) in which all patients on renal replacement therapy (RRT) are registered. This study describes the first experience with PROMs in Dutch routine dialysis care. We aim to evaluate the introduction of the national registry of PROMs by answering the following research questions:

1. What is the response rate and how does the response rate vary among centres? Which differences in characteristics are observed between responders and non-responders?

2. What is the HRQOL and symptom burden of patients receiving dialysis, which variation in scores is observed among centres, and to which extent can variation in scores be explained by differences in patient population?

3. What are patients' experiences and views on the use of PROMs in clinical practice?

Materials and Methods

Study design and patients

The registry of PROMs was introduced in routine nephrological care through a pilot study among adult patients on dialysis in 16 Dutch centres from September 2016 to April 2017. These centres treat 26% of all Dutch patients receiving dialysis. Patients undergoing any type of dialysis were included. Clinicians invited their patients to complete the online PROMs at 3 time-points: at baseline, 3 and 6 months after study start. This frequency was considered suitable by patients [23] and is expected to be sufficient for centres to become familiar with PROMs. Aiming at optimal incorporation of PROMs in routine care, centres were free to develop the process of inviting and motivating patients that fits their workflow.[24, 25] Clinicians could decide not to invite a patient, for example because of the patient's holiday or medical condition. At 6 months, PROMs were available to complete in the following languages: Dutch, English, Turkish and Arabic.

PROMs: HRQOL and symptom burden questionnaires

The PROMs consist of two questionnaires: the 12-item Short-Form (SF-12) health survey to assess HRQOL and the Dialysis Symptom Index (DSI) to assess symptom burden. These questionnaires were carefully selected in close collaboration with patients, professionals, the Dutch Kidney Patients Association (NVN) and the quality institution Nefrovisie.[23] Literature also recommends the SF-12 as appropriate questionnaire to assess HRQOL in routine care, but no recommendation is provided for the assessment of symptom burden.[20] Therefore, a four-phase mixed methods study was conducted to select the best suitable symptom questionnaire, in collaboration with patients and experts, and by using existing symptom questionnaires and literature. In this study, the DSI was found the most relevant, complete and comprehensible symptom questionnaire for routine assessment in patients with advanced CKD. The details of this selection process have been described elsewhere.[23]

The SF-12 is a generic questionnaire consisting of 12 questions regarding physical and mental HRQOL, especially developed for large-scale monitoring.[26] Within the dialysis population, the SF-12 is frequently used and has shown to be a preferred and valid questionnaire.[20, 27] Norm-based scoring algorithms were used to calculate physical (PCS) and mental (MCS) component scores. Component scores range from 0 to 100, with higher scores indicating better HRQOL. PCS and MCS scales are standardized to the U.S. population with a mean of 50 and a standard deviation (SD) of 10.[26, 28]

The DSI is a 30-item disease-specific symptom questionnaire to assess physical and emotional symptom burden.[29] To ensure comprehensiveness for individual

patients, an open-ended question was added to report three additional symptoms.[23] Patients indicate for each symptom if it was present (yes/no) during the past week and, if so, how much it bothered (5-point scale ranging from 1 'not at all' to 5 'very much'). The number (0-30 symptoms) and burden (score ranging from 0 [no symptoms] to 150 [all 30 symptoms are present and are very burdensome]) of symptoms were calculated, with higher scores indicating higher symptom burden.[30] Scores were calculated for patients that filled in ≥28 questions, whereby missing symptoms were assumed absent (burden score 0).[30]

Potentially explanatory factors

From Renine we obtained patient, disease and treatment characteristics describing the study population: age, sex, primary kidney disease (according to European Renal Association – European Dialysis and Transplantation Association codes [31]), social economic status (SES; using zip code [32]), dialysis modality and time on RRT (using date of RRT initiation).

Statistical analysis

Statistical analyses were performed using SPSS version 23.0. *P*-values<0.05 were considered statistically significant. Variables are shown as mean (SD) or percentages. Non-normally distributed variables were log-transformed and presented as geometric mean (SD). Missing values for patient, disease and treatment characteristics (Table 1) were assumed 'missing at random' and estimated using multiple imputation.[33, 34] Ten imputed datasets were created.[34] The imputation model included all patient, disease and treatment characteristics (see potentially explanatory factors), centre, response, if patients received support completing PROMs, death during follow-up, cause of death and all outcomes (PCS, MCS, symptom number and burden score).[34, 35]

Patients who died or for which the centre indicated that they did not invite the patient were excluded from analyses for relevant time-points (Figure 1). Patients were considered a responder if they participated at least once. Student's t-test and Chi-squared tests were used to compare characteristics of responders and non-responders. To compare response rates between time-points and centre-volume (number of dialysis patients), Chi-squared test and linear regression analysis were performed, respectively. For patients who participated at multiple time-points, their first measurement was used in HRQOL and symptoms analyses (Figure 1).

MCS, PCS, symptom number and burden scores were calculated for responders who completed the full questionnaire (Figure 1). To explore variation among centres, MCS, PCS and symptom burden scores were assessed per centre and

compared to the overall study population through indirect standardization. To that end, the following steps were taken: first, an expected score was calculated per patient for each outcome separately by using a multivariable linear regression model including patient, disease and treatment characteristics as predictors. Second, mean expected and observed scores were calculated for each centre. Third, adjusted PROM-scores per centre were calculated as follows: *(Observed centre mean – Expected centre mean) + overall mean*, hereby creating centre scores comparable to the overall study population. Crude and adjusted PROM-scores are shown in funnel plots.[36] Funnel plots were created in R version 3.4.2.

To examine to what extent variation among centres can be explained by differences in patient population, intraclass correlation (ICC) – also referred to as 'rankability' – was calculated using multilevel regression analysis (MLRA).[37-39] ICC is the proportion of variance in MCS, PCS or symptom burden scores that occurs at centre level. This variance may be attributable to centre-factors or to the patient population (of responders) of centres.[37, 38] Patient, disease and treatment characteristics were included as fixed effects and centres as random effect in the MLRA model. Comparison of ICC before and after including characteristics in the model (i.e. comparing crude and adjusted ICC) shows to which extent centre variation can be explained by differences in characteristics of centre populations.[38]

Patients' experiences and preferences

As PROMs are intended to become part of regular care, we wanted to know more about patients' experiences with and preferences for discussing PROM-scores with their healthcare professional. At 3 months, all patients were asked if they would like to share and discuss their PROM-scores with their healthcare professional. Hereafter, in each centre, professionals received an individual digital report from 5 randomly selected patients who gave consent. Professionals were invited to discuss the report with these patients at their next consultation visit. This report contained patient's responses and PROM-scores with a comparison to all responders and – for MCS and PCS – the general Dutch population. At 6 months, patients and professionals were asked how they experienced the conversation about PROM-scores. Patients also reported which professional discussed the PROM-scores with them and how satisfied they were with the conversation (5-point scale: 1-5, poor-excellent).

Additionally, the use of PROMs was evaluated in a focus group with patients receiving dialysis. Patients were recruited by NVN via e-mail and social media. During the focus group, patients' views and preferences concerning the use of PROMs in clinical practice were discussed. The focus group lasted 2.5 hours and was chaired

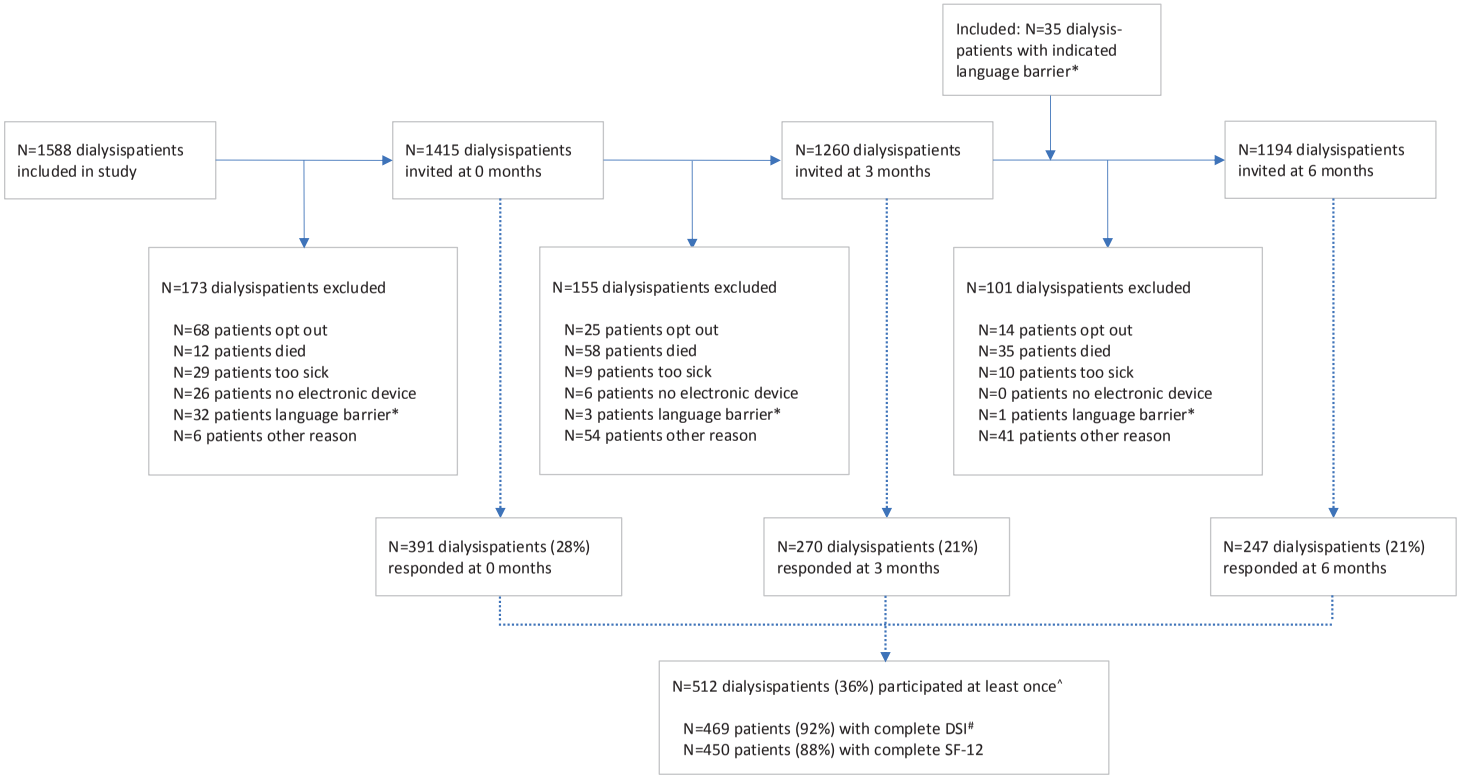

Figure 1. Flow chart for the number of patients included, invited and participating at each time-point.

* *Patients that were excluded because of a language barrier at 0 or 3 months were again included at 6 months: PROMs were also available in English, Turkish and Arabic at 6 months.*

^ *In total, 1440 patients were invited at least at one time-point.*

\# *The DSI was considered complete if ≥28 questions had been answered.*

Abbreviations: DSI, Dialysis Symptom Index; SF-12, 12-item Short-Form; PROMs, patient-reported outcome measures.

by a health educator (KP). Patients' discussion was recorded in detail by handwritten field notes and, when possible, verbatim by the chair and two observers (HB and FD). All written information was analysed using Atlas.ti. Statements were analysed by a researcher trained in qualitative research (EvdW) and discussed with an experienced qualitative researcher (YM).

Results

Response rate

Figure 1 shows the number of patients that were invited and responded across the time-points. In total, 1440 patients were invited at least once. The main reasons not to invite a patient were the medical condition of patients and that patients indicated that they did not want to be invited. In total, 512 patients (36%) responded at least once and altogether completed 908 PROMs (24%) across the three time-points.

The response rate was higher at baseline with 28% compared to 21% at 3 and 6 months ($p<0.001$). Figure 2 presents response rates per centre at all time-points. A large variation among centres was found with response rates ranging from 6% to 70%.

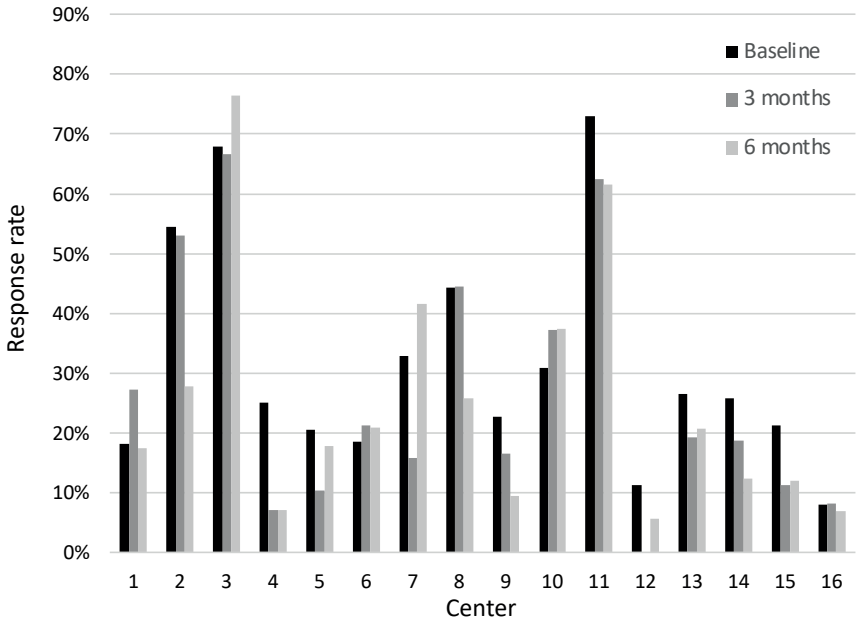

Figure 2. Response rates per time-point in 16 pilot centres.

Centres are ranked (low to high) according to the number of patients on dialysis included at baseline. Larger centres (i.e. higher number of patients included at baseline) had a slightly lower response rate compared to smaller centres: the response rate decreases with 2% for each additional 10 patients (p<0.001).

Table 1. Characteristics of responders and non-responders (N=1440)

	Responder* N=512	Non-responder* N=928	*p*-value
Sex, male [a]	342 (67.9)	484 (57.1)	<0.001
Age, mean (years) [b]	66.6 (13.8)	64.7 (16.0)	0.022
SES [c]			<0.001
Low	119 (24.1)	305 (36.5)	
Middle	309 (62.6)	430 (51.5)	
High	66 (13.4)	100 (12.0)	
Primary kidney disease [d]			0.005
Glomerulonephritis/sclerosis	55 (12.5)	98 (12.8)	
Pyelonephritis	23 (5.2)	40 (5.2)	
Polycystic kidney disease	42 (9.5)	40 (5.2)	
Hypertension	72 (16.4)	158 (20.6)	
Renal vascular disease	67 (15.2)	96 (12.5)	
Diabetes mellitus	84 (19.1)	194 (25.3)	
Miscellaneous	97 (22.0)	142 (18.5)	
Dialysis modality [e]			0.121
HD centre	407 (82.6)	695 (82.3)	
HD home	18 (3.7)	50 (5.9)	
PD	68 (13.8)	99 (11.7)	
Time on RRT, mean (years) [f #]	2.5 (3.8)	3.1 (3.4)	0.005

Values are shown in N (%) or mean (SD)
**Patients are considered responder if they participated at least once. Non-responders are invited at least once, but never participated.*
[a] Sex is available for 504 (98.4%) responders and 847 (91.3%) non-responders, [b] Age is available for 504 (98.4%) responders and 846 (91.2%) non-responders, [c] SES is available for 494 (96.5%) responders and 835 (90.0%) non-responders, [d] Primary kidney disease is available for 440 (85.9%) responders and 768 (82.8%) non-responders, [e] Dialysis modality is available for 493 (96.3%) responders and 844 (90.9%) non-responders, [f] Time on RRT is available for 497 (97.1%) responders and 847 (91.3%) non-responders.
[#] Time on RRT is shown as geometric mean (SD).
Abbreviations: SES, social economic status; HD, haemodialysis; PD, peritoneal dialysis; RRT, renal replacement therapy.

Responders

Table 1 shows the characteristics of responders (N=512) compared to non-responders (N=928). Responders were more frequently male, older, had a higher SES and started RRT more recently. Responders' primary kidney disease was more frequently polycystic kidney disease and less frequently hypertension or diabetes. Responders needed on average 12.2 (SD: 6.1) minutes to complete the PROMs. In total, 211 out of 512 patients (41%) received some support to complete the PROMs, ranging from 7% to 65% across centres. When support was provided, the support mainly consisted of: reading questions aloud (81%), filling in patients' answers (79%), translating of questions (6%), and completing the questionnaire on their behalf (e.g. their partner; 8%). Eleven patients (5%) indicated that other support was provided, such as assistance in using an electronic device or discussing questions with relatives to remember their experiences. Furthermore, some centres with high response rates indicated that they provided tablets, so that patients could complete the PROMs while receiving dialysis treatment. The non-Dutch questionnaires that were available at 6 months, were used twice: once in English and once in Arabic.

Table 2. Top 10 most frequent and most burdensome symptoms*

	Symptom frequency	N (%)	Symptom burden^	Mean (SD)
1	Feeling tired or lack of energy	366 (76.4)	Difficulty becoming sexually aroused	3.42 (1.4)
2	Dry skin	283 (58.7)	Trouble falling asleep	3.26 (1.1)
3	Trouble staying asleep	260 (54.3)	Decreased interest in sex	3.25 (1.5)
4	Muscle cramps	246 (51.0)	Feeling tired of lack of energy	3.24 (1.0)
5	Itching	240 (50.0)	Bone or joint pain	3.23 (1.1)
6	Bone or joint pain	225 (47.0)	Trouble staying asleep	3.18 (1.1)
7	Dry mouth	223 (46.8)	Dry skin	3.04 (1.2)
8	Trouble falling asleep	206 (43.2)	Numbness or tingling in feet	2.99 (1.0)
9	Shortness of breath	207 (43.1)	Restless legs or difficulty keeping legs still	2.94 (1.0)
10	Decreased interest in sex	193 (41.8)	Itching	2.88 (1.0)

** Symptom frequency and burden reported using the Dialysis Symptom Index (DSI): top 10 out of 30 symptoms. Symptoms were available for 459 to 484 patients (90% to 95%).*
^ Average burden score (range: 1-5) reported when symptom was present.

Patient-reported outcomes

Patients experienced on average 10.8 (SD: 6.1) out of 30 symptoms, ranging between 8.0-14.8 symptoms across centres. The overall mean symptom burden score was 30.7 (SD: 22.0) on a scale ranging from 0 (no symptoms) to 150 (all 30 symptoms bother 'very much'). Table 2 presents the 10 most frequently experienced symptoms and 10 most burdensome symptoms. The most common symptom was fatigue, which was experienced by 76% of the patients. 'Difficulty becoming sexually aroused' was – if present – reported as the most bothersome symptom, with a mean score of 3.4 on the 5-point scale. Figure 3 presents the variation among centres in symptom burden score in comparison with the overall mean score.
The mean (SD) scores for physical and mental HRQOL were 35.6 (10.2) and 47.7 (10.6), respectively. Figure 4 and 5 present the variation among centres in PCS and MCS in comparison to the overall mean scores.

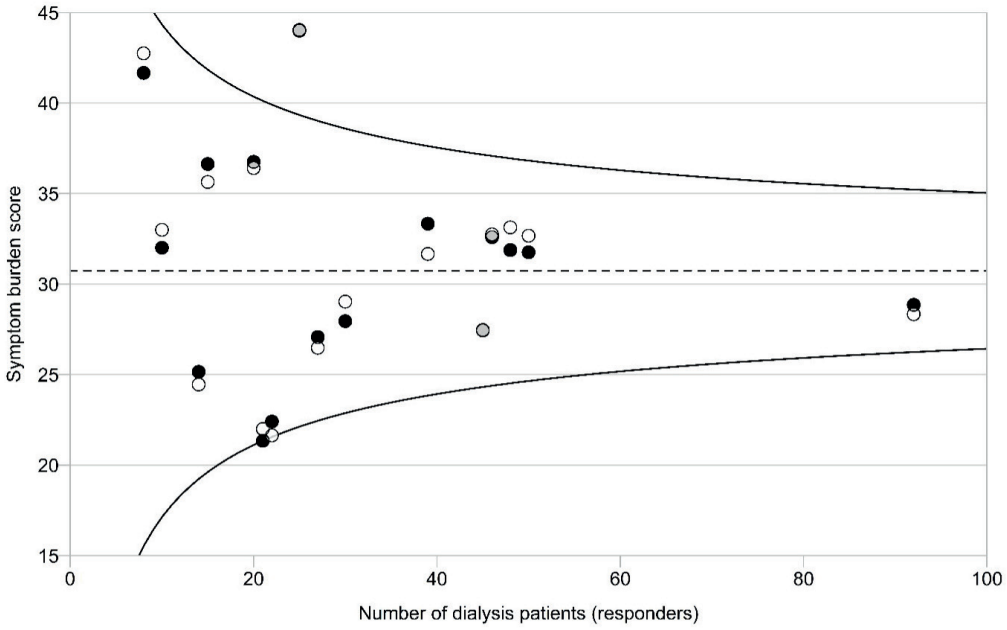

Figure 3. Observed and adjusted mean symptom burden score in 16 pilot centres.
Circles represent the mean observed (white circles) and adjusted (black circles) symptom burden score for each centre. Overlapping part of circles is depicted grey. The overall mean (dotted line) is used as reference in the comparison with each centre. The 95%-CI (curved lines) is provided around the overall mean. The mean score of one centre is outside the 95%-CI, indicating a statistically significant higher symptom burden score compared to the overall mean.*
**Adjusted for sex, age, SES, primary kidney disease, dialysis modality and time on RRT.*
Abbreviations: 95%-CI, 95%-confidence interval; SES, social economic status; RRT, renal replacement therapy.

Variance at centre level

The part of the observed variance in symptom burden, PCS and MCS scores explained by differences among centres was 2.6% (p=0.34), 1.0% (p=0.64) and 1.5% (p=0.45), respectively. The adjusted ICC was 3.1% (p=0.32), 0.6% (p=0.80) and 2.0% (p=0.41), respectively.

Patient experiences and preferences

At 3 months, 214 patients (79%) indicated that they wanted to share and discuss their results on HRQOL and symptom burden with their clinician. In total, 71 individual reports were sent to professionals: 5 patients in each centre, unless fewer patients gave their consent at 3 months (e.g. one centre had no responders at 3

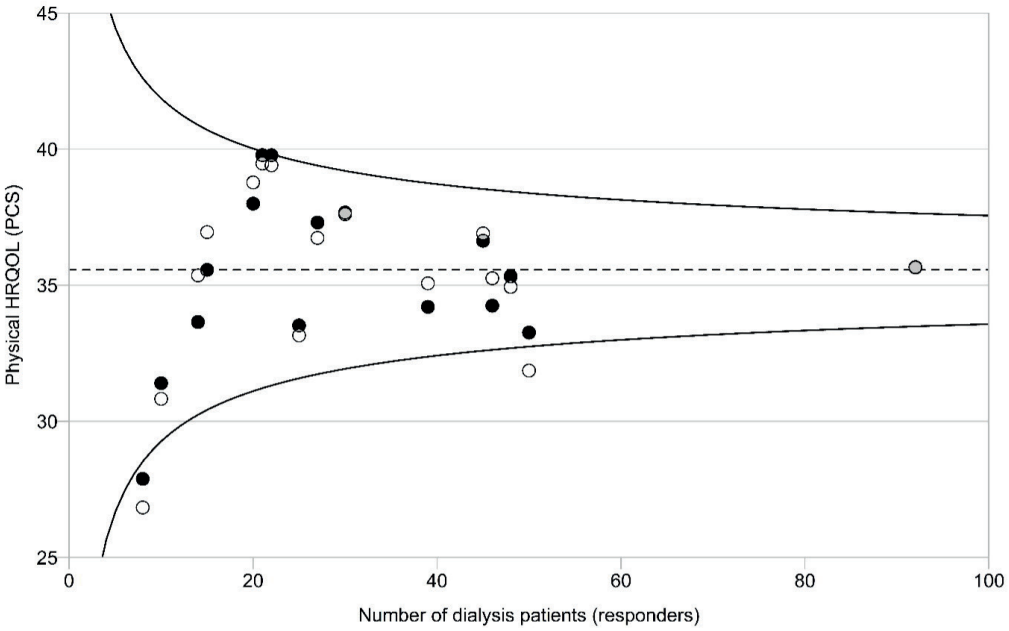

Figure 4. Observed and adjusted mean physical HRQOL (PCS) in 16 pilot centres.
Circles represent the mean observed (white circles) and adjusted (black circles) score for physical HRQOL per centre. Overlapping part of circles is depicted grey. The overall mean PCS (dotted line) is used as reference in the comparison with each centre. The 95%-CI (curved lines) is provided around the overall mean PCS. The adjusted mean score of one centre is outside the 95%-CI, indicating a statistically significant lower PCS compared to the overall mean PCS.*
**Adjusted for sex, age, SES, primary kidney disease, dialysis modality and time on RRT.*
Abbreviations: 95%-CI, 95%-confidence interval; HRQOL, health-related quality of life; PCS, physical component score; SES, social economic status; RRT, renal replacement therapy.

months). At 6 months, 16 patients from 10 different centres indicated that they had discussed the PROM-scores and gave feedback on how they experienced the conversation. Patients discussed the results with a nephrologist (N=11), a nurse (N=8) and/or a social worker (N=2). Patients rated the way in which results were discussed with a mean score of 3.8 (SD: 0.8, score range: 1-5; poor-excellent). Professionals also appreciated discussing patients' PROM-scores and experienced it as insightful. Additionally, professionals indicated that their involvement is important for implementing PROMs into routine care. Moreover, response rates were highest in centres where professionals indicated that they had put a lot of effort into informing and inviting patients.

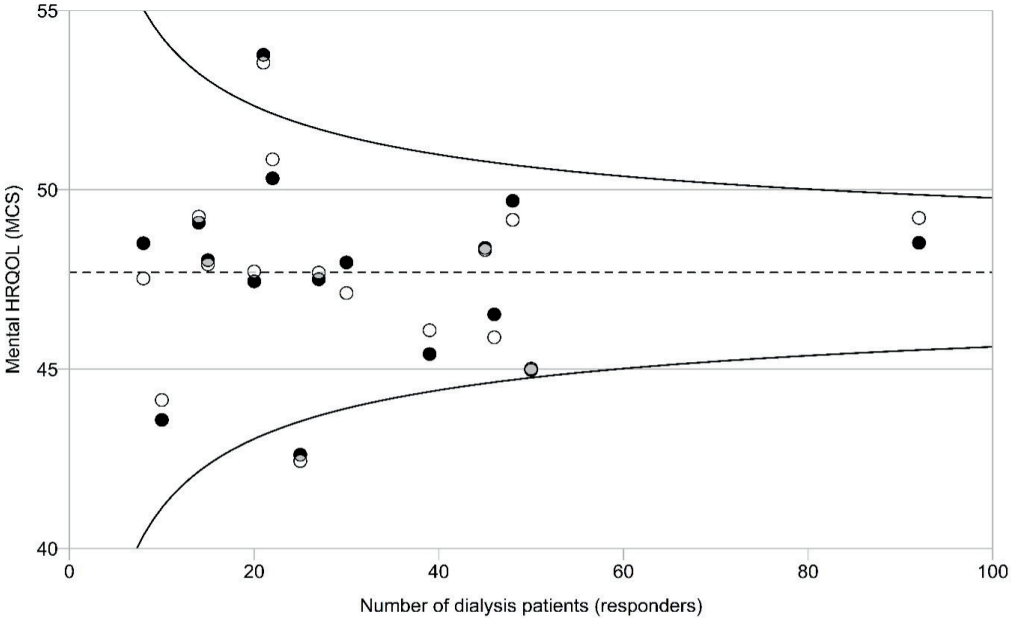

Figure 5. Observed and adjusted mean mental HRQOL (MCS) in 16 pilot centres.
Circles represent the mean observed (white circles) and adjusted (black circles) score for mental HRQOL per centre. Overlapping part of circles is depicted grey. The overall mean MCS (dotted line) is used as reference in the comparison with each centre. The 95%-CI (curved lines) is provided around the overall mean MCS. The mean scores of two centres are outside the 95%-CI: one above and one below the funnel, indicating a statistically significant higher and lower MCS compared to the overall mean MCS, respectively.*
**Adjusted for sex, age, SES, primary kidney disease, dialysis modality and time on RRT.*
Abbreviations: 95%-CI, 95%-confidence interval; HRQOL, health-related quality of life; MCS, mental component score; SES, social economic status; RRT, renal replacement therapy.

Eight patients participated in the focus group: 7 patients were male, aged 33-78 years old, 6 patients received haemodialysis and 2 patients peritoneal dialysis. Five themes were discussed: 'online tool', 'communication about content and purpose', 'benefits of using PROMs', 'feedback is crucial', and 'interpreting PROM-scores'. Examples of corresponding quotations by patients are presented in Table 3. Overall, patients were satisfied with the content, length and structure of the PROMs and the online completion was mentioned as an advantage. Communication about the content and the purpose of PROMs was not always clear for patients. Additional information is needed when receiving the invitation and when completing PROMs. Furthermore, patients indicated that the use of PROMs can contribute to their treatment by providing insight into patient's experienced health for both the clinician and the patient. Additionally, it may enhance patient-clinician communication, as it offers guidance during and in preparation of the conversation. Patients indicated that provision of individual feedback, written and oral, is crucial

Table 3. Examples of corresponding quotations by 8 patients receiving dialysis for the identified themes

Themes	Illustrative quotations
Online tool	"When filling it [the questionnaire] in online, you can also save and keep track of changes [in PROM-scores over time] yourself. This can be an advantage."
Communication about content and purpose	"Titles like PROMs, DSI and SF-12 make no sense. Use clear terms that appeal to the patients, such as 'symptom questionnaire' or 'quality of life questionnaire'."
Benefits of using PROMs	"The questionnaires can be used as a kind of checklist. To help you remember things. (…) The questionnaires help to come up with ideas." "Questionnaires help patients in initiating conversations. Some subjects are difficult to discuss." "You can adjust your treatment goal and plan according to these changes [in PROM-scores] over time, and this can be discussed with your healthcare professional."
Feedback is crucial	"Getting feedback on the results [PROM-scores] should be the basis of each PROMs measurement. After all, it is about your treatment." "Healthcare professionals have the important task to conduct the conversation well. Not every patient is out-spoken and active enough [to express needs and experiences]."
Interpreting PROM-scores	"It is nice to know what other kidney patients score, this gives some context…You want to know if a score of 46 is high, low or average." "I am not very interested in the average [PROM-] score in my hospital… Hospital scores should be available for patients (...) and local patients advocates to address quality improvement."

and that clinicians play an important role in this. Patients mentioned that individual feedback should be presented in a relevant context. They stressed the need for a reference score (e.g. average score of similar patients) to interpret their own results, not to compare their results.

Discussion

This study describes the first experience with PROMs in Dutch routine dialysis care. Overall, response rates were low with high variability among centres. Patients receiving dialysis experienced a high symptom burden and a decreased HRQOL. With regard to these PROM-scores, no centre effect could be observed. Patients believed that discussing HRQOL and symptom burden scores with their healthcare professional was highly insightful and valuable. Individual feedback on PROM-scores was considered crucial.

This is the first study presenting results on HRQOL and symptom burden in Dutch routine dialysis care setting. Patients receiving dialysis experienced a decreased physical HRQOL with an average score of 36 compared to 51 in the general Dutch population (aged 60-69).[40] Mental HRQOL was comparable to the general Dutch population.[40] The substantial symptom burden found is comparable to literature as well.[3, 23, 30] In line with a recent study [41], this study shows that the most common symptoms are not necessarily the ones that bother patients the most. The importance of certain symptoms may be different for each patient. Therefore, it is important to monitor and discuss the presence and burden of symptoms in order to understand what is most important to each patient. Further research is needed on how individual PROM-scores can be best used to address their needs.

Patients and professionals were very positive about the use of PROMs, in which they considered provision of individual feedback to be crucial. These first results are promising and imply that PROMs are suitable for use at individual level. The number of patients (n=16, 23%) that indicated to have discussed their PROM-scores seems low, but is proportionally similar compared to the response rate at 6 months. Moreover, the real number of patients that discussed their PROM-scores is probably higher, for instance because they discussed their report after the third time-point. Since all patients and professionals who discussed the PROM-scores highly appreciated the conversation, we decided to send the individual reports of the remaining patients (who gave consent) to their professionals and to include individual PROM reports into the electronic registration system.

Results from the focus group suggest that PROMs can provide insight into experienced health and needs, improve patient-professional communication and in-

crease shared decision-making. Similar potential benefits of PROMs are described in literature [9-13], however, there is a paucity of evidence on whether and how the use of PROMs actually leads to improvements in patients' outcomes. There are some studies suggesting that using PROMs will lead to better outcomes, for example: a randomized controlled trial in routine cancer care showed that web-based symptom monitoring resulted in improved HRQOL after 6 months, less hospital admissions and better 1-year survival, even though no specific guidance was provided to professionals on how to respond to reported symptoms.[42] Scholars also argue that patients receiving dialysis expect improvements when using PROMs, for instance: improved symptom experience as a consequence of improved patient-professional communication about symptoms.[41] However, further research is needed to investigate whether and how the use of PROMs leads to long term improvements in healthcare quality and outcomes in patients receiving dialysis.

The low response rate in this study is similar to the response rate (31%) of the Scottish Renal Registry when first introducing PROMs, confirming that it is challenging to incorporate PROMs into routine care.[18] Several factors may explain our results. First, professionals play an important role in informing and motivating patients. Highest response rates were observed in centres where professionals were highly engaged in the process. Therefore, interventions to increase professionals' engagement may be beneficial. Previous studies show that training and guidance on why and how to use PROMs and how to act in response to individual PROM-scores may facilitate the uptake of PROMs by professionals.[24, 43, 44] In the Scottish registry, interventions to improve patient information letters and staff awareness indeed resulted in an increase of their response rate to 48%.[18] Second, the process of inviting patients was regulated by each centre independently to promote incorporation into their workflow. A drawback of this approach may be that not every centre organized this in a structured way or had the desired facilities (e.g. availability of resources such as a process coordinator, printer and internet access) and consequently, some patients may not have been invited. Moreover, differences across centres existed with regard to the type and amount of support that patients received when filling in PROMs (e.g. availability of electronic devices in centres), by whom support is provided (e.g. medical staff or partner) and at which location (home or medical centre). It is possible that the centres' support and the possibility to complete PROMs on site, contributed to higher response rates. On the other hand, the availability or lack of support in centres could also have influenced patients' responses. However, we did not observe differences among centres with regard to PROs. Third, some patients are more likely to participate than others. In line with literature, we found that older patients with a higher SES [18] and male

[45] patients were more likely to participate. Further research focussing on non-responders is needed to gain more insight into barriers and potential facilitators for participation in order to implement recruitment strategies tailored to these more difficult-to-reach patients.[46, 47]

Higher response rates are needed for optimal use of PROMs at patient level (e.g. individualized prognosis) and aggregated level (e.g. evaluation of healthcare quality).[9] Based on this study and literature, we provide the following recommendations to increase the response rate. First, provide additional training and support to increase engagement of healthcare professionals and to reinforce the professionals' feeling of being comfortable and able to handle PROM-scores.[48, 49] Second, recruitment strategies should be improved and, given that dialysis patients regularly encounter healthcare professionals, recruitment strategies should particularly focus on tailored communication (e.g. on personal relevance and confidentiality) and support (e.g. completing PROMs online).[25] Third, communication between stakeholders should be improved, for instance by supportive resources such as provision of material to inform patients, individualized reports on PROM-scores, and updates on centres' experiences (best practices), response rates and outcomes.[25, 48] Fourth, logistics should be further developed to improve response rates and to support professionals and patients in using PROMs in clinical practice, for example: provide individual reports directly after PROMs completion, incorporate PROMs into the electronic health record, and send automated invitations (e.g. prior to patient's upcoming consultation visit [24]) and reminders to complete PROMs.[50] Finally, we propose to assess and discuss PROM-scores twice per year, as we believe this provides insight into patient's outcomes over time with minimal burden to patients and professionals. Some centres suggested using PROMs during a more extended consultation, such as an annual check-up, to discuss PROs progression over time, patients' needs and treatment goals.

The low response rate and selective response are important results, but also limitations in this study. For instance, our results suggest that there is no relevant centre-effect on patients' HRQOL and symptom burden, however, possibly real centre-effects could not be detected due to low and selective responses. Furthermore, responders are likely to be more health conscious and involved in healthcare compared to non-responders (i.e. healthy responder bias). For example, the patients who shared their experience about discussing PROM-scores may be more involved and may have a more positive attitude towards using PROMs in clinical practice, which should be taken into account when interpreting the results. Additionally, the selective response may have led to effect underestimation of patients' outcomes: symptom burden is likely to be higher and HRQOL lower in the

total dialysis population. However, information about non-responders was also presented and can therefore be taken into account when interpreting the results. Although current data may be insufficient to evaluate healthcare quality, the electronic registration of PROMs as part of Renine is designed in such a way that future data may be used for this purpose.[9] We believe that it is a major strength that PROMs can be used both at individual level in clinical practice and at aggregated level to evaluate healthcare quality. Possibly, this combination is crucial, as the use of PROMs for individual patient's treatment may be the most important factor in reaching sufficient response rates to enable evaluation of healthcare quality.

Another strength is the multicentre study design and methods used in this study. With 16 participating centres, a substantial sample of all Dutch dialysis patients was included. Additionally, by leaving centres free to incorporate PROMs into their workflow, a broad variation of in-centre processes was included, which may provide valuable information (e.g. insight into best practices for using PROMs in clinical settings) and may eventually promote adaptation and implementation of PROMs into clinical practice (e.g. due to limited workflow disruptions and research processes that are in line with priorities of patients and professionals).[13, 24, 25] Moreover, all relevant stakeholders (e.g. patients, healthcare professionals and researchers) were involved from the start, resulting in widely supported PROMs that fit clinical practice and research.[13, 24, 25] Besides, during the developmental phase much attention has been paid to the electronic registration system and selection of valid questionnaires.[23, 24] The pilot study confirms that the questionnaires were suitable and feasible, with only minor suggestions for improvement. Finally, by making use of both quantitative and qualitative methods, we obtained a broad picture of perceived benefits and barriers for implementing PROMs into nephrological care and possibilities for improvement.

In conclusion, first results from the Dutch registry of PROMs in patients receiving dialysis showed low response rates with a high centre variability. Achieving higher response rates is challenging and requires extra encouragement of patients and professionals. Patients experienced a high symptom burden and a decreased physical HRQOL. Discussing symptom and HRQOL results was greatly appreciated and considered crucial for the use of PROMs in routine care. Further research is needed to investigate how collection and use of PROMs can be successfully integrated into routine care in order to improve healthcare quality and outcomes.

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