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Original Article

ORIGINAL ARTICLE

Remote symptom monitoring with patient-reported outcome measures in outpatients with chronic kidney disease (PROKID): a multicentre randomised controlled non-inferiority study

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ABSTRACT

Background. The increasing incidence of chronic kidney disease (CKD) is straining the capacity of outpatient clinics. Remote healthcare delivery might improve CKD follow-up compared with conventional face-to-face follow-up. Patient-reported outcomes (PROs) are used to empower remote follow-up and patient engagement. The consequences of shifting from face-to-face follow-up to remote outpatient follow-up on kidney function, health resource utilisation and quality of life remain unknown.

Methods. We conducted a multicentre pragmatic non-inferiority trial at three outpatient clinics in the Central Denmark Region. A total of 152 incident outpatients with CKD were randomised (1:1:1) to either PRO-based, PRO-telephone follow-up or standard of care (SoC). The primary outcome was the annual change in kidney function measured by the slope of the estimated glomerular filtration rate (eGFR). The non-inferiority margin was an eGFR of 2.85 ml/min/1.73 m^2/year. Mean differences were estimated using intention-to-treat (ITT), per protocol and random coefficient models.

Results. Mean eGFR slope differences between PRO-based and SoC were −0.97 ml/min/1.73 m^2/year [95% confidence interval (CI) −3.00–1.07] and −1.06 ml/min/1.73 m^2/year (95% CI −3.02–0.89) between PRO-telephone and SoC. Non-inferiority was only established in the per-protocol analysis due to CIs exceeding the margin in the ITT group. Both intervention groups had fewer outpatient visits: −4.95 (95% CI −5.82 to −4.08) for the PRO-based group and −5.21 (95% CI −5.95 to −4.46) for the PRO-telephone group. We found no significant differences in quality of life, illness perception or satisfaction.

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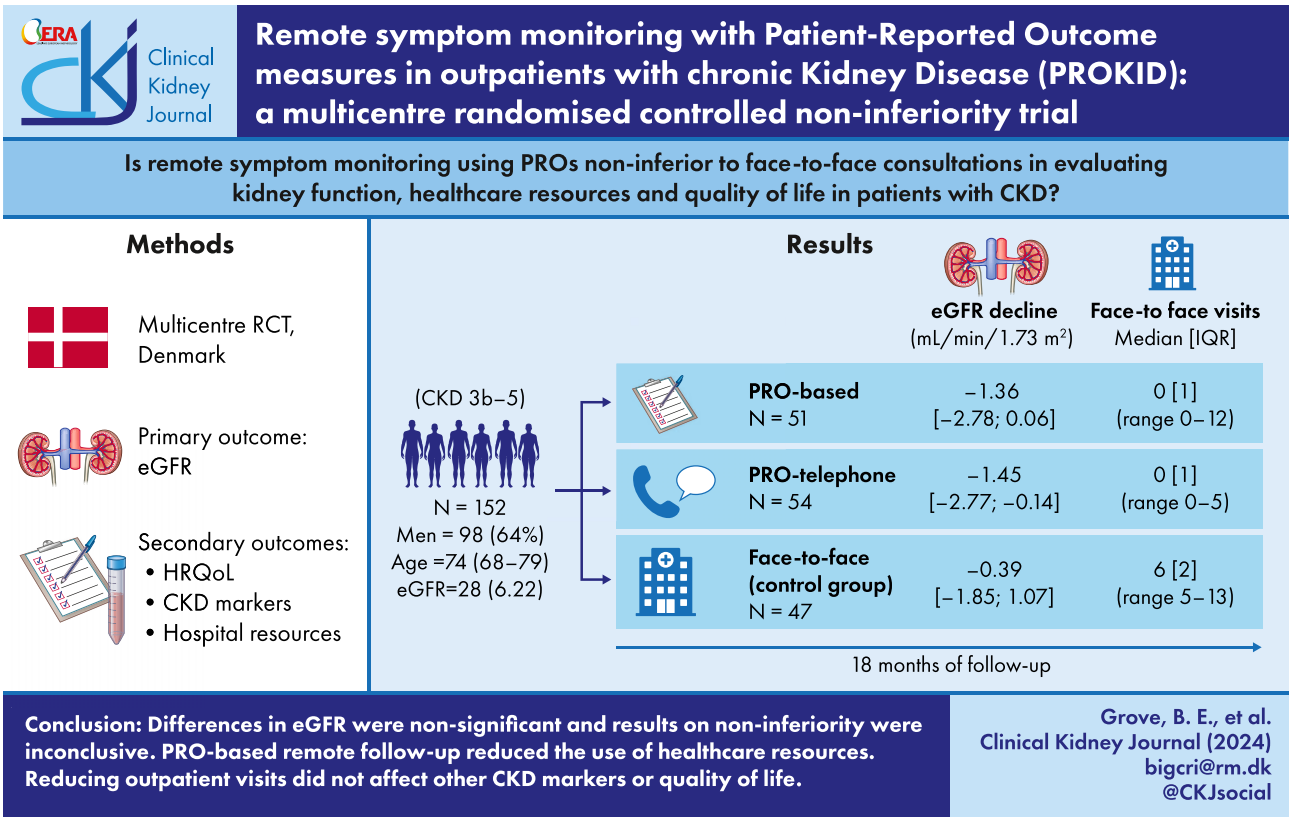
Conclusion. Differences in the eGFR slope between groups were non-significant and results on non-inferiority were inconclusive. Thus, transitioning to remote PRO-based follow-up requires close monitoring of kidney function. Reducing patients' attendance in the outpatient clinic was possible without decreasing either quality of life or illness perception.
ClinicalTrials.gov identifier: NCT03847766

GRAPHICAL ABSTRACT



Keywords: chronic kidney disease, outpatient care, patient-reported outcome measures, randomized controlled trial, remote symptom monitoring

KEY LEARNING POINTS

What was known:

- During the last decade, there has been increasing outpatient activities and the use of telephone consultations.
- Remote symptom monitoring using patient-reported outcomes (PROs) has been investigated in other populations of chronic and malignant diseases, but its potential in patients with chronic kidney disease (CKD) remains unknown.

This study adds:

- No differences in the patients' kidney function across the intervention groups were found and patients' quality of life, satisfaction and illness perception were not affected.
- Implementing PRO-based remote follow-up reduced face-to-face consultations but increased the number of telephone consultations.
- Remote PRO-based follow-up had no negative effect on other CKD markers.

Potential impact:

- Close monitoring and an awareness of preserving kidney function is crucial in transitioning from the standard of care to remote follow-up.
- Remote PRO-based follow-up decreases the need for face-to-face outpatient visits.

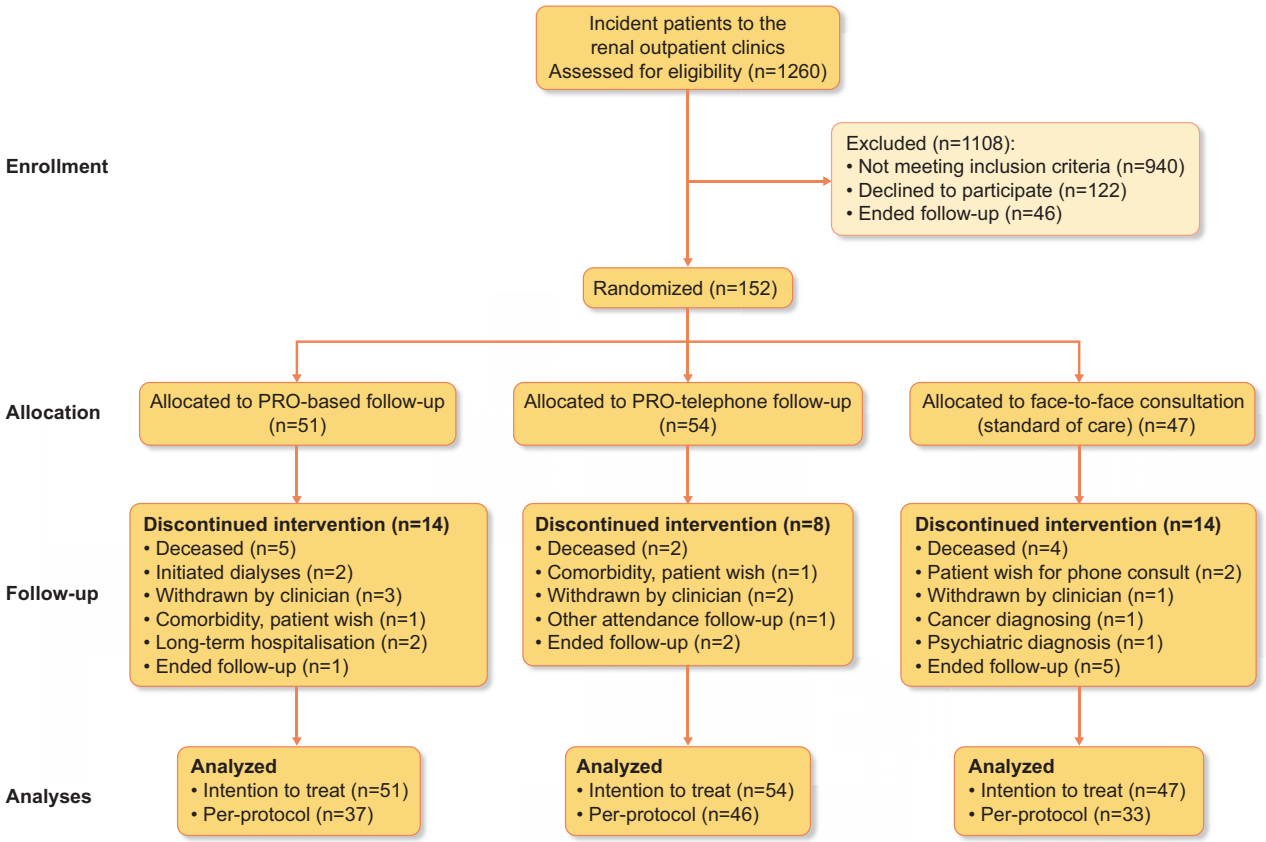


Figure 1: CONSORT flow diagram.

INTRODUCTION

Globally, the incidence of people with chronic kidney disease (CKD) and the demand to deliver more healthcare is increasing [1, 2]. In Denmark, patients with CKD are referred to specialist care for diagnosis and treatment in hospitals when the estimated glomerular filtration rate (eGFR) reaches 30–40 ml/min/1.73 m^2 [3]. Providing care for people with CKD stages 3b–5 requires monitoring kidney function, symptom burden and overall well-being [4, 5]. Patients' health conditions may be captured using patient-reported outcomes (PROs) collected through disease-specific questionnaires [6, 7]. Using PROs in outpatient care may provide additional information about patient perceptions of their health [8, 9]. When regular outpatient visits are replaced with disease-specific questionnaires, it is termed 'PRO-based remote follow-up' [10]. The effects of using PRO in remote care have been investigated in other populations and have been shown to improve symptom control [11, 12], patient–clinician communication [13], satisfaction and supportive care [14, 15] and decreased outpatient appointments [16, 17]. Evidence for the effects of remote care for patients with CKD is not yet established, even though studies have shown that, e.g., telephone consultations have been widely adopted as a safe option for receiving care during the coronavirus disease 2019 (COVID-19) pandemic [18].

To investigate the efficacy and safety of remote symptom monitoring in patients with CKD, we conducted a multicentre randomised non-inferiority study (PROKID) with two different intervention groups compared with a standard-of-care (SoC) group. The intervention groups were either entirely managed by PROs or PROs supported by telephone consultations. The primary endpoint was non-inferiority in the difference of the eGFR slope. Secondary endpoints were the difference in quality of life (QOL), illness perception and the use of healthcare resources.

We hypothesised that the eGFR slope change was non-inferior between patients in the remote PRO-based follow-up groups compared with patients receiving the SoC.

MATERIALS AND METHODS

Study design and participants

The PROKID study is a multicentre non-inferiority randomised controlled study carried out at Aarhus University Hospital, Gødstrup Hospital and Region Hospital Central, Viborg, Denmark. Patients were included from January 2019 until August 2021 with 18 months of follow-up. Patients were eligible if they were newly referred to the renal outpatient clinic, ≥18 years of age, with an eGFR of 10–40 ml/min/1.73 m^2 and did not exhibit cognitive dysfunction. The main exclusion criteria were projected risk of progression to end-stage kidney disease (ESKD) within 12 months, inability to answer a questionnaire or suffering from terminal illness (Fig. 1). The design and procedures of the study have been published previously [19]. The Consolidated Standard of Reporting Trial (CONSORT) Extension for Non-inferiority [20] and CONSORT PRO [21] extension checklists were followed (Supplementary Table S1). The study was conducted following the Helsinki Declaration, and the Danish Data

Protection Agency granted permission to store and use confidential data (no. 1-16-02-873-17). Verbal and signed written consent was obtained from each patient before enrolment.

Randomisation

Participants were randomly allocated (1:1:1) to either PRO-based, PRO-telephone or SoC. Computer-generated randomisation was used and project nurses carried out randomisation after enrolment and the patients completed a baseline questionnaire. Blinding was not possible.

Interventions

All patients in the study were followed for 18 months with six planned contacts and had blood samples taken at a local clinic or hospital before contact. Irrespective of group allocation, patients were allowed to initiate contact between visits.

Patients randomised to the PRO intervention responded to a disease-specific questionnaire either on paper or electronically through a generic web PRO system before each consultation [6, 22] that included self-reported weight and blood pressure (BP). These PRO data were available to physicians in the electronic health record [6].

PRO-based follow-up

The questionnaire was used as a decision aid together with other clinical data for triaging patient care and contact. A physician assessed the questionnaires, provided feedback on responses and blood tests by secure email and called the patient or scheduled a face-to-face visit if necessary or if it was desired by the patient.

PRO-telephone follow-up

The questionnaire was used as communication support and a symptom monitoring aid during the telephone consultation. The patients' responses, results of blood tests and BP and weight were discussed.

SoC (control group)

Patients receiving the SoC were seen by the physician and had BP and weight measured by the nurse in the outpatient clinic.

Primary outcome

The primary outcome was the difference in the slope of eGFR per year between the intervention groups and the SoC group.

Secondary outcomes

The secondary outcomes were the difference in other CKD markers [urine albumin:creatinine ratio (UACR), plasma potassium, plasma phosphate and BP], ESKD, hospitalisations and PROs, including health-related quality of life (HRQOL), measured by the EuroQoL five dimension (EQ-5D) index and EQ-5D visual analogue scale (VAS) [23], and illness perception (IP) measured by the Brief Illness Perception Questionnaire (BIPQ) [24]. Healthcare evaluation comprises confidence, satisfaction, involvement and safety measured by single items from the Danish Cancer Society's Patient-Reported Experience Measure questionnaire [25]. Registered contacts included all outpatient telephone consultations and face-to-face consultations. Outpatient visits included all face-to-face consultations. Additional information on the nature of resource utilisation was obtained from the medical records and captured in a database (REDCap) [26]. An overview of outcomes has been published [19].

Sample size

Based on a literature review, we assumed that the expected loss in eGFR would be ≈5 ml/min/1.73 m^2/year in all groups [27]. The sample size was calculated using a non-inferiority margin of 2.85 ml/min/1.73 m^2/year between the groups [19, 27]. This estimate was based on existing literature [28], clinical judgements [20] and the assumption that the study participants would present a consistent eGFR during the follow-up period [27]. Given 90% statistical power and a *P*-value of 0.05, we needed 34 patients in each group to detect non-inferiority group differences. To examine secondary outcomes and account for attrition, a total of 152 patients were enrolled.

Statistical methods

All randomised participants were included in the intention-to-treat (ITT) analyses. Per-protocol analysis included patients who completed all six contacts in their allocated group. Each intervention group was compared with the SoC group. Normally distributed baseline data were presented with means and standard deviations (SDs); otherwise, medians and interquartile ranges (IQRs) were reported. Sum scores followed guidelines for handling missing items for each score.

Kidney function

The primary outcome was the mean difference (MD) and a two-sided 95% confidence interval (CI) in a change in kidney function measured as the slope of eGFR within and between the groups. A random coefficient mixed model was used [29]. Before the analyses, outliers were identified and longitudinal plots of the data over time were constructed for visual presentation. Model assumptions were checked by comparing observed and expected within-subject SDs and correlations and by inspecting plots of residuals versus fitted values and QQ plots. The model included fixed and random (time) effects for the intercept and coefficient. We performed a sensitivity analysis adjusting for sex, age and comorbidity.

Secondary outcomes

CKD markers were analysed by calculating the MD from baseline to the end of follow-up and compared between groups. Whenever possible, an ITT approach was used. PRO data were analysed in the per-protocol population. Between- and within-group differences were calculated using a linear mixed regression model. Longitudinal plots of the PRO data over time were constructed to visualise the presentation of data. Between-group differences in the categorical variables, such as the utilization of healthcare, were summarised and reported as numbers and percentages. The MD between groups was assessed by linear regression. Due to an expected skewed distribution, 95% CIs will be found using the bootstrap method with 1000 replications [30]. Two-sided *P*-values $<.05$ were considered to indicate statistical significance.

Table 1: Baseline characteristics.

Variables	Total ($N = 152$)	SoC ($n = 47$)	PRO-telephone follow-up ($n = 54$)	PRO-based follow-up ($n = 51$)
Age (years), median (IQR)	74 (68–79)	74 (64–79)	74 (68–78)	75 (68–80)
Male, *n* (%)	98 (64)	32 (68)	31 (57)	35 (68)
eGFR (ml/min/1.73 m^2)	28.67 (6.22)	28.29 (6.60)	28.98 (6.49)	28.72 (6.43)
Systolic BP (mmHg)	133 (21)	133 (21)	132 (20)	136 (21)
Diastolic BP (mmHg)	75 (12)	77 (12)	75 (13)	75 (12)
Pulse (bpm)	72 (13)	74 (15)	71 (12)	71 (13)
Charlson Comorbidity Index	1.96 (1.33)	2.02 (1.24)	1.91 (1.28)	1.96 (1.48)
Plasma phosphate (mmol/l)	1.16 (0.25)	1.21 (0.30)	1.15 (0.22)	1.15 (0.24)
Plasma albumin (g/l)	37.70 (3.01)	38.09 (3.16)	37.65 (3.28)	37.38 (2.56)
UACR (mg/ml), median (IQR)	75 (476)	106 (558)	62 (574)	56 (230)
Plasma potassium (mmol/l)	4.36 (0.60)	4.28 (0.43)	4.45 (0.71)	4.32 (0.60)
Haemoglobin (mmol/l)	7.83 (1.10)	7.90 (1.32)	7.81 (0.98)	7.8 (1.02)
Education, *n* (%)				
Low (<10 years)	37 (24)	10 (21)	14 (26)	13 (25)
Medium/high (≥10 years)	100 (66)	32 (68)	35 (65)	33 (65)
Missing	15 (10)	5 (11)	5 (9)	5 (10)
Labour market affiliation, *n* (%)				
Employed	20 (13)	9 (19)	7 (13)	4 (8)
Retired	119 (78)	33 (70)	43 (80)	43 (84)
Missing	13 (9)	5 (11)	4 (7)	4 (8)
QOL (EQ-5D index)				
Median (IQR)	0.878 (0.755–0.959)	0.815 (0.660–0.939)	0.912 (0.819–1)	0.858 (0.758–0.952)
Mean (SD)	0.82 (0.21)	0.78 (0.19)	0.86 (0.21)	0.81 (0.20)
Missing, *n* (%)	5 (3)	3 (6)	1 (2)	1 (2)
QOL (EQ-5D-VAS)				
Median (IQR)	70 (50–80)	62.5 (50–80)	80 (60–85)	70 (50–80)
Mean (SD)	67.36 (21.09)	63.98 (20.23)	70.84 (22.76)	66.64 (19.72)
Missing, *n* (%)	5 (3)	3 (6)	1 (2)	1 (2)
Illness perception score	37.73 (11.95)	40.59 (10.71)	34.42 (12.03)	38.56 (12.35)
Missing, *n* (%)	14 (9)	5 (10)	6 (11)	3 (6)

Values are presented as mean (SD) unless stated otherwise.

RESULTS

From January 2019 to August 2021, 320 newly referred patients with CKD were found eligible for possible inclusion in the PROKID trial and a total of 152 (48%) accepted participation. A total of 25 (16%) patients left the study or died, 11 (7%) after randomisation, leaving 116 (76%) patients for the per-protocol analyses (Fig 1). Non-completer analyses showed that dropouts were older ($P = .04$) and had a higher level of comorbidity ($P = .01$) and a lower level of concentration ($P = .02$) (Supplementary Table S2). Demographic and clinical characteristics at baseline were balanced ($P < .05$) between the groups (Table 1).

Kidney function

We found no statistical differences in the eGFR slope across the intervention groups. Nevertheless, as the lower limit of the CIs extended the non-inferiority threshold in both PRO-based intervention groups, non-inferiority was not established for the primary outcome in the ITT analysis (Fig. 2). A difference in eGFR slope when comparing each of the PRO intervention groups with the SoC was −0.97 ml/min/1.73 m^2/year (95% CI −3.00–1.07) and −1.06 ml/min/1.73 m^2/year (95% CI −3.02–0.89), respectively (Table 2). As the CI includes zero and the non-inferiority margin, the results in the ITT population are inconclusive. In the per-protocol analysis, non-inferiority was established. The adjusted analyses reached the same results

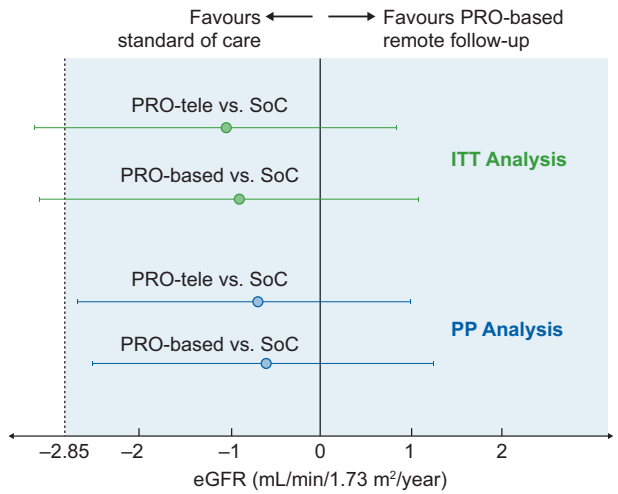


Figure 2: Forrest plot displaying the difference in the slope of eGFR between the PRO intervention groups and the SoC. ITT and per-protocol analyses.

(Supplementary Table S3). While a decrease in the eGFR slope was noted within all groups, only in the PRO-telephone group was a statistically significant decrease observed, with an eGFR slope of −1.45 ml/min/1.73 m^2/year (95% CI −2.77 to −0.14) (Table 3 and Fig. 3).

Table 2: Differences in the change in the eGFR slope between the PRO-based intervention groups and the SoC 18 months after randomisation.

		PRO-based versus SoC		PRO-telephone versus SoC	
Intervention	n	Change in eGFR[a] (ml/min/1.73 m^2/year) (95% CI)	P-value	Change in eGFR[b] (ml/min/1.73 m^2/year) (95% CI)	P-value
ITT	152	−0.97 (−3.00–1.07)	.35	−1.06 (−3.02–0.89)	.28
PP	116	−0.62 (−2.58–1.35)	.54	−0.86 (−2.74–1.02)	.36

PP: per-protocol.
[a]The estimated mean difference in eGFR slopes between the PRO-based remote follow-up and SoC group.
[b]The estimated mean difference in eGFR slopes between the PRO-telephone and SoC group.
Random coefficient mixed models were used.

Table 3: Decline in eGFR within each of the intervention groups 18 months after randomisation.

Intervention	SoC eGFR decline (ml/min/1.73 m^2/year) (95% CI) (n = 47/33)	PRO-telephone eGFR decline (ml/min/1.73 m^2/year) (95% CI) (n = 54/46)	PRO-based eGFR decline (ml/min/1.73 m^2/year) (95% CI) (n = 51/37)
ITT	−0.39 (−1.85–1.07)	−1.45* (−2.77 to −0.14)	−1.36 (−2.78–0.06)
PP	−0.20 (−1.63–1.23)	−1.06 (−2.28–0.15)	−0.82 (−2.17–0.54)

PP: per-protocol.
Linear mixed model regression was used. A negative value means a decrease in eGFR.
*Statistically significant ($P < .05$).

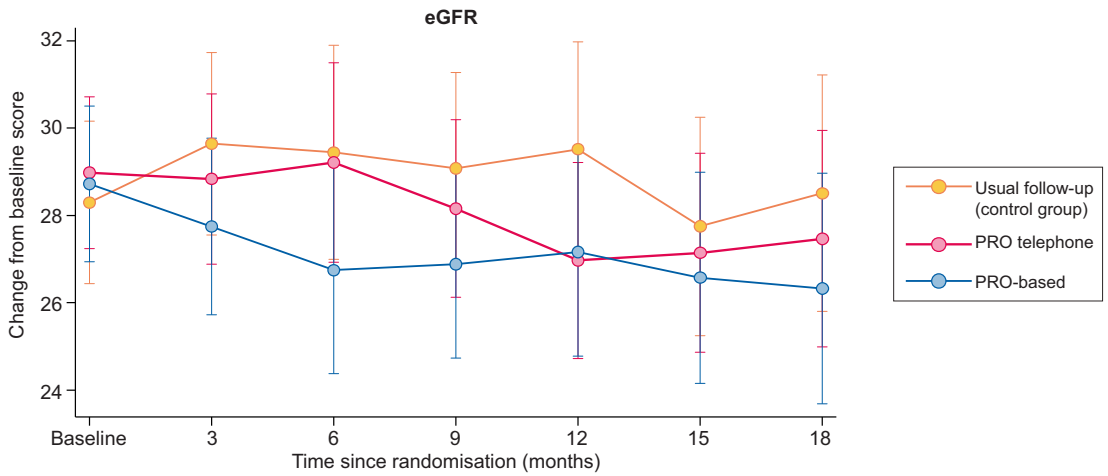


Figure 3: Change in eGFR within and between the intervention groups.

Healthcare utilisation

Patients who received the PRO-based intervention had significantly fewer contacts with the outpatient clinic than those who received the SoC [MD −3.04 (95% CI −4.43 to −1.64)] (Table 4). The total number of contacts to the outpatient clinic was highest in the PRO-telephone group, with a median of 7 (IQR 2) contacts, followed by a median of 6 (IQR 3) contacts in the SoC group and a median of 3 (IQR 4) registered contacts for the patients in the PRO-based group (Table 4). Both intervention groups had fewer outpatient visits compared with the SoC, with an MD of −4.95 (95% CI −5.82 to −4.08) for the PRO-based intervention and −5.21 (95% CI −5.95 to −4.46) for the PRO-telephone group. Accordingly, patients in the intervention groups had more frequent telephone consultations compared with the SoC, with an MD of 1.99 (95% CI 1.19–2.80) for the PRO-based intervention and 5.80 (95% CI 5.02–6.58) for the PRO-telephone group. Supplementary Table S4 outlines an overview of the type of contact.

HRQOL

A higher not statistically significant difference in self-reported outcomes (EQ-VAS) was seen in the PRO-based follow-up group

Table 4: Healthcare utilisation during the 18-month follow-up period among outpatients with CKD (ITT population = 152).

Variables	SoC ($n = 47$)	PRO-telephone ($n = 54$)	PRO-based follow-up ($n = 51$)	Mean difference[a] PRO-telephone versus SoC (95% CI)	Mean difference[a] PRO-based versus SoC (95% CI)
Follow-up time (months)					
Total	708	888	762		
Median (IQR)	18 (6)	18 (0)	18 (6)	1.38 (−0.50–3.26)	−0.12 (−2.22–1.97)
All registered contacts					
Total	315	394	191		
Median (IQR) (range)	6 (3) (0–19)	7 (2) (0–17)	3 (4) (0–20)	0.59 (−0.66–1.84)	−3.04 (−4.43 to −1.64)
Contacts per month, mean (SD)	0.45 (0.16)	0.45 (0.15)	0.24 (0.20)	−0.01 (−0.07–0.06)	−0.22 (−0.29 to −0.14)
Outpatient visits[b], median (IQR) (range)	6 (2) (5–13)	0 (1) (0–5)	0 (1) (0–12)	−5.21 (−5.95 to −4.46)	−4.95 (−5.82 to −4.08)
Outpatient visits per month, mean (SD)	0.39 (0.10)	0.04 (0.08)	0.06 (0.11)	−0.35 (−0.38 to −0.31)	−0.33 (−0.38 to −0.29)
Telephone consultations[c], median (IQR) (range)	0 (1) (0–8)	6 (2) (6–14)	3 (3) (0–10)	5.80 (5.02–6.58)	1.99 (1.19–2.80)
Telephone consultation per month, mean (SD)	0.07 (0.13)	0.40 (0.10)	0.19 (0.17)	0.33 (0.38–0.38)	0.13 (0.07–0.19)
Additional contacts[d], median (IQR) (range)	1 (2) (0–11)	1 (2) (0–11)	1 (3) (0–14)	0.22 (−0.72–1.16)	0.37 (−0.67–1.40)

[a]The ITT MDs and 95% CIs were obtained after linear regression by using the bootstrap method with 1000 replications [30].
[b]Including the scheduled visits in the usual follow-up group (control group).
[c]Including the scheduled telephone consultations in the PRO-telephone group.
[d]Number of additional contacts between scheduled contacts.

as compared with the SoC [MD 4.56 points (95% CI −3.55–12.67)] (Supplementary Table S5). Patients in the SoC group reported the lowest QOL from the onset of the study and did not change in level during follow-up (Fig. 4). We found no between-group differences in the EQ-5D index score.

Illness perception

Patients in the PRO-based intervention groups reported a more threatening view of their illness during follow-up compared with the SoC group, although none of the difference was statistically different (Fig. 4 and Supplementary Table S5).

Healthcare evaluation

No statistically significant differences were found between the SoC and intervention groups regarding evaluation of healthcare (satisfaction, involvement, safety and confidence). Fig. 4 outlines the development over time (numbers shown in Supplementary Table S5). More than 95% of the patients in all three groups answered that they were 'very satisfied/satisfied' with their mode of control.

No differences in the CKD markers such as BP and UACR were found (Supplementary Table S6).

DISCUSSION

We hypothesised that a change in kidney function, measured by the slope of eGFR, was non-inferior between patients in the two PRO-based intervention groups compared with patients receiving the SoC. We found no significant differences in the slope of eGFR, and results regarding non-inferiority were inconclusive. Patients in the PRO-based intervention groups had an overall reduction of face-to-face consultations and more telephone consultations. No significant differences between the groups were found in the clinical data, patients' QOL, illness perception and health service evaluation.

In the ITT analyses, we did not reach non-inferiority in the slope of eGFR, as the lower bound of the CIs reached the non-inferior limit. In the per-protocol analyses, the slope of the eGFR decline between the SoC and intervention groups was not significantly different and all the estimates were within the non-inferiority margin. Thus the per-protocol analyses demonstrated non-inferiority and are considered equally important [31]. The overall results regarding non-inferiority were inconclusive [20].

A commonly used minimum clinically important difference in eGFR has been reported in various studies ranging from 1 to 5 ml/min/1.73 m^2/year [28, 32]. Thus the differences across the intervention groups ranging from eGFR −0.97 to −1.06 ml/min/1.73 m^2/year with CIs reaching the non-inferiority limit, represent a clinically meaningful difference. However, the non-inferiority limit must be determined carefully and will always depend on the specific context and population [33]. During the follow-up period, the decrease in eGFR within the intervention groups was modest, ranging from −0.39 to −1.45 ml/min/1.73 m^2. These findings were lower than those from a recent meta-analysis, including CKD 3–5 cohorts [34]. We recruited patients with an eGFR of 10–40 ml/min/1.73 m^2, however, the contrast may be caused by the low-risk CKD population in our study.

Patients in the PRO-based intervention groups had significantly fewer contacts and fewer outpatient visits than the SoC group. Effectiveness in terms of utilization of healthcare in a remote care intervention has been investigated in other studies, reporting a lower number of outpatient visits in the intervention groups among patients with rheumatoid arthritis [17, 35], inflammatory bowel disease [36, 37], type 1 diabetes [38] and cancer [39]. Our study stands out from the other research endeavours, as the PRO questionnaire assessed patients' need for contact. Combining the PRO questionnaires and blood samples formed the basis for triaging patient care and the type of

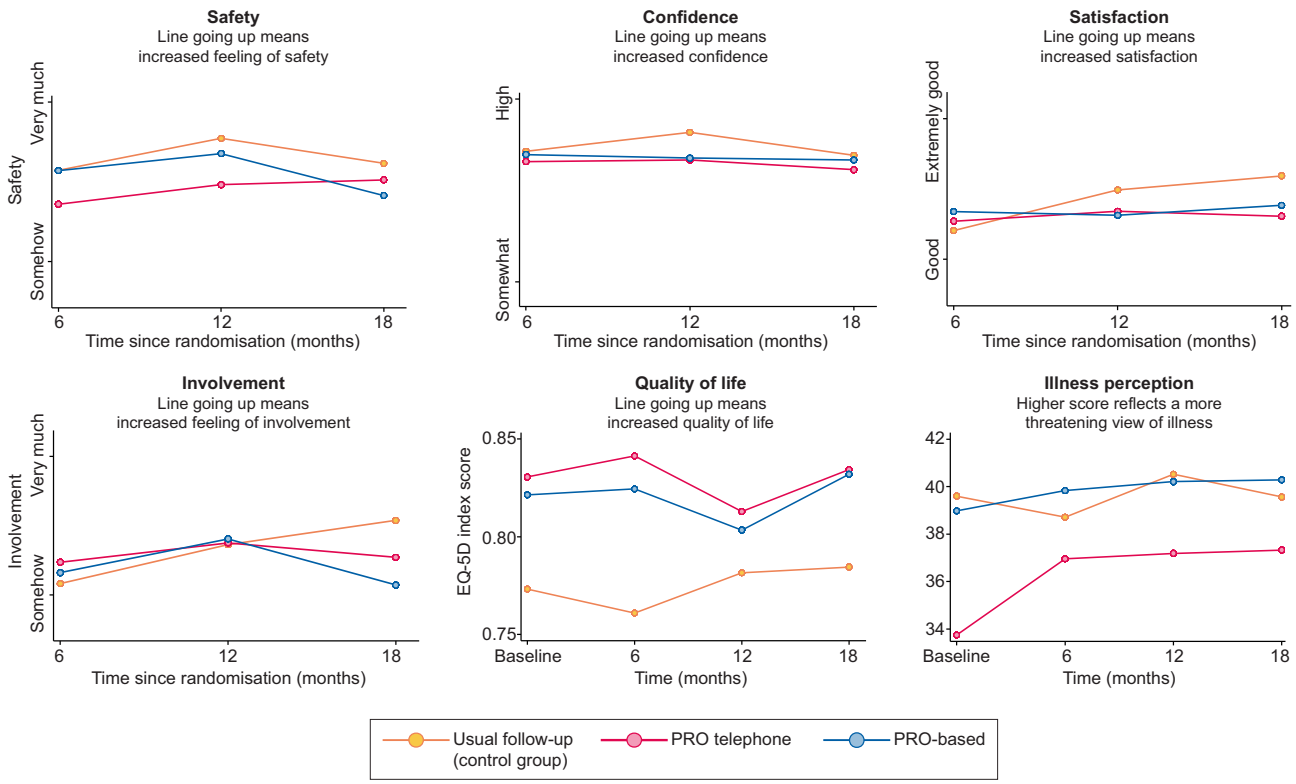


Figure 4: Change in PROs during the 18 months of follow-up. Per-protocol population = 116.

contact. In evaluating the resource utilisation of this intervention, it is essential to note that patients in the SoC group were consulting both a physician and a nurse, whereas patients in the intervention groups primarily interacted with a physician, and only saw a nurse if a nursing task was deemed relevant by the physician. A process evaluation following the PROKID trial outlines the distribution and nature of visits [40].

Self-rated QOL at baseline was high, but lower than that of the general Danish population at 0.90 (SD 0.16) [41]. No significant differences were observed in the change in the QOL within or between the groups, and only minor changes were detected.

Our findings showed a non-significant increase in IP compared with the SoC. Nonetheless, we argue that knowledge of the individual's illness representation can be valuable in healthcare settings. It may help healthcare providers to tailor their communication and treatment plans accordingly [42].

Qualitative studies have found that both patients and physicians were overall confident in using a remote approach [40, 43]. This finding was supported in our study, as >95% of the patients reported confidence and satisfaction with this mode of follow-up. No statistically significant differences in patient satisfaction and health service evaluation across the intervention groups were found. If patients felt unconfident or unsatisfied with the follow-up mode, we would presumably have seen a higher non-adherence rate. Non-adherence to health technology interventions is a well-known problem [44]. We had a reasonably high completion rate among the participants, as 116/152 (76%) completed the study according to the protocol. The implementation strategy, which involved the active participation of clinicians and patients during the development phase, may have contributed to this outcome [19, 22].

Strengths and limitations

One strength of this study lies in its pragmatic randomised design, which enabled the production of feasible results by aligning the research with real-life conditions in routine clinical care.

Among the 320 patients eligible for the study, 46 ended follow-up after the first consultation, leaving 152 (48%) agreeing to participate. We recruited newly referred patients from three different outpatient clinics in three hospitals and the study population had similar characteristics to the source population [40], which enhanced the external validity. However, we excluded patients who were expected to have a rapid decline in kidney function. This decision was made to encompass patients with relatively stable kidney function and to minimise attrition induced by the risk of reaching ESKD. This could potentially impact the external validity and lead to a risk of being underpowered. A potential risk of selection bias might occur, as only patients who were capable of completing a questionnaire, considered to have a stable disease pathway and possessed cognitive abilities were included. The study should be approached with caution when attempting to apply its findings to an older population with greater comorbidity, as the individuals who discontinued participation were older and had more underlying health conditions.

A major limitation arose from the inconclusive results regarding non-inferiority, hindering the ability to definitively conclude the non-inferiority of PRO-based interventions over the SoC. A total of 36 patients left the study. Non-adherence to the intervention may have influenced the results, potentially leading to an underestimation of the intervention's effect compared with what would have been observed if all patients had

followed the intervention [45]. The underlying reasons for the loss of follow-up were similar between the groups and unrelated to the intervention. Data for the primary outcome were complete except for the deceased ($n = 11$). Thus the risk of bias due to missing data was low. Moreover, the attrition analysis revealed no difference regarding the primary outcome. However, several patients ended follow-up in the outpatient clinic, especially in the SoC group, often due to their preference for remote care consultations [40] and probably as a consequence of the COVID-19 pandemic. Conversely, COVID-19 heightened the motivation and engagement among physicians, as they benefitted from the remote monitoring of patients in the trial. Even post-pandemic, remote monitoring will remain crucial for providing and triaging healthcare services. Thus PRO-based interventions may help older adults by continuously monitoring their health status and reducing the burden on outpatient clinics.

CONCLUSION

In conclusion, differences in the slope of eGFR across the intervention groups were non-significant and our results regarding non-inferiority were inconclusive. Implementing PROs in remote care for patients with CKD may substitute for or replace some of the traditional outpatient visits without compromising patients' QOL, satisfaction or IP. In changing healthcare delivery modes, where remote patient management is increasing, remote PROs may help improve care. Even though the results were ambiguous regarding the non-inferiority of eGFR, we recommend close monitoring and tightened focus on maintaining kidney function during the shift from traditional outpatient follow-up to remote monitoring.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

All authors were involved in drafting or reviewing the article, with careful attention to the actual intellectual content. All authors approved the final version to be submitted for publication. The first author had complete access to all study data and is accountable for maintaining the integrity and precision of the data analysis.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared upon request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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