Health-related quality of life and symptom burden in patients on haemodialysis

Oevelen, M. van; Bonenkamp, A.A.; Sluijs, A.V. van der; Bos, W.J.W.; Douma, C.E.; Buren, M. van; ... ; DOMESTICO Study Grp

ORIGINAL ARTICLE

Nephrol Dial Transplant, 2024, **39**, 436–444
https://doi.org/10.1093/ndt/gfad179
Advance access publication date: 14 August 2023

Health-related quality of life and symptom burden in patients on haemodialysis

Mathijs van Oevelen[1], Anna A. Bonenkamp[2,3], Anita van Eck van der Sluijs[4,5], Willem Jan W. Bos[1,6], Caroline E. Douma[7], Marjolijn van Buren[1,8], Yvette Meuleman[9], Friedo W. Dekker[9], Brigit C. van Jaarsveld[3] and Alferso C. Abrahams[4]; on behalf of the DOMESTICO study group[†]

[1]Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands
[2]Department of Internal Medicine, Jeroen Bosch Hospital, 's Hertogenbosch, The Netherlands
[3]Department of Nephrology, Amsterdam Cardiovascular Sciences, Amsterdam University Medical Center, Amsterdam, The Netherlands
[4]Department of Nephrology and Hypertension, University Medical Center Utrecht, Utrecht, The Netherlands
[5]Department of Internal Medicine, Deventer Hospital, Deventer, The Netherlands
[6]Department of Internal Medicine, St. Antonius Hospital, Nieuwegein, The Netherlands
[7]Department of Internal Medicine, Spaarne Gasthuis, Hoofddorp, The Netherlands
[8]Department of Nephrology, Haga Hospital, The Hague, The Netherlands
[9]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands
Correspondence to: Mathijs van Oevelen; E-mail: M.van_Oevelen@lumc.nl
[†]The DOMESTICO Group Members are in the supplementary material.

Watch the video of this contribution at https://academic.oup.com/ndt/pages/author_videos

ABSTRACT

Background. Patients on haemodialysis (HD) generally experience poor health-related quality of life (HRQoL) and a broad range of physical and mental symptoms, but it is unknown whether this differs between younger and older patients. We aimed to describe the trajectories of HRQoL and symptom burden of patients <70 and ≥70 years old and to assess the impact of symptom burden on HRQoL.

Methods. In incident Dutch HD patients, HRQoL and symptoms were measured with the 12-item Short Form Health Survey and Dialysis Symptom Index. We used linear mixed models for examining the trajectories of HRQoL and symptom burden during the first year of dialysis and linear regression for the impact of symptom burden on HRQoL.

Results. In 774 patients, the trajectories of physical HRQoL, mental HRQoL and symptom burden were stable during the first year of dialysis. Compared with patients <70 years of age, patients ≥70 years reported similar physical HRQoL {mean difference −0.61 [95% confidence interval (CI) −1.86–0.63]}, better mental HRQoL [1.77 (95% CI 0.54–3.01)] and lower symptom burden [−2.38 (95% CI −5.08–0.32)]. With increasing symptom burden, physical HRQoL declined more in older than in younger patients ($\beta = -0.287$ versus −0.189, respectively; *P*-value for interaction = .007). For mental HRQoL, this decrease was similar in both age groups ($\beta = -0.295$ versus −0.288, $P = .847$).

Conclusion. Older HD patients generally experience a better mental HRQoL and a (non-statistically significant) lower symptom burden compared with younger patients. Their physical HRQoL declines more rapidly with increasing symptom burden.

Keywords: ageing, dialysis, end-stage renal disease, kidney failure, patient-reported outcomes

INTRODUCTION

Dialysis-dependent patients generally experience a lower health-related quality of life (HRQoL) than the general population, patients with earlier stages of chronic kidney disease (CKD) and kidney transplant recipients [1–3]. Apparently, dialysis treatment, although often lifesaving, has a major impact on patients' lives, both physically, mentally and socially. HRQoL is often influenced by the presence of physical and emotional symptoms [4–7]. On average, patients on dialysis experience a high symptom burden and report having >10 symptoms [8].

Although the dialysis population is ageing rapidly, little is known about the trajectories of HRQoL and symptom burden of younger and older dialysis patients. A recent European study found a stabilisation of HRQoL and symptom burden after dialysis initiation in patients ≥65 years of age [9, 10]. It is unknown whether the same holds true when including patients of all ages, including those <65 years old. It is also currently unknown whether the impact of symptom burden on HRQoL differs between age groups. Therefore, we aimed to describe the trajectories of HRQoL and symptom burden of younger and older patients during the first year of dialysis and to assess the impact of symptom burden on HRQoL in both age groups.

MATERIALS AND METHODS

Study design and population

For this study, data from the Dutch nOcturnal and hoME dialysis Study To Improve Clinical Outcomes (DOMESTICO) were used,

Received: April 13, 2023; Editorial decision: August 5, 2023

KEY LEARNING POINTS

What was known:

- Dialysis often has a major impact on patients' lives, both physically, mentally and socially.
- In older patients, health-related quality of life (HRQoL) and symptom burden deteriorate rapidly in the years preceding dialysis initiation, after which a stabilisation is seen. However, it remains unknown whether the trajectories of HRQoL and symptom burden differ between younger and older patients.
- Symptoms play an important role in HRQoL, but it remains unknown if the impact of symptoms differs between younger and older dialysis patients.

This study adds:

- Younger (<70 years) and older (≥70 years) patients both have stable trajectories of HRQoL and symptom burden during their first year of haemodialysis (HD). Older patients, however, generally experience better mental HRQoL and a lower symptom burden.
- Both the prevalence and severity of individual symptoms was lower among older patients, as compared with younger patients. Younger patients more often reported feeling sad, lightheadedness, having difficulty concentrating, headaches, feeling irritable, nausea, feeling anxious, diarrhoea and vomiting. Older patients more often reported leg swelling.
- In older patients, the impact of symptoms on physical HRQoL is greater than observed in younger patients. For mental HRQoL, the effect was similar among both age groups.

Potential impact:

- Knowledge on HRQoL and symptom burden trajectories of both younger and older patients helps to inform patients on what to expect after dialysis is initiated: despite the impact of dialysis, HD patients—most notably, older patients—showed no further deterioration of HRQoL during their first year of treatment.
- Because symptoms impact the physical HRQoL of older patients, adequate monitoring, discussing and treatment of symptoms is warranted.
- Future studies should assess which symptoms impact patients' HRQoL most and whether treatment of those symptoms would consequently improve HRQoL.

a nationwide observational cohort study in the Netherlands and Belgium with 59 participating centres. The rationale and design of DOMESTICO was published previously [11]. In summary, DOMESTICO will assess differences between patients on home dialysis with in-centre dialysis in terms of HRQoL, clinical outcomes and costs. Patients ≥18 years of age who started maintenance dialysis from December 2017 onwards were included. Patients with a life expectancy of <3 months or an expected kidney transplantation within 3 months were excluded. For the present substudy, we included all patients who started in-centre HD prior to 19 January 2021, as DOMESTICO is currently ongoing. This allowed for a minimum follow-up duration of 1 year. This article adheres to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [12] (Supplementary Table S1).

Patient-reported outcome measures (PROMs)

For the present study we used data on HRQoL and symptoms collected at dialysis initiation and after 3, 6 and 12 months. Patients completed questionnaires on paper or using online forms, with help from others if needed, as long as patients themselves provided the answers. HRQoL was measured using the 12-item Short Form Health Survey (SF-12) [13, 14]. The SF-12 is summarised into a Physical Component Summary (PCS) score and a Mental Component Summary (MCS) score, hereafter referred to as physical HRQoL and mental HRQoL. These scores range from 0 to 100, with higher scores indicating better HRQoL. Both scores are norm-based, with the mean of 50 being standardised to the US general population. Symptoms were measured using the kidney disease–specific Dialysis Symptom Index (DSI), consisting of the 30 most common physical and emotional symptoms in this population [15]. Patients indicated the presence of each symptom (yes/no) and, if present, the symptom's severity on a 5-point Likert scale ranging from 1 (not at all bothersome) to 5 (very bothersome). An overall symptom burden score was calculated by summation of the severity of each of the 30 symptoms, resulting in an overall score ranging from 0 (no symptoms) to 150 (30 symptoms with a maximal severity) [16].

Statistical analyses

The main determinant for all analyses was age at dialysis initiation, which was dichotomised to <70 years (reference) and ≥70 years (comparison). This cut-off value for age was determined *a priori* and based on comparability with other large nationwide study initiatives [17].

HRQoL at dialysis initiation was compared between age groups using unpaired *t*-tests. The trajectory of HRQoL during the first year of dialysis treatment was examined using linear mixed models while incorporating all available measurements for individual patients. This allowed us to describe the trajectory of HRQoL for younger and older patients (i.e. within-groups results) and to compare these two age groups (i.e. between-groups comparison). Age (dichotomised) was used as a fixed covariate. To detect differences in the trajectories of HRQoL between both groups, an interaction with time was added to the model. Results were not adjusted for expected between-group differences, such as sex and comorbidities, because of the descriptive nature of these analyses. Results of the between-groups comparison were reported as the mean difference over the 1-year observation period.

The presence and severity of symptoms at the start of dialysis treatment were compared between patients <70 and ≥70 years of age using chi-squared tests. The overall symptom burden at dialysis initiation was compared using a *t*-test. The trajectory in symptom burden during the first year of dialysis treatment was examined using linear mixed models, with similar methodology as the assessment of HRQoL. Again, the trajectories of symptom burden for both age groups were described and a comparison made between younger and older patients.

Finally, the impact of overall symptom burden on physical and mental HRQoL at dialysis initiation was assessed using linear

regression analysis. To compare the impact of age (dichotomised), an interaction term with the symptom burden score was added to the model.

Categorical variables are displayed as frequencies with percentages. Normally distributed variables are displayed as means with standard deviations (SDs) and non-normally distributed variables as medians with interquartile ranges (IQRs). All analyses were performed using SPSS version 28.0 (IBM, Armonk, NY, USA), except for the linear mixed models, which were performed using Stata version 14 (StataCorp, College Station, TX, USA). A significance level (alpha) of 0.05 was used and results of the longitudinal analyses were reported with 95% confidence intervals (CIs). In the longitudinal analyses, missing values were assumed to be missing at random and estimated using multiple imputation [18]. Up to 10 iterations and predictive mean matching using 20 imputed datasets were used. The imputation model included patients' age and sex, moment of measurement and all individual responses on both the SF-12 and the DSI. Questionnaires with >50% missing answers were considered insufficient and were excluded [19].

Sensitivity analyses

Four sensitivity analyses were performed. We performed two sensitivity analyses for the longitudinal assessment of HRQoL and symptom burden by excluding patients who died and excluding patients who did not complete the 1-year follow-up (i.e. patients who died, received a kidney transplant, withdrew their consent, withdrew from dialysis or had recovery of kidney function). This was done since younger and older patients are potentially at an unequal risk for not completing the 1-year follow-up due to expected differences in mortality risk and probability of receiving a kidney transplant. We performed two additional sensitivity analyses for the longitudinal analyses to assess the effect of multiple imputation, using complete case analysis, and the influence of the selected cut-off for age by using a different age contrast (i.e. age <50 versus ≥80 years).

RESULTS

In total, 777 patients started in-centre HD, of which 3 patients were excluded because they did not complete a questionnaire. This led to a total of 774 included patients, of whom 381 (49.2%) were <70 years and 393 (50.8%) were ≥70 years of age. Baseline characteristics are shown in Table 1. Most notably, older patients more often had renovascular and diabetic kidney disease, were living together, had a low education level and had more comorbidities. The 1-year follow-up was complete for 622 patients (80.4%; Supplementary Table S2). Younger patients more often received a kidney transplant (9.2%, compared with 5.3% in patients ≥70 years old), while older patients more often died (7.6%, compared with 3.1% in patients <70 years old).

HRQoL at HD initiation

At baseline, physical HRQoL was similar for both age groups: 35.3 ± 9.6 and 35.3 ± 10.1 for patients <70 years and ≥70 years, respectively ($P = .972$). However, mental HRQoL was significantly higher among older patients: 45.7 ± 10.5 for patients <70 years and 47.6 ± 9.7 for patients ≥70 years ($P = .014$).

Trajectory of HRQoL after HD initiation

When comparing the two age groups, during the first year of dialysis, physical HRQoL scores of older patients were comparable with those of younger patients [mean difference −0.61 (95% CI −1.86–0.63), $P = .334$). However, the mental HRQoL of older patients was higher compared with that of younger patients [mean difference 1.77 (95% CI 0.54–3.01), $P = .005$]. In other words, older patients reported a 1.77-point higher mental HRQoL score during the first year of dialysis treatment.

The trajectories of HRQoL scores are shown in Fig. 1. Physical HRQoL slightly increased for patients <70 years of age throughout the first year of dialysis, while it remained stable for patients ≥70 years. Mental HRQoL increased slightly in both groups. The interaction term for time and age was statistically significant for physical HRQoL, indicating a different trend in physical HRQoL over time between younger and older patients. This can be seen in Fig. 1: between 3 and 6 months, when patients <70 years of age had an increase in HRQoL whereas patients ≥70 years had a decrease. For mental HRQoL, no significant differences in trends over time between age groups were detected.

Presence and severity of symptoms and overall symptom burden at HD initiation

At dialysis initiation, patients <70 years of age more often reported feeling sad, lightheadedness, having difficulty concentrating, headaches, feeling irritable, nausea, feeling anxious, diarrhoea and vomiting (Fig. 2). Patients ≥70 years of age more often reported leg swelling. Mean symptom severity scores for all individual symptoms of patients <70 years were comparable with or higher than those of patients ≥70 years (Supplementary Figure S1). The mean overall symptom burden at dialysis initiation was higher in patients <70 years compared with patients ≥70 years (35.7 ± 22.7 versus 31.6 ± 19.2, respectively, $P = .013$).

Trajectory of overall symptom burden after HD initiation

During the first year of HD, older patients reported somewhat lower symptom burden scores compared with younger patients, although this difference was not statistically significant [mean difference −2.38 (95% CI −5.08–0.32), $P = .084$]. The trajectory of symptom burden is shown in Fig. 3. Among both younger and older patients, symptom burden decreased slightly during the first 3 months and thereafter stabilised. The interaction with time was statistically significant, indicating a different trend between both age groups, which can be seen in Fig. 3: the symptom burden of patients <70 years slightly decreased between 3 and 6 months and then slightly increased between 6 and 12 months. For patients ≥70 years of age, this was the opposite.

Impact of symptom burden on HRQoL at HD initiation

In younger patients, the overall symptom burden score explained 18.7% of the variance of the physical HRQoL (Fig. 4). In older patients, this was 28.6%. With increasing symptom burden, the decline in physical HRQoL was less in younger patients compared with older patients ($\beta = -0.189$ versus -0.287, respectively, P-value for interaction .007).

For mental HRQoL, the explained variance by the symptom burden score was more comparable for younger and older patients (37.1% and 31.2%, respectively). With increasing symptom burden, the decline in mental HRQoL was similar between younger and older patients ($\beta = -0.295$ and -0.288, respectively, $P = .847$).

Sensitivity analyses

In summary, the sensitivity analyses showed that most results remained stable (Fig. 5 and Supplementary Table S3), with one exception: when comparing patients <50 years of age with

Table 1: Baseline characteristics of the study cohort.

Characteristics	Total cohort (*N* = 774)	<70 years (*n* = 381)	≥70 years (*n* = 393)
Age (years), median (IQR)	70 (59–76)	58 (47–65)	76 (73–80)
Male, *n* (%)	513 (66.3)	241 (63.3)	272 (69.2)
Primary kidney disease, *n* (%)			
Renovascular disease	181 (23.4)	68 (17.8)	113 (28.8)
Diabetic kidney disease	135 (17.4)	60 (15.7)	75 (19.1)
Glomerulonephritis	81 (10.5)	55 (14.4)	26 (6.6)
Polycystic kidney disease	44 (5.7)	33 (8.7)	11 (2.8)
Pyelonephritis, interstitial nephritis and urolithiasis	38 (4.9)	16 (4.2)	22 (5.6)
Other or unknown	295 (38.1)	149 (39.1)	146 (37.2)
Social status, *n* (%)			
Married or living together	468 (60.5)	209 (54.9)	259 (65.9)
Single, divorced or widowed	281 (36.3)	159 (41.7)	122 (31.0)
Education level, *n* (%)[a]			
Low	218 (28.2)	87 (22.8)	131 (33.3)
Middle	256 (33.1)	134 (35.2)	122 (31.0)
High	221 (28.6)	120 (31.5)	101 (25.7)
Comorbidity, *n* (%)			
Charlson-Deyo Comorbidity Score, median (IQR)[b]	4 (2–5)	3 (2–4)	4 (3–5)
Diabetes mellitus	269 (34.8)	107 (28.1)	162 (41.2)
Malignancy	114 (14.7)	38 (10.0)	76 (19.3)
Ischaemic heart disease	198 (25.6)	63 (16.5)	135 (34.4)
Peripheral and/or cerebrovascular disease	196 (25.3)	67 (17.6)	129 (32.8)
HD characteristics			
Treatment hours per week, median (IQR)	12 (9–12)	12 (9–12)	12 (9–12)
eGFR at dialysis start (ml/min/1.73 m^2), median (IQR)[c]	7.4 (5.4–9.6)	7.2 (5.2–9.3)	7.6 (5.7–10.0)
Vascular access at dialysis start, *n* (%)			
Arteriovenous fistula	238 (30.7)	108 (28.3)	130 (33.1)
Arteriovenous graft	13 (1.7)	6 (1.6)	7 (1.8)
Central venous catheter	279 (36.0)	147 (38.6)	132 (33.6)
HRQoL at dialysis initiation, mean ± SD[d]			
SF-12 PCS score	35.3 ± 9.8	35.3 ± 9.6	35.3 ± 10.1
SF-12 MCS score	46.6 ± 10.2	45.7 ± 10.5	47.6 ± 9.7
Overall symptom burden, mean ± SD[e]	33.7 ± 21.1	35.7 ± 22.7	31.6 ± 19.2

Some characteristics contain missing data: social status, *n* = 25 (3.2%); education level, *n* = 79 (10.2%); comorbidity score, *n* = 20 (2.6%); diabetes, *n* = 20 (2.6%); malignancy, *n* = 19 (2.5%); ischaemic heart disease, *n* = 20 (2.6%); peripheral and/or cerebrovascular disease, *n* = 19 (2.5%); HD treatment hours, *n* = 240 (31.0%); eGFR at dialysis initiation, *n* = 277 (35.8%); vascular access, *n* = 244 (31.5%); HRQoL, *n* = 115 (14.9%) and overall symptom burden, *n* = 146 (18.9%).
[a]Education levels are grouped based on the coding system for the Dutch educational system by Verhage *et al.* [33]. The patient's highest finished level of education is grouped into seven categories that were merged into ordinal categories: low (Verhage 1–4, i.e. up to 'low-level secondary education'), mid (5, i.e. 'average-level secondary education') and high (6–7, i.e. 'high-level secondary education or university degree').
[b]This commonly used adaptation of the Charlson Comorbidity Index scores the presence of the same 17 health conditions but does not score age and scores the presence of lymphoma and leukaemia together with non-metastasised malignancies [34]. The minimum score is 2 due to the presence of chronic kidney disease, the maximum score is 29.
[c]Calculated using the 2009 Chronic Kidney Disease Epidemiology Collaboration formula without race [35].
[d]Range 0–100; higher scores indicate better HRQoL.
[e]Range 0–150; higher scores indicate the presence of more symptoms and/or a higher severity per symptom.

patients ≥80 years (total *n* = 215), the estimated mean difference in physical HRQoL increased, with patients <50 years old having a better physical HRQoL.

DISCUSSION

Our study showed that older HD patients (≥70 years) had a similar physical HRQoL but a better mental HRQoL than younger patients (<70 years) at dialysis initiation and during their first year of treatment. During this year, HRQoL remained stable, both in younger and older patients. Regarding symptoms, older patients generally reported fewer symptoms and with lower severity, resulting in a lower overall symptom burden, but with increasing symptom burden, the physical HRQoL of older patients decreased more profoundly than observed in younger patients. The impact of symptoms on mental HRQoL was similar for both age groups.

HRQoL

In general, the physical HRQoL of all patients in our cohort was significantly lower than observed in the general Dutch population (35.3 versus 50.3, respectively, using the SF-12), while for mental HRQoL the difference was less pronounced (46.6 versus 52.9) [20]. This illustrates the substantial physical impact that kidney failure, its associated comorbidities and dialysis treatment have on patients' lives, but also shows the remarkable mental resilience of dialysis patients. It is reassuring that patients, most notably older patients, are able to maintain their HRQoL, despite frequent hospital visits, risk of dialysis-related complications and a high risk of mortality. Indeed, we perhaps would have expected a greater decline in HRQoL among older patients, as they are particularly susceptible to these risks. Previous studies in incident HD patients assessing the effect of age are scarce and have produced contradictory results. One study found that increasing age was associated with worse physical

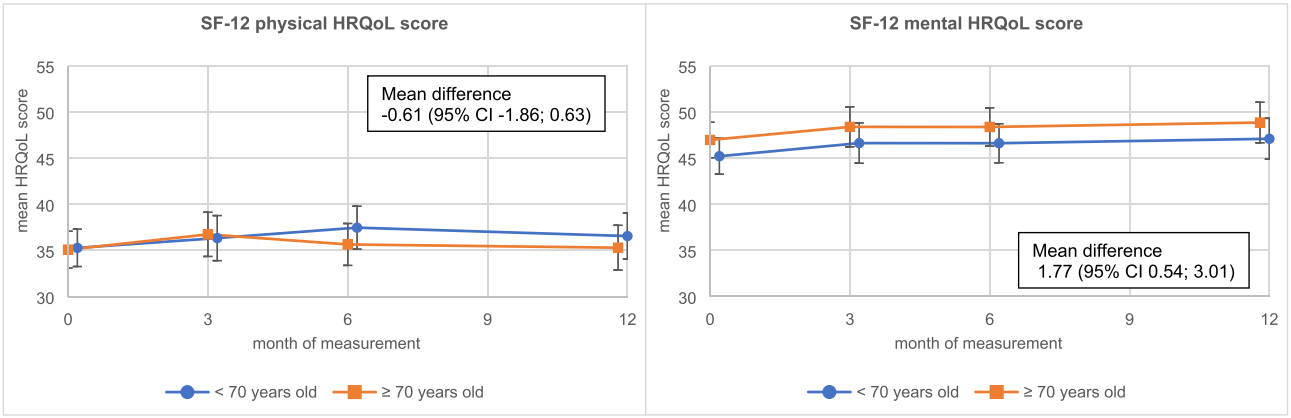

Figure 1: Longitudinal assessment of physical and mental HRQoL. Graphs show the estimated mean scores of the PCS score (left) and the MCS score (right) of the SF-12 with error bars indicating the 95% CIs. Mean differences indicate the mean difference over the 1-year observation period, using patients <70 years old as the reference and patients ≥70 years old as the comparison. Note that scores range from 0 to 100 and higher scores indicate better HRQoL. Mean scores and differences are estimated using linear mixed models.

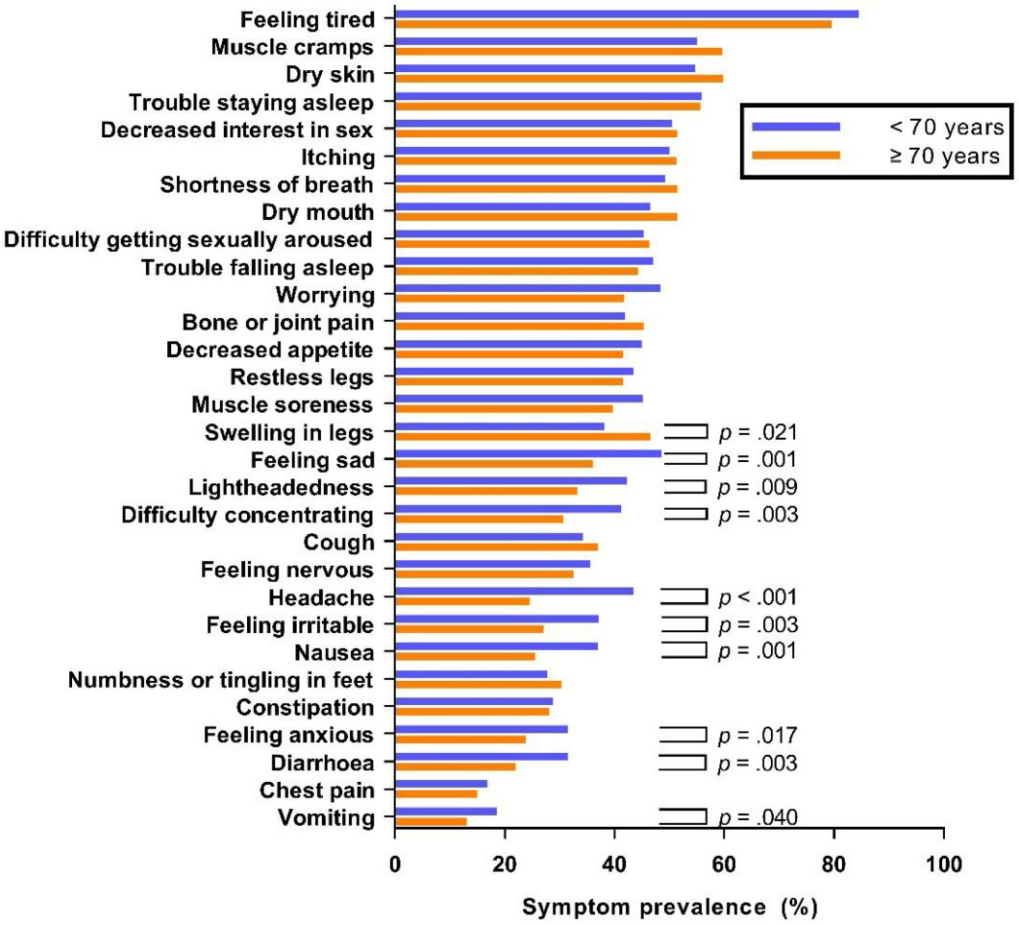

Figure 2: Prevalence of all 30 symptoms at dialysis initiation among younger (blue) and older (orange) patients, in order of descending prevalence. Statistically significant differences between age groups are shown with their *P*-values.

HRQoL measured 3 months after dialysis initiation [21]. For mental HRQoL, no association with age was found. In the Dutch NECOSAD study, seven of eight subdomains of the SF-36 were negatively associated with age, also measured 3 months after the start of dialysis [22]. The European EQUAL study assessed HRQoL longitudinally and found that after a marked deterioration in the year preceding dialysis, both physical and mental HRQoL stabilised shortly after dialysis was started [9]. In a subgroup analysis for age, the trajectory was similar for patients 65–74 years of age and ≥75 years. Hence our current study adds to this knowledge by showing that similar stabilisation is found in Dutch HD patients of all ages. In general, changes over time were small and likely clinically irrelevant: estimates of the minimally clinically important difference for HRQoL, measured with

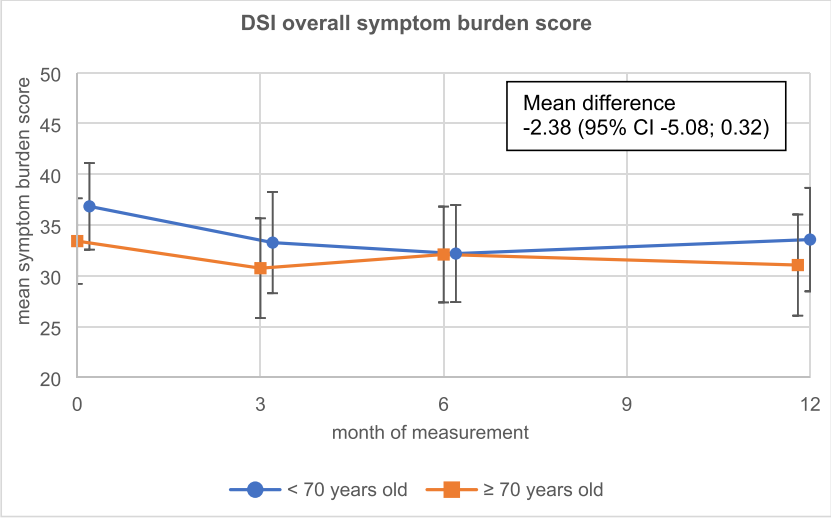

Figure 3: Longitudinal assessment of overall symptom burden. Graphs show the estimated mean scores of the total symptom burden score, measured using the 30-item DSI, with error bars indicating the 95% CIs. Mean difference indicates the mean difference over the 1-year observation period, using patients <70 years old as the reference and patients ≥70 years old as the comparison. Note that scores range from 0 to 150, with higher scores indicating more symptoms and/or higher experienced severity of symptoms. Mean scores and differences are estimated using linear mixed models.

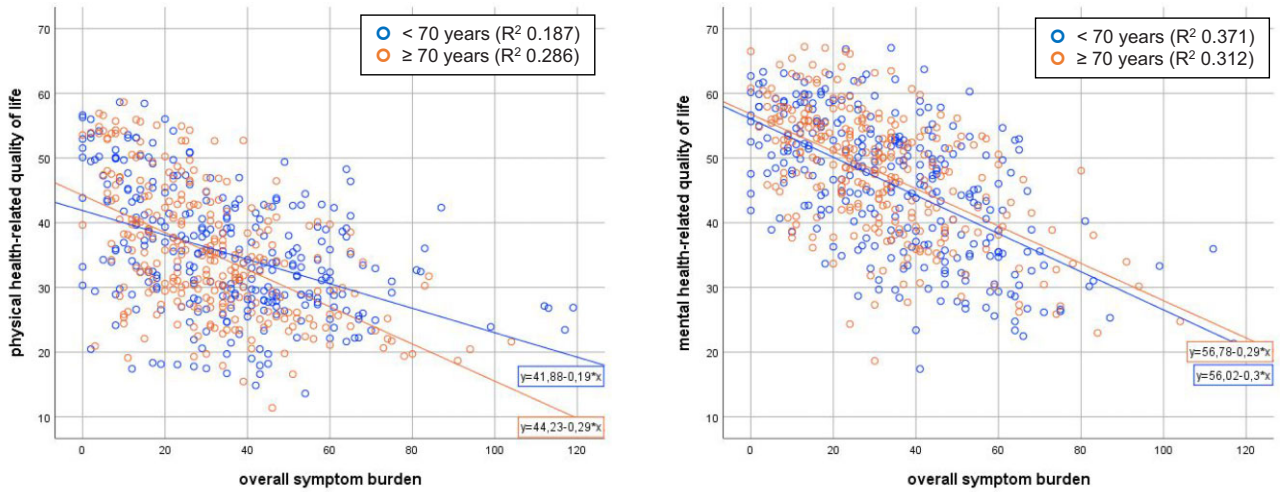

Figure 4: Scatterplot showing the association of overall symptom burden with physical HRQoL (left) and mental HRQoL (right), measured at the start of HD. Note that symptom burden scores range from 0 to 150, with higher scores indicating the presence of more symptoms and/or a higher severity per symptom. HRQoL scores range from 0 to 100, with higher scores indicating better QoL.

the SF-36, range from 2 to 9 points, depending on the population studied [23, 24].

Symptom burden

Older patients overall had a lower symptom burden, with an equal or lower prevalence and severity of nearly all individual symptoms compared with younger patients. So far, only two longitudinal studies assessed the potential influence of age on the symptom burden trajectory of patients with CKD. A French study found no association between age and 5-year symptom trajectories in nearly 2800 patients with eGFR <60 ml/min/1.73 m^2 [25]. In the EQUAL study, patients 65–75 years of age and ≥75 years had a comparable trajectory of symptom burden after dialysis was started [10]. Both results are in line with our findings, demonstrating a stable symptom burden during the first year of dialysis in both younger and older patients.

Impact of symptom burden on HRQoL

Our study found a strong impact of the overall symptom burden on HRQoL, with physical HRQoL being more affected in older patients compared with younger patients. A causal association between symptoms and HRQoL is biologically plausible. In the framework by Wilson and Cleary [26], symptoms directly influence a patient's functional status, in turn affecting the general health perception and ultimately HRQoL. Indeed, previous studies described this association between symptoms and HRQoL, but none compared younger and older patients [5, 7, 16]. One study described that the physical HRQoL of dialysis patients of all ages is more profoundly influenced by either the number of symptoms or the symptoms' severity, as compared with mental HRQoL [16]. Our study adds that the impact of symptoms on physical HRQoL is greater in patients ≥70 years of age compared with younger patients.

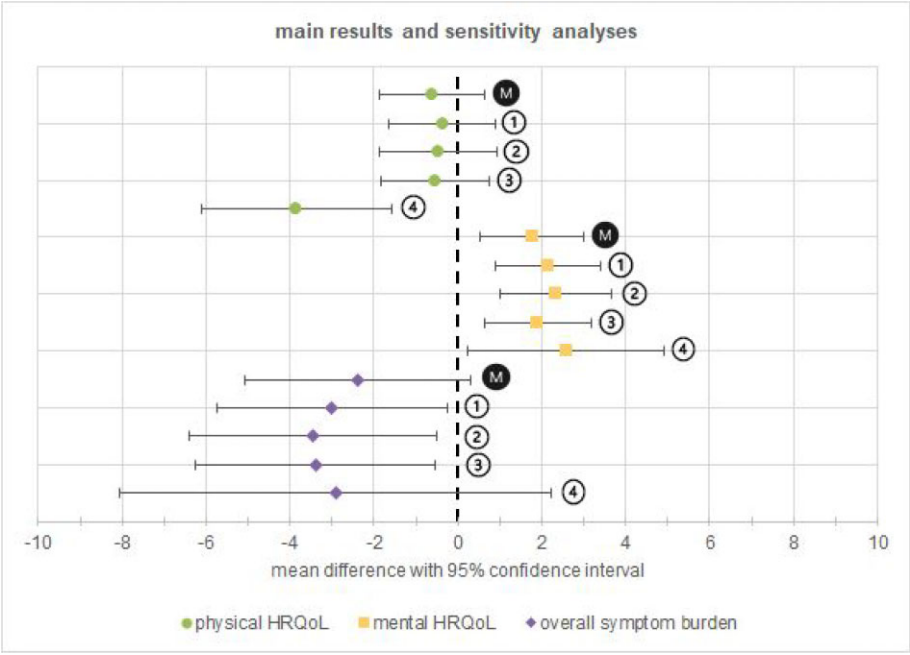

Figure 5: Results of the main and sensitivity analyses. The x-axis shows mean differences of the longitudinal analyses and their 95% CIs, using patients <70 years old as the reference and ≥70 years old as the comparison. Note that higher scores for HRQoL and lower scores for symptom burden indicate better performance. The result (M) depicts the study's main results (number of patients included in the analysis, $N = 774$), (1) the first sensitivity analysis with exclusion of patients who died within the first year ($n = 732$), (2) the second sensitivity analysis with exclusion of patients who did not complete their first year, i.e. due to death, kidney transplantation, recovery of kidney function, withdrawal of informed consent or loss to follow-up ($n = 622$), (3) the third sensitivity analysis with inclusion of complete cases only ($n = 659$ for HRQoL, $n = 628$ for symptom burden) and (4) the fourth sensitivity analysis, comparing patients <50 years of age (reference) with patients ≥80 years of age ($n = 215$).

Potential explanations

There are several potential explanations for the observed limited difference in physical HRQoL, mental HRQoL and symptoms between younger and older patients, even though older age often comes with more comorbidity, functional dependence and higher dialysis-related risks. First, coping strategies may differ between younger and older patients. Older persons are generally better at emotional regulation, e.g. by avoiding stressors, positively reappraising the effects of negative events, adapting their daily life, adjusting their goals and pacing their activities [27]. In a way, their past experiences help them cope with the increased burden that is associated with ageing, chronic illness and the end of life. Second, social comparison, a behavioural strategy where people compare certain aspects of themselves to those of others, may also differ between the young and the old: younger patients with chronic illnesses are more often among healthier peers and, as such, their perception of their own health could be worse than that of older patients [28, 29]. In addition, ageing is expected by the general population to be accompanied by physical deterioration. For younger adults, chronic health conditions are more likely to be regarded as abnormal events, influencing the person's perception of health. Third, the required adaptation to health problems often differs between younger and older patients since it is dependent on patients' social roles, life expectations and goals. For example, younger patients are more often confronted with the risk of unemployment as their kidney function deteriorates, while for many older patients, career responsibilities are no longer present or less influential. In younger patients, chronic illness may interfere with their desired central family role. In summary, it is possible that having better coping strategies, being around less healthy peers and having less-restraining social roles could have helped the older patients in our study to perceive their HRQoL more positively and their symptoms as less burdensome compared with the younger patients.

Clinical interpretation and directives for future research

Our study has several clinical implications. Having data on the trajectory of HRQoL after dialysis initiation helps to inform patients about what to expect regarding the trajectory of HRQoL. Our observation that increasing symptom burden was associated with a lower physical HRQoL, most notably among older patients, suggests the importance of monitoring, discussing and, if possible, alleviating symptoms to improve HRQoL. Extra attention should be paid to the symptoms that are most common, burdensome and modifiable. Future studies should assess if multidisciplinary treatment strategies to reduce symptom burden indeed result in improvement of HRQoL and which subgroups of patients are most likely to benefit. An example of such a study is currently ongoing in Australia and New Zealand [30]. In addition, the trajectory of individual symptoms should be studied, as potentially some symptoms are better alleviated with dialysis than others and symptoms might influence HRQoL differently.

Strengths and limitations

To our knowledge, this is the first study to directly compare HRQoL and symptom burden between younger and older dialysis patients, using a large prospective cohort that includes patients of all ages. By using multiple measurements within the first year, the trajectory of HRQoL could be studied in detail. By using linear mixed models, all measurements were included, even if patients died or withdrew within the first year. Multiple sensitivity analyses were performed to assess the robustness of our results.

By combining the SF-12 and DSI, both generic and kidney disease–specific outcomes were measured. In the Netherlands, the DSI was chosen with input from the Dutch Kidney Patients Association as the standard in nephrology care for its brevity and completeness while being developed and validated in populations with advanced kidney disease [31].

Our study has a few caveats. First, we only included patients on in-centre HD and it is unknown how generalisable our results are to patients receiving other types of dialysis treatment (i.e. home HD or peritoneal dialysis). Comparison between treatment modalities is often difficult, as generally younger, less frail and more functionally independent patients are started on home therapies. Second, we assessed only patients who started dialysis, while older and frailer patients are more likely to abstain from dialysis. Although previous studies demonstrated that patients who opt for conservative care have the potential to reach a comparable HRQoL as patients treated with dialysis, poor HRQoL could be associated with the odds to start dialysis [32]. Hence it is important not to causally apply our results to patients prior to their decision to start dialysis or not. The risk of selection bias after dialysis initiation appears to be limited in our study. Although older patients were more likely to die and younger patients more likely to receive a kidney transplant, and both odds are potentially associated with HRQoL, our sensitivity analyses showed results similar to our main analyses. Third, the trajectory of HRQoL and symptom burden after our 1-year study period remains unknown. However, particularly for older patients, a year is still quite extensive due to the high risk of mortality: in our cohort, 5.4% died within the first year of dialysis. Finally, patients with a low HRQoL and/or a high symptom burden could choose to forego answering PROMs, potentially limiting the generalisability of the results to the whole HD population. This selection, however, is unlikely related to age as the exposure of interest.

Conclusion

In conclusion, younger and older HD patients experience HRQoL and symptoms differently, with older patients generally experiencing better mental HRQoL and a lower symptom burden. In both age groups, the association between symptoms and HRQoL is marked, but physical HRQoL declines more rapidly with increasing symptom burden in older patients. Clinicians should discuss and treat individual symptoms where possible and future research should evaluate whether treatment of these symptoms also results in reduced symptom burden and consequently an improvement in HRQoL.

SUPPLEMENTARY DATA

Supplementary data are available at *ndt* online.

ACKNOWLEDGEMENTS

We would like to thank the patients and the staff of the participating dialysis centres for contributing to the results of this work. A full list of the DOMESTICO study group members is presented as Supplementary File 1. All patients provided written informed consent upon enrolment. Primary ethical approval was obtained from the medical research ethics committee of the VU University Medical Center Amsterdam (reference number: 2017.491, NL63277.029.17, 17 December 2017).

FUNDING

DOMESTICO is supported by grants from the Netherlands Organisation for Health Research and Development, Dutch Kidney Foundation, Fresenius Medical Care Deutschland, Baxter, Dirinco, AstraZeneca, Cablon Medical, Eurocept Homecare, Novartis, CSL Vifor, Bayer and Alnylam. The sponsors did not play a role in the design and/or conductance of either DOMESTICO or the present substudy.

AUTHORS' CONTRIBUTIONS

All authors were involved in the study design, data interpretation and drafting of the manuscript. A.A.B., A.E.S., F.W.D., B.v.J. and A.C.A. are primary investigators of DOMESTICO and involved in the data collection. M.v.O. performed the main analyses. A.A.B. performed the linear mixed models. All authors approved the final version.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request and with permission of the DOMESTICO steering committee.

CONFLICT OF INTEREST STATEMENT

A.E.S. received speaker fees from Baxter, outside the submitted work. W.J.B. received grant support from Zilveren Kruis Insurance, outside the submitted work. F.W.D. received grant support from Vifor, Astellas and Chiesi, outside the submitted work. A.C.A. received speaker fees from Baxter, Fresenius Medical Care Deutschland and Cablon Medical and grant support from the Dutch Kidney Foundation and Baxter, outside the submitted work. M.v.O., A.C.A., M.v.B. and W.J.B. are investigators for the DIALysis or not: Outcomes in older kidney patients with GerIatriC Assessment (DIALOGICA) study, which is supported by Leading the Change, a Dutch healthcare efficiency evaluation project by Zorgevaluatie Nederland. All other authors declare no competing interests.

REFERENCES

1. Gorodetskaya I, Zenios S, McCulloch CE *et al.* Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney Int* 2005;**68**:2801–8. https://doi.org/10.1111/j.1523-1755.2005.00752.x
2. Krishnan A, Teixeira-Pinto A, Lim WH *et al.* Health-related quality of life in people across the spectrum of CKD. *Kidney Int Rep* 2020;**5**:2264–74. https://doi.org/10.1016/j.ekir.2020.09.028
3. Wang Y, Hemmelder MH, Bos WJW *et al.* Mapping health-related quality of life after kidney transplantation by group comparisons: a systematic review. *Nephrol Dial Transplant* 2021;**36**:2327–39. https://doi.org/10.1093/ndt/gfab232
4. Davison SN, Jhangri GS. Impact of pain and symptom burden on the health-related quality of life of hemodialysis patients. *J Pain Symptom Manage* 2010;**39**:477–85. https://doi.org/10.1016/j.jpainsymman.2009.08.008
5. Yong DS, Kwok AO, Wong DM *et al.* Symptom burden and quality of life in end-stage renal disease: a study of 179 patients on dialysis and palliative care. *Palliat Med* 2009;**23**:111–9. https://doi.org/10.1177/0269216308101099
6. Raj R, Ahuja KD, Frandsen M *et al.* Symptoms and their recognition in adult haemodialysis patients: interactions with quality of

life. *Nephrology (Carlton)* 2017;**22**:228–33. https://doi.org/10.1111/nep.12754
7. Voskamp PWM, van Diepen M, Evans M *et al.* The impact of symptoms on health-related quality of life in elderly pre-dialysis patients: effect and importance in the EQUAL study. *Nephrol Dial Transplant* 2019;**34**:1707–15. https://doi.org/10.1093/ndt/gfy167
8. Van der Willik EM, Hemmelder MH, Bart HAJ *et al.* Routinely measuring symptom burden and health-related quality of life in dialysis patients: first results from the Dutch registry of patient-reported outcome measures. *Clin Kidney J* 2021;**14**:1535–44. https://doi.org/10.1093/ckj/sfz192
9. De Rooij ENM, Meuleman Y, de Fijter JW *et al.* Quality of life before and after the start of dialysis in older patients. *Clin J Am Soc Nephrol* 2022;**17**:1159–67. https://doi.org/10.2215/CJN.16371221
10. De Rooij ENM, Meuleman Y, de Fijter JW *et al.* Symptom burden before and after dialysis initiation in older patients. *Clin J Am Soc Nephrol* 2022;**17**:1719–29. https://doi.org/10.2215/CJN.09190822
11. Van Eck van der Sluijs A, Bonenkamp AA, Dekker FW *et al.* Dutch nOcturnal and hoME dialysis Study To Improve Clinical Outcomes (DOMESTICO): rationale and design. *BMC Nephrol* 2019;**20**:361. https://doi.org/10.1186/s12882-019-1526-4
12. Von Elm E, Altman DG, Egger M *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007;**147**:573–7. https://doi.org/10.7326/0003-4819-147-8-200710160-00010
13. Ware J Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;**34**:220–33. https://doi.org/10.1097/00005650-199603000-00003
14. Loosman WL, Hoekstra T, van Dijk S *et al.* Short-Form 12 or Short-Form 36 to measure quality-of-life changes in dialysis patients? *Nephrol Dial Transplant* 2015;**30**:1170–6. https://doi.org/10.1093/ndt/gfv066
15. Weisbord SD, Fried LF, Arnold RM *et al.* Development of a symptom assessment instrument for chronic hemodialysis patients: the Dialysis Symptom Index. *J Pain Symptom Manage* 2004;**27**:226–40. https://doi.org/10.1016/j.jpainsymman.2003.07.004
16. Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. *Clin J Am Soc Nephrol* 2009;**4**:1057–64. https://doi.org/10.2215/CJN.00430109
17. Van Oevelen M, Abrahams AC, Bos WJW *et al.* DIALysis or not: Outcomes in older kidney patients with GerIatriC Assessment (DIALOGICA): rationale and design. *BMC Nephrol* 2021;**22**:39. https://doi.org/10.1186/s12882-021-02235-y
18. Eekhout I, de Vet HC, Twisk JW *et al.* Missing data in a multi-item instrument were best handled by multiple imputation at the item score level. *J Clin Epidemiol* 2014;**67**:335–42. https://doi.org/10.1016/j.jclinepi.2013.09.009
19. Ware JE, Snow KK, Kosinski M *et al. SF-36 Health Survey: Manual and Interpretation Guide*. Boston: Health Institute, New England Medical Center, 1997.
20. Centraal Bureau voor de Statistiek. [Health, lifestyle, healthcare consumption; 2000–2009], https://opendata.cbs.nl/statline/#/CBS/nl/dataset/03799/table?dl=47491 [accessed 22 November 2022].
21. Lee J, Kim YC, Kwon S *et al.* Impact of health-related quality of life on survival after dialysis initiation: a prospective cohort study in Korea. *Kidney Res Clin Pract* 2020;**39**:426–40. https://doi.org/10.23876/j.krcp.20.065.
22. Merkus MP, Jager KJ, Dekker FW *et al.* Quality of life in patients on chronic dialysis: self-assessment 3 months after the start of treatment. The Necosad Study Group. *Am J Kidney Dis* 1997;**29**:584–92. https://doi.org/10.1016/S0272-6386(97)90342-5
23. Erez G, Selman L, Murtagh FE. Measuring health-related quality of life in patients with conservatively managed stage 5 chronic kidney disease: limitations of the Medical Outcomes Study Short Form 36: SF-36. *Qual Life Res* 2016;**25**:2799–809. https://doi.org/10.1007/s11136-016-1313-7
24. Maruish ME. *User's Manual for the SF-36v2 Health Survey*. 3rd ed. Lincoln, RI: QualityMetric, 2011.
25. Faye M, Legrand K, Le Gall L *et al.* Five-year symptom trajectories in nondialysis-dependent CKD patients. *Clin J Am Soc Nephrol* 2022;**17**:1588–97. https://doi.org/10.2215/CJN.06140522
26. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA* 1995;**273**:59–65. https://doi.org/10.1001/jama.1995.03520250075037
27. Piazza JR, Charles ST, Almeida DM. Living with chronic health conditions: age differences in affective well-being. *J Gerontol Ser B* 2007;**62**:P313–21. https://doi.org/10.1093/geronb/62.6.P313
28. Buunk AP, Gibbons FX. Social comparison: the end of a theory and the emergence of a field. *Organ Behav Hum Decis Process* 2007;**102**:3–21. https://doi.org/10.1016/j.obhdp.2006.09.007
29. Callan MJ, Kim H, Matthews WJ. Age differences in social comparison tendency and personal relative deprivation. *Pers Individ Differ* 2015;**87**:196–9. https://doi.org/10.1016/j.paid.2015.08.003
30. Greenham L, Bennett PN, Dansie K *et al.* The Symptom Monitoring with Feedback Trial (SWIFT): protocol for a registry-based cluster randomised controlled trial in haemodialysis. *Trials* 2022;**23**:419. https://doi.org/10.1186/s13063-022-06355-0
31. Van der Willik EM, Meuleman Y, Prantl K *et al.* Patient-reported outcome measures: selection of a valid questionnaire for routine symptom assessment in patients with advanced chronic kidney disease – a four-phase mixed methods study. *BMC Nephrol* 2019;**20**:344. https://doi.org/10.1186/s12882-019-1521-9
32. Verberne WR, van den Wittenboer ID, Voorend CGN *et al.* Health-related quality of life and symptoms of conservative care versus dialysis in patients with end-stage kidney disease: a systematic review. *Nephrol Dial Transplant* 2021;**36**:1418–33. https://doi.org/10.1093/ndt/gfaa078
33. Verhage F. *Intelligentie en Leeftijd Onderzoek Bij Nederlanders Van Twaalf tot Zevenenzeventig Jaar [Intelligence and age: Research study in Dutch individuals aged twelve to seventy-seven]*. Assen, The Netherlands: Van Gorcum/Prakke & Prakke, 1964.
34. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;**45**:613–9. https://doi.org/10.1016/0895-4356(92)90133-8
35. Levey AS, Stevens LA, Schmid CH *et al.* A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;**150**:604–12. https://doi.org/10.7326/0003-4819-150-9-200905050-00006

Received: April 13, 2023; Editorial decision: August 5, 2023