

Quality of Life in Caregivers of Patients Randomized to Standard- Versus Extended-Hours Hemodialysis



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Introduction: Caregivers are essential for the health, safety, and independence of many patients and incur financial and personal cost in this role, including increased burden and lower quality of life (QOL) compared to the general population. Extended-hours hemodialysis may be the preference of some patients, but little is known about its effects on caregivers.

Methods: Forty caregivers of participants of the ACTIVE Dialysis trial, who were randomized to 12 months extended (median 24 hours/wk) or standard (12 hours/wk) hemodialysis, were included. Utility-based QOL was measured by EuroQOL-5 Dimension-3 Level (EQ-5D-3L) and Short Form-6 Dimensions (SF-6D) and health-related QOL (HRQOL) was measured by the 36-Item Short Form Health Survey (SF-36) physical component summary (PCS) and mental component summary (MCS) and the Personal Wellbeing Index (PWI) at enrolment and then every 3 months until the end of the study.

Results: At baseline, utility-based QOL and HRQOL were similar in both groups. At follow-up, caregivers of people randomized to extended-hours dialysis experienced a greater decrease in utility-based QOL measured by EQ-5D-3L compared with caregivers of people randomized to standard hours (-0.18 ± 0.30 vs. -0.02 ± 0.16 , $P = 0.04$). There were no differences between extended- and standard-hours groups in mean change in SF-6D (0.03 ± 0.12 vs. -0.04 ± 0.1 , $P = 0.8$), PCS (-1.2 ± 9.8 vs. -5.6 ± 9.8 , $P = 0.2$), MCS (-4.1 ± 11.2 vs. -0.5 ± 7.1 , $P = 0.4$), and PWI (2.3 ± 17.6 vs. 0.00 ± 20.4 , $P = 0.9$).

Conclusion: Poorer utility-based QOL, as measured by the EQ-5D-3L, was observed in caregivers of patients receiving extended-hours hemodialysis in this small study. Though the findings are exploratory, the possibility that mode of dialysis delivery negatively impacts on caregivers supports the prioritization of research on burden and impact of service delivery in this population.

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KEYWORDS: caregiver; Co-ACTIVE; extended dialysis; hemodialysis; quality of life

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Caregivers play an important role in supporting the independence of people receiving dialysis, including through assistance with activities of daily living (ADL) such as personal hygiene, dressing, and feeding, and instrumental ADL such as shopping, housework, and

meal preparation. Caregivers of people receiving hemodialysis may also be responsible for tasks such as transport to and from dialysis, preparation of meals appropriate for people with kidney disease, and medical/nursing tasks such as setup and assisting with dialysis treatment in patients performing home dialysis.^{1–3} Caregivers of patients receiving dialysis treatment experience significantly increased burden and reduced QOL compared with the general population.^{4,5} Marital adjustment and sleep quality may be adversely affected.^{6–9} In addition, caregivers incur significant financial burden equivalent to an average of US\$6954 per year lost or foregone in the United States, through loss of work and out-of-pocket expenses related to caregiving.¹⁰ Yet, caregivers are essential to health systems, as the estimated cost of replacing informal caregivers with paid services in Australia is \$60.3 billion per year, approximately 60% of the health and social work industry.¹¹ Unfortunately, there are limited high-quality studies evaluating QOL, or interventions to improve QOL, in caregivers of dialysis patients.^{12,13}

Standard hemodialysis regimens typically involve thrice-weekly sessions of 4 to 5 hours duration. More intensive hemodialysis regimens, which may involve increased duration or frequency, have been associated with improved biochemical parameters and reduced medication burden for patients.^{14–17} Despite a lack of proven benefit in terms of either QOL or survival,^{14,18} some patients may prefer extended-hours hemodialysis as a lifestyle choice or for biochemical or medication benefits. However, little is known about how more intensive dialysis regimens affect caregivers.¹⁹ It is possible that such regimens may result in greater reductions in caregiver QOL, because of increased demands on time, need for physical assistance, and other responsibilities for caregivers. Conversely, more intensive dialysis regimens could result in improvements in caregiver QOL, by improving the health of the patients for whom they care.

The ACTIVE trial (A Clinical Trial of Intensive Dialysis) was an international, multicenter trial in which QOL, cardiovascular effects, laboratory outcomes, medication usage, and safety were assessed in patients who were randomized to receive either extended-hours (≥ 24 hours/wk) or standard-hours (≤ 18 hours/wk) hemodialysis.^{14,20} Our study, Caregivers of ACTIVE (Co-ACTIVE), was a longitudinal cohort substudy of the ACTIVE trial, where we sought to investigate the effects of hemodialysis on caregivers' QOL.

METHODS

Study Design

Co-ACTIVE was a prospective, observational study that examined QOL and burden in caregivers of patients

enrolled in the ACTIVE study. The design and results of the ACTIVE study have been previously described in detail.¹⁴ Briefly, ACTIVE was an international, multicenter, randomized controlled trial where adult patients receiving maintenance hemodialysis received either standard- (≤ 18 hours/wk) or extended-hours (≥ 24 hours/wk) hemodialysis. Co-ACTIVE was conducted in parallel with ACTIVE study, and caregiver data were collected at the same time points as patient data for the ACTIVE study (enrolment and then every 3 months until study end at month 12).

The study was approved by the Metro South Hospital and Health Service Human Research and Ethics Committee, Queensland, Australia (HREC/12/QPAH/267). Each center obtained additional approvals as required by local practice. Written informed consent was obtained from all participants.

Study Participants

Patients enrolled in the ACTIVE study were invited to nominate their primary caregiver to participate in Co-ACTIVE. As Co-ACTIVE was initiated after recruitment for ACTIVE had already begun, not all sites and participants were eligible. Caregivers were not blinded to patient treatment arm allocation (standard vs. extended hours).

Demographic data, including age, sex, marital status, and ethnicity were collected at baseline by written questionnaire. Caregivers also completed a purpose-designed Co-ACTIVE study questionnaire that included caregiver relationship to the patient, duration of being a caregiver, caregiver role and responsibilities, and impacts of caregiving ([Supplementary Material S1](#)).⁵ This study questionnaire was translated by local staff for participants from non-English speaking backgrounds.

Outcome Measures

Caregiver utility-based QOL was measured with the EQ-5D-3L and SF-6D, and HRQOL was measured with the SF-36 PCS and MCS and the PWI. Health utility aims to assign a single value (on a 0–1, dead to full health, scale) and may be useful for economic evaluation²¹; however, HRQOL measures may provide a more nuanced, multidimensional coverage of QOL assessment, and thus both were used in this study. Validated translations of these instruments were used for participants who were from non-English speaking backgrounds. Patients who could not read or complete their questionnaires were excluded from study participation. The instruments were completed by caregivers at study entry and then at 3-month intervals for 12 months (the same time points as the dialysis recipients). For the EQ-5D-3L, UK population preference weighting was used

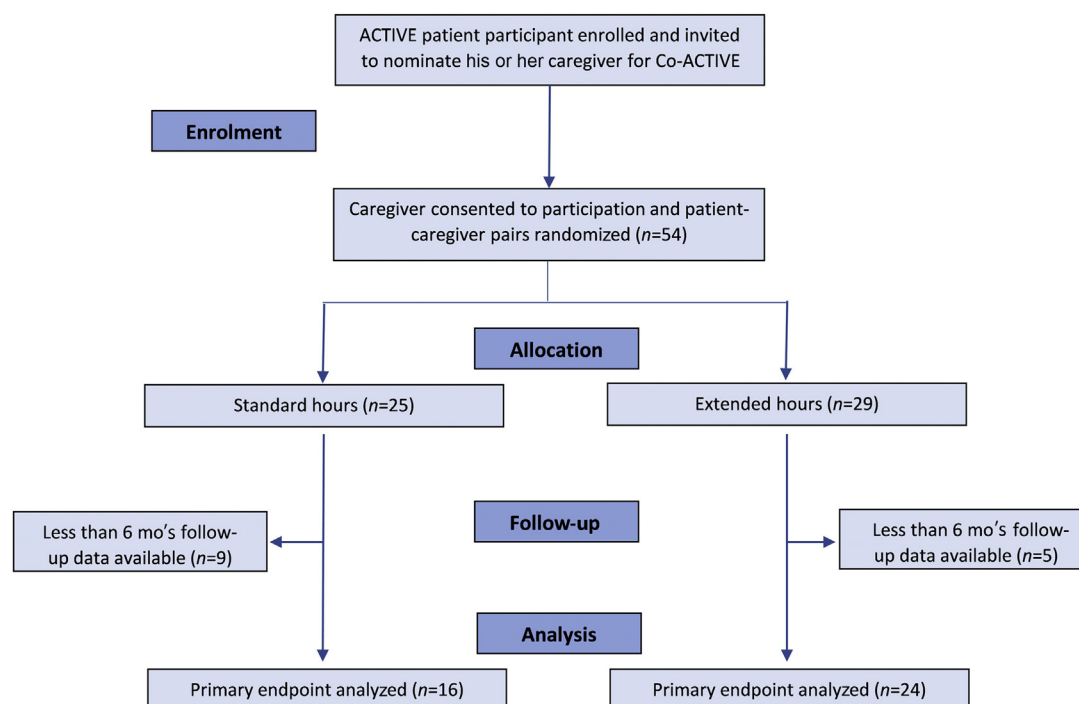


Figure 1. Participant flow through the study.

to maintain consistency with the ACTIVE study.¹⁴ As the majority of caregivers were from China, SF-6D preference weights from a Hong Kong population were used (preference weights from a mainland Chinese population were unavailable).²²

The primary outcome was the difference in change in EQ-5D-3L from baseline to last available follow-up measurement between standard- and extended-hours dialysis caregivers. Caregivers who did not have at least 6 months of follow-up data were excluded from the final analysis as per the prespecified Statistical Analysis Plan to ensure sufficient time for the intervention to produce effects on HRQOL. Secondary outcomes included the change in caregiver SF-6D, SF-36 PCS and MCS, and PWI from baseline to follow-up in standard- and extended-hours groups. Change in QOL measures of caregivers were compared to those of patients (ACTIVE trial participants) as an exploratory outcome.

Statistical Analysis

Descriptive statistics were reported as mean \pm standard deviation, or median (interquartile range) as appropriate. Comparative analysis of continuous data was performed using *t*-test or Kruskal-Wallis for parametric and nonparametric data, respectively. Comparisons of categorical data were performed with χ^2 test. For participants who had missing 12-month HRQOL data, the last-observation carried forward method was used. Analyses were performed on intention-to-treat basis.

Statistical analyses were performed using Stata, version 15.0 (StataCorp, College Station, TX).

RESULTS

Baseline Characteristics

Forty caregivers participated in the Co-ACTIVE study and were eligible for inclusion in the analysis (Figure 1). Most caregivers were female, cared for a spouse or partner, and lived at the same residence (Table 1). Standard- and extended-hours groups were not significantly different in terms of age (54.6 ± 10.3 vs. 53.4 ± 13.0 years, $P = 0.9$) or sex (female 71.4% vs. 59.1%, $P = 0.4$). The majority of caregivers were Asian, because recruitment for the ACTIVE study was occurring predominantly in China at the time. As such, all participants were receiving hemodialysis within a facility, as is usual practice in mainland China,^{23,24} and so continued with a thrice-weekly schedule. Most caregivers had attained at least high school-level education, and approximately one-third had attained postsecondary education. More than half had been a caregiver for more than 2 years.

Most caregivers were required to assist with at least 1 instrumental ADL such as household chores, shopping, transport, and medications. A smaller proportion were required to assist with basic ADLs such as showering and mobility. More than one-third of caregivers spent 3 or more hours per day performing caregiving duties. At baseline (prior to randomization of dialysis recipients to standard- or extended-hours

Table 1. Baseline characteristics of caregivers

Characteristic	Standard hours (n = 16)	Extended hours (n = 24)
Age, yr, mean (SD)	54.6 (10.3)	53.4 (13.0)
Sex, %		
Female	71.4	59.1
Marital status, %		
Married/ <i>de facto</i>	92.9	100
Single	7.1	—
Divorced/separated	—	—
Widowed	—	—
Ethnicity, %		
Asian	92.9	95.5
Caucasian	7.1	—
Other	—	4.5
Education, %		
Primary school	7.1	13.6
High school	64.3	45.5
University/TAFE	28.6	40.9
Occupation, %		
Paid employment	40	21.7
Pension (aged/carer's/retired)	40	56.5
Homemaker	13.3	17.4
Unemployed	—	4.4
Other	6.7	—
Person cared for, %		
Spouse/partner	78.6	60.9
Parent	—	4.4
Child	7.1	17.3
Sibling	7.1	—
Friend	—	4.4
Other	7.2	13.0
Duration of being a caregiver, %		
<6 mo	7.1	9.1
6 mo–2 yr	28.6	27.3
3–9 yr	57.1	54.5
10–19 yr	7.2	9.1
Residence of the dialysis patient, %		
With caregiver	87.5	86.4
Alone	—	—
Another household	6.25	13.6
Other	6.25	—
Daily time spent caring, %		
<1 h	13.3	13.1
1–2 h	33.4	29.0
3–6 h	13.3	15.8
7–12 h	33.4	29.0
>12 h	6.6	13.1
Caregiver responsibilities, %		
Assists with showering/toileting	14.3	17.7
Assists with mobility	14.3	17.7
Assists with household chores	100	94
Assists with medications	42.9	23.5
Assists with shopping/banking	42.9	58.8
Assists with transport	42.9	50

(Continued on following page)

hemodialysis), there were no significant differences in EQ-5D-3L (0.920 ± 0.12 vs. 0.911 ± 0.12 , $P = 0.8$), SF-6D (0.74 ± 0.1 vs. 0.71 ± 0.1 , $P = 0.4$), SF-36 PCS (50.0 ± 7.3 vs. 47.9 ± 8.5 , $P = 0.4$), SF-36 MCS (50.4 ± 10.0 vs.

Table 1. (Continued)

Characteristic	Standard hours (n = 16)	Extended hours (n = 24)
Caregiver utility-based QOL/HRQOL, mean \pm SD		
EQ-5D-3L	0.920 ± 0.12	0.911 ± 0.12
SF-6D	0.74 ± 0.1	0.71 ± 0.1
SF-36 PCS	50.0 ± 7.3	47.9 ± 8.5
SF-36 MCS	50.4 ± 10.0	48.3 ± 8.8
PWI	63.8 ± 21.1	62.5 ± 23.8

EQ-5D-3L, EuroQoL-5 Dimension-3 Level; MCS, Mental Component Summary; PCS, Physical Component Summary; PWI, Personal Wellbeing Index; SF-6D, Short Form-6 Dimensions; SF-36, 36-Item Short Form Health Survey; TAFE, technical and further education.

Some respondents did not answer all questions.

48.3 ± 8.8 , $P = 0.4$), or PWI (63.8 ± 21.1 vs. 62.5 ± 23.8 , $P = 0.8$) scores.

Utility-Based QOL and Health-Related QOL

At study conclusion, EQ-5D-3L was lower than baseline in both caregiver groups, but the mean reduction in QOL was significantly greater in caregivers of patients receiving extended-hours hemodialysis, compared with caregivers of patients receiving standard-hours hemodialysis (-0.18 ± 0.30 vs. -0.02 ± 0.16 , $P = 0.04$) (Table 2, Figure 2a).

There was no significant difference between standard- and extended-hours groups in mean change in utility-based QOL as measured by SF-6D (-0.04 ± 0.1 vs. 0.03 ± 0.12 , $P = 0.8$) (Figure 2b). Change in HRQOL was similar between groups when measured by SF-36 PCS (-5.6 ± 9.8 vs. -1.2 ± 9.8 , $P = 0.2$), SF-36 MCS (-0.5 ± 7.1 vs. -4.1 ± 11.2 , $P = 0.4$), and PWI (0.00 ± 20.4 vs. -2.3 ± 17.6 , $P = 0.9$) (Figure 2c–e).

When baseline patient and caregiver scores were compared to one another, mean SF-36 PCS was significantly lower in patients than caregivers, in both the standard- (39.81 ± 7.24 vs. 50.0 ± 7.3 , $P < 0.01$) and extended-hours groups (40.58 ± 12.2 vs. 47.9 ± 8.5 , $P = 0.04$) (Table 3). However, there were no significant differences between patients and caregivers in the change in any measure, in either the standard- or extended-hours groups.

DISCUSSION

Caregivers of patients receiving hemodialysis in our study were required to spend substantial time each day performing caregiving tasks. Most had been in their caregiving role for years, and most commonly cared for a partner with whom they lived. A significantly greater decrease of -0.18 in EQ-5D-3L was observed in caregivers of patients receiving extended-hours hemodialysis. Although the minimum clinically important difference (MCID) has been reported at approximately this value,²⁵ albeit with some uncertainty, a decrease of 0.18 on a utility scale of 0 to 1 (dead to full health)

Table 2. Changes in utility-based QOL and HRQOL scores of caregivers

Utility-based QOL/ HRQOL measure	Standard hours, mean change (SD)	Extended hours, mean change (SD)	P value
EQ-5D-3L	-0.02 (0.16)	-0.18 (0.30)	0.04
SF-6D	-0.04 (0.1)	0.03 (0.12)	0.8
SF36 PCS	-5.6 (9.8)	-1.2 (9.8)	0.2
SF-36 MCS	-0.5 (7.1)	-4.1 (11.2)	0.4
PWI	0.00 (20.4)	2.3 (17.6)	0.9

EQ-5D-3L, EuroQoL-5 Dimension-3 Level; MCS, Mental Component Summary; PCS, Physical Component Summary; PWI, Personal Wellbeing Index; SF-6D, Short Form-6 Dimensions; SF-36, 36-Item Short Form Health Survey.

represents a substantial reduction in QOL. For context, a systematic review by Wyld and colleagues reported a utility-based QOL value for having a kidney transplant of 0.82, that is, a decrement from full health of 0.18.²⁶ This suggests that caregivers of patients receiving extended-hours hemodialysis in Co-ACTIVE experienced a decrement in utility-based QOL of a similar magnitude to them having a kidney transplant themselves. Moreover, similar utility values have also been observed in caregivers of patients with dementia or cancer receiving chemotherapy.^{27,28} It should be noted that there were no significant between-group differences detected in utility-based QOL as measured by SF-6D, or in HRQOL as measured by SF-36 PCS or MCS, or PWI, although these instruments measure different domains and dimensions of QOL; thus, some variation between results would be anticipated. As a result, the true magnitude and clinical significance of the effects of extended-hours dialysis on caregiver QOL remains somewhat unclear.

There are few previous randomized trials evaluating the effect of hemodialysis on caregivers. The Frequent Hemodialysis Network (FHN) Nocturnal trial found a trend to higher perceived caregiver burden, as measured by the Cousineau scale of perceived burden, in patients randomized to receive daily home nocturnal dialysis compared with conventional dialysis in-center or at home.^{29–31} However, there was no difference in perceived caregiver burden between those randomized to receive daily facility hemodialysis compared with conventional facility dialysis in the FHN Daily Trial.^{31,32} It is important to note, however, that the FHN trials did not directly measure caregiver burden but instead assessed the patient's perception of his or her caregiver's burden.

It is possible that extended-hours hemodialysis may adversely affect caregiver QOL through increased time, transport, and other demands. Our participant population included only facility dialysis patients and thus both standard- and extended-hours participants continued with a thrice-weekly dialysis schedule. Thus, as previously suggested, dialysis being

performed by paid health care workers may have potentially helped to lessen any increased burden of extended-hours dialysis.^{31,32} In our study, it did not appear that improvements in patient health with extended-hours dialysis would have mitigated increased caregiver burden, as the results of the larger ACTIVE trial did not show any significant improvements in patient QOL, blood pressure, or cardiac parameters with this treatment.^{14,33} In addition, we did not identify any significant differences between patients and caregivers in change in any HRQOL or utility-based QOL measure.

Strengths of our study include its design as part of an international, randomized controlled trial and its use of validated HRQOL and utility-based QOL measures. The EQ-5D-3L was selected as the primary outcome measure owing to its more widespread use and to be consistent with the main ACTIVE study. However, we used multiple health utility and HRQOL measures, as there is no single accepted and validated tool for evaluating QOL in the caregiver population. In fact, a previous systematic review and meta-analysis identified the use of 70 different quantitative measures of QOL and burden in studies of caregivers of dialysis recipients.¹² Moreover, although some domains of QOL are shared between different measures, they do differ in the view provided of the underlying concepts. To our knowledge, our study is the first to examine several direct measures of caregiver QOL with extended versus standard hemodialysis treatment. However, our study has limitations, including small sample size and relatively short follow-up. Selection bias may have been present regarding the characteristics of those who agreed to participate in the study. It is not clear how generalizable the results of our study are, as country-specific social and cultural factors may influence caregiver perception of responsibilities and QOL, and the majority of participants were from China. Finally, the patients in the Co-ACTIVE cohort were all receiving facility hemodialysis, so the results may not be applicable to those patients performing home hemodialysis.

In conclusion, the Co-ACTIVE study demonstrated a statistically greater decrease in utility-based QOL measured by EQ-5D-3L in caregivers of patients randomized to receive extended-hours hemodialysis compared with those receiving standard-hours. Given the limited sample size, and as no significant difference was found in change in SF-6D, SF-36 MCS or PCS, or PWI, the results should be regarded as exploratory. However, it is not unreasonable to suggest that different ways of delivering dialysis for people with end-stage kidney disease may impact on the QOL of

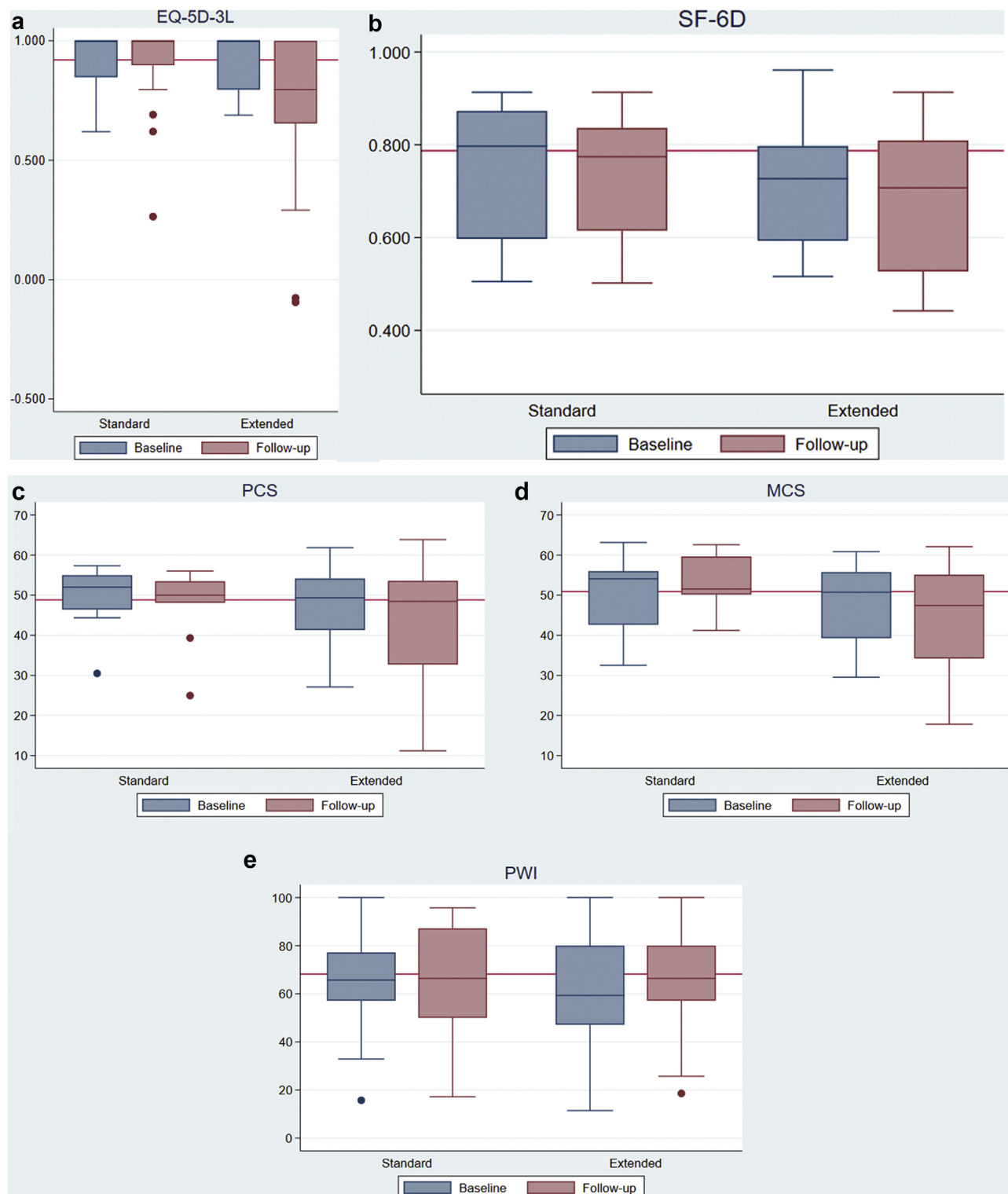


Figure 2. Scores in caregivers of patients randomized to standard- and extended-hours hemodialysis: (a) EQ-5D-3L (Chinese general population norm = 0.920, SD 0.17)³⁴; (b) SF-6D (Chinese general population norm = 0.787, SD 0.15)²²; (c) SF-36 PCS (Chinese general population norm = 48.8)³⁵; (d) SF-36 MCS (Chinese general population norm = 50.9)³⁵; (e) PWI (Chinese general population norm for age 51–55 years = 68.2, SD 14.2).³⁶ EQ-5D-3L, EuroQoL-5 Dimension-3 Level; MCS, Mental Component Summary; PCS, Physical Component Summary; PWI, Personal Wellbeing Index; SF-6D, Short Form-6 Dimensions; SF-36, 36-Item Short Form Health Survey.

their caregivers. The findings of our study support prioritization of research, including qualitative studies, to better understand the burden and impact of dialysis

service delivery on caregivers, and assist in directing health care funding and provision of financial and social support for these important health care providers.

Table 3. Utility-based QOL and HRQOL in patients and caregivers randomized to standard and extended hours

	Standard hours			Extended hours		
	Patients, mean (SD)	Carers, mean (SD)	P value	Patients, mean (SD)	Carers, mean (SD)	P value
EQ-5D-3L						
Baseline	0.772 (0.255)	0.920 (0.12)		0.80 (0.25)	0.911 (0.12)	
Follow-up	0.78 (0.2)	0.9 (0.21)		0.76 (0.31)	0.71 (0.32)	
Change from baseline to follow-up	0.005 (0.27)	−0.02 (0.16)	0.9	−0.04 (0.16)	−0.18 (0.30)	0.06
SF-36 PCS						
Baseline	39.81 (7.24)	50.0 (7.3)		40.58 (12.2)	47.9 (8.5)	
Follow-up	40.25 (9.22)	47.13 (8.49)		41.0 (12.05)	45.02 (12.97)	
Change from baseline to follow-up	0.21 (6.5)	−5.34 (8.77)	0.2	−0.66 (8.41)	−1.06 (9.28)	0.6
SF-36 MCS						
Baseline	49.83 (10.98)	50.4 (10.0)		50.1 (10.95)	48.3 (8.8)	
Follow-up	47.02 (13.39)	51.42 (8.17)		49.96 (12.29)	44.74 (12.41)	
Change from baseline to follow-up	0.5 (9.35)	−2.21 (8.68)	0.6	−0.57 (8.25)	−4.21 (11.63)	0.3
SF6D						
Baseline	0.67 (0.14)	0.74 (0.1)		0.7 (0.16)	0.71 (0.1)	
Follow-up	0.65 (0.18)	0.73 (0.14)		0.69 (0.17)	0.68 (0.16)	
Change from baseline to follow-up	0.0003 (0.12)	−0.037 (0.096)	0.6	−0.02 (0.12)	−0.03 (0.12)	0.8

EQ-5D-3L, EuroQoL-5 Dimension-3 Level; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-6D, Short Form-6 Dimensions; SF-36, 36-Item Short Form Health Survey.

DISCLOSURE

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AUTHOR CONTRIBUTIONS

Study inception and design: NG, KH, LZ, JdZ, AC, VP, MeJ. Data collection: LZ, DH, MiJ, BS, JW, CL, ZL. Data analysis and interpretation: MN, RK, NG, BS, KH, MeJ. Manuscript preparation: MN, NG, RK. Revision and approval of final manuscript: all authors

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References.

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