

## ACTIVE Primary Results paper Online Supplementary Material

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## Methods

### Imputation

Single imputation was performed for EQ-5D defined quality of life if the measure was missing in accordance with the EQ-5D User Guide ([www.euroqol.org](http://www.euroqol.org)). If the patient died before the 12 months follow-up then quality of life was scored as 0. If the patient reached the end of the study duration before 12 months or if the quality of life score at 12 month was missing then the last available measure was used. There was no imputation for LVMI as there was only one post-randomisation measure.

### Equation for stdKt/v

Standardised kt/v was calculated using the following equations described in the 2015 Update of the KDOQI Clinical Practice Guideline for Hemodialysis Adequacy<sup>1</sup> to estimate true std Kt/v from spKt/v. The fixed volume model was used as measures of residual native kidney clearance were not collected in this study. Residual native clearance is likely to have been negligible for most participants given the median duration on dialysis of 2.5 years at recruitment.

$$eKt/V = spKt/V(t/(t + 30))$$

$$stdKt/V = \frac{10,080 \frac{1 - e^{-eKt/V}}{t}}{\frac{1 - e^{-eKt/V}}{eKt/V} + \frac{10,080}{Nt} - 1}$$

1. Daugirdas JT, Depner TA, Inrig J, Mehrotra R, Rocco MV, Suri RS, Weiner DE, Greer N, Ishani A, MacDonald R, Olson C, Rutks I, Slinin Y, Wilt TJ, Rocco M, Kramer H, Choi MJ, Samaniego-Picota M, Scheel PJ, Willis K, Joseph J, Brereton L. KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 Update. *Am. J. Kidney Dis.* 2015;66(5):884-930.

**Appendix Table 1. Blood flow rate (mls/min) and dialysis flow rate (mls/min) by treatment group over study period**

	Standard		Extended		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	p-value
<b>Blood flow rate (mls/min)</b>					
Baseline	278.6 (36.8)	280.0 (250.0; 300.0)	279.2 (39.8)	288.0 (250.0; 300.0)	0.0010
Follow up	283.8 (48.4)	280.0 (250.0; 300.0)	261.6 (42.9)	250.0 (230.0; 300.0)	
<b>Dialysate flow rate (mls/min)</b>					
Baseline	503.9 (84.5)	500.0 (500.0; 500.0)	514.0 (69.7)	500.0 (500.0; 500.0)	0.0215
Follow up	502.3 (71.7)	500.0 (500.0; 500.0)	478.4 (64.4)	500.0 (500.0; 500.0)	

P-values are from a Linear mixed model with random intercept including randomisation and time categories with baseline as reference

**Appendix Table 2. Details of dialysis treatment characteristics used throughout the study**

<b>Characteristic</b>		<b>Standard N=100</b>	<b>Extended N=100</b>	<b>Total N=200</b>
Membrane	Asahi	3.0%	1.0%	2.0%
	Baxter	6.0%	7.0%	6.5%
	Baxter then Bellco	1.0%	0.0%	0.5%
	Bellco	0.0%	1.0%	0.5%
	D-Tec	1.0%	1.0%	1.0%
	Fresenius	67.0%	70.0%	68.5%
	Fresenius then Nipro	1.0%	0.0%	0.5%
	Gambro	9.0%	9.0%	9.0%
	Nipro	6.0%	2.0%	4.0%
	Toray	1.0%	0.0%	0.5%
	Wego	2.0%	2.0%	2.0%
	Not reported	3.0%	7.0%	5.0%
Flux	High	89.0%	82.0%	85.5%
	Low	7.0%	10.0%	8.5%
	High then low	1.0%	0.0%	0.5%
	Low then high	0.0%	1.0%	0.5%
	Not reported	3.0%	7.0%	5.0%
Biocompatibility	Cellulose	4.0%	3.0%	3.5%
	Synthetic	93.0%	90.0%	91.5%
	Not reported	3.0%	7.0%	5.0%

Characteristics of dialysis treatment were mostly constant throughout the study. Proportions of those whose dialysis treatments changed during the study are indicated. Seven participants were treated with cellulose membranes throughout the study: 1 in Australia, 1 in Canada and 5 in China.

**Appendix Table 3. Number of patients with measures of small molecule clearance at baseline and throughout follow up by dialysis location<sup>1</sup>**

	In-center and satellite-based participants		Home-based participants	
	Baseline	Follow up <sup>2</sup>	Baseline	Follow up
	N=149	N=145	N=51	N=49
Urea Reduction Ratio (%)	78 (52.3%)	99 (68.3%)	32 (62.7%)	26 (53.1%)
Kt/V	47 (31.5%)	66 (45.5%)	28 (54.9%)	25 (51.0%)

1. ACTIVE used values obtained from routine clinical practice. Not all participants had a measure of small molecular clearance measured every 3 months. The table depicts the numbers of patients who had measures of small molecular clearance during the study.
2. Numbers in followup exclude participants who had withdrawn or died before follow-up assessments

**Appendix Table 4. Impact of extended dialysis hours on measures of small molecule clearance among participants with baseline measures**

	Standard		Extended		Between-Group difference	P-value
	n	mean (sd)	n	mean (sd)	Mean difference (95% CI)	
Urea Reduction Ratio (%)						
Baseline	58	69.67 ( 10.29)	52	72.35 ( 8.52)	2.67 ( -0.92, 6.27)	
3-month	55	69.62 ( 9.29)	50	78.06 ( 8.84)	8.44 ( 4.92, 11.96)	
6-month	52	69.65 ( 8.63)	45	79.82 ( 6.89)	10.17 ( 6.99, 13.35)	
9-month	48	68.40 ( 9.58)	47	77.68 ( 8.22)	9.29 ( 5.65, 12.92)	
12-month	49	69.49 ( 8.97)	52	75.85 ( 9.51)	6.36 ( 2.70, 10.01)	
Average intervention effect <sup>1</sup>					7.12 ( 4.91, 9.33)	<.0001
Single pool Kt/v						
Baseline	42	1.39 ( 0.35)	33	1.43 ( 0.31)	0.04 ( -0.11, 0.19)	
3-month	41	1.47 ( 0.40)	34	1.96 ( 0.74)	0.50 ( 0.23, 0.76)	
6-month	39	1.41 ( 0.33)	35	1.95 ( 0.69)	0.54 ( 0.29, 0.78)	
9-month	36	1.40 ( 0.30)	34	1.93 ( 0.56)	0.54 ( 0.33, 0.75)	
12-month	37	1.40 ( 0.26)	33	1.83 ( 0.61)	0.43 ( 0.21, 0.65)	
Average intervention effect <sup>1</sup>					0.48 ( 0.27, 0.68)	<.0001
Standardised Kt/V <sup>2</sup>						
Baseline	42	2.53 ( 0.42)	33	2.76 ( 0.85)	0.23 ( -0.07, 0.53)	
3-month	41	2.72 ( 0.55)	34	3.81 ( 1.39)	1.10 ( 0.63, 1.57)	
6-month	39	2.56 ( 0.46)	35	4.25 ( 3.86)	1.69 ( 0.45, 2.93)	
9-month	36	2.83 ( 1.51)	34	3.65 ( 0.92)	0.83 ( 0.23, 1.43)	
12-month	37	2.83 ( 1.40)	33	3.62 ( 1.20)	0.79 ( 0.17, 1.42)	
Average intervention effect <sup>1</sup>					1.29 ( 0.61, 1.96)	0.0003

1. Average effect of intervention for all followup visits adjusted for baseline.
2. Calculated from measuring spKt/V using a fixed volume model. Residual kidney function data was not collected in the study.

**Appendix Table 5. Baseline characteristics of participants contributing to MRI analyses of the ACTIVE Dialysis Trial**

<b>Characteristics</b>	<b>Standard (N = 44)</b>	<b>Extended (N = 51)</b>	<b>Total (N = 95)</b>
Age at randomisation (years)			
Mean (SD)	50.2 (12.08)	50.0 (13.23)	50.1 (12.64)
Median (Q1, Q3)	51.0 (42.0, 58.9)	50.5 (39.6, 62.1)	50.9 (40.2, 59.4)
Gender			
Male	26/44 (59.1%)	31/51 (60.8%)	57/95 (60.0%)
Female	18/44 (40.9%)	20/51 (39.2%)	38/95 (40.0%)
Primary cause of renal disease			
Diabetic Nephropathy	17/44 (38.6%)	11/51 (21.6%)	28/95 (29.5%)
Hypertension/Vascular Nephrosclerosis	4/44 (9.1%)	5/51 (9.8%)	9/95 (9.5%)
Glomerulonephritis	16/44 (36.4%)	23/51 (45.1%)	39/95 (41.1%)
Reflux Nephrology	1/44 (2.3%)	1/51 (2.0%)	2/95 (2.1%)
Polycystic Kidney Disease	1/44 (2.3%)	4/51 (7.8%)	5/95 (5.3%)
Other or unknown	5/44 (11.4%)	7/51 (13.8%)	12/95 (12.7%)
Co-morbidity			
Diabetes Mellitus	20/44 (45.5%)	15/51 (29.4%)	35/95 (36.8%)
Hypertension	36/44 (81.8%)	40/51 (78.4%)	76/95 (80.0%)
Any Cardiovascular disease	14/44 (31.8%)	12/51 (23.5%)	26/95 (27.4%)
Symptomatic Ischaemic Heart Disease	6/44 (13.6%)	5/51 (9.8%)	11/95 (11.6%)
Angina	3/44 (6.8%)	2/51 (3.9%)	5/95 (5.3%)
Acute Myocardial Infarction	1/44 (2.3%)	1/51 (2.0%)	2/95 (2.1%)
Previous Coronary Artery Bypass Graft/ Percutaneous Transluminal Coronary Angioplasty	3/44 (6.8%)	2/51 (3.9%)	5/95 (5.3%)
Congestive Heart Failure	7/44 (15.9%)	5/51 (9.8%)	12/95 (12.6%)
Cerebrovascular Disease	2/44 (4.5%)	3/51 (5.9%)	5/95 (5.3%)
Peripheral Vascular Disease	5/44 (11.4%)	1/51 (2.0%)	6/95 (6.3%)
Smoking status			
Never smoked	27/44 (61.4%)	32/51 (62.7%)	59/95 (62.1%)
Past cigarette smoker	9/44 (20.5%)	9/51 (17.6%)	18/95 (18.9%)
Current cigarette smoker	8/44 (18.2%)	10/51 (19.6%)	18/95 (18.9%)
Country			
Australia	11/44 (25.0%)	18/51 (35.3%)	29/95 (30.5%)
Canada	2/44 (4.5%)	3/51 (5.9%)	5/95 (5.3%)
China	29/44 (65.9%)	30/51 (58.8%)	59/95 (62.1%)
New Zealand	2/44 (4.5%)	0/51 (0.0%)	2/95 (2.1%)
Ethnicity			
Caucasian	7/44 (15.9%)	12/51 (23.5%)	19/95 (20.0%)
Aboriginal or Torres Strait Islander	0/44 (0.0%)	1/51 (2.0%)	1/95 (1.1%)
Maori	1/44 (2.3%)	2/51 (3.9%)	3/95 (3.2%)
Pacific Islander	3/44 (6.8%)	2/51 (3.9%)	5/95 (5.3%)
Asian	31/44 (70.5%)	32/51 (62.7%)	63/95 (66.3%)



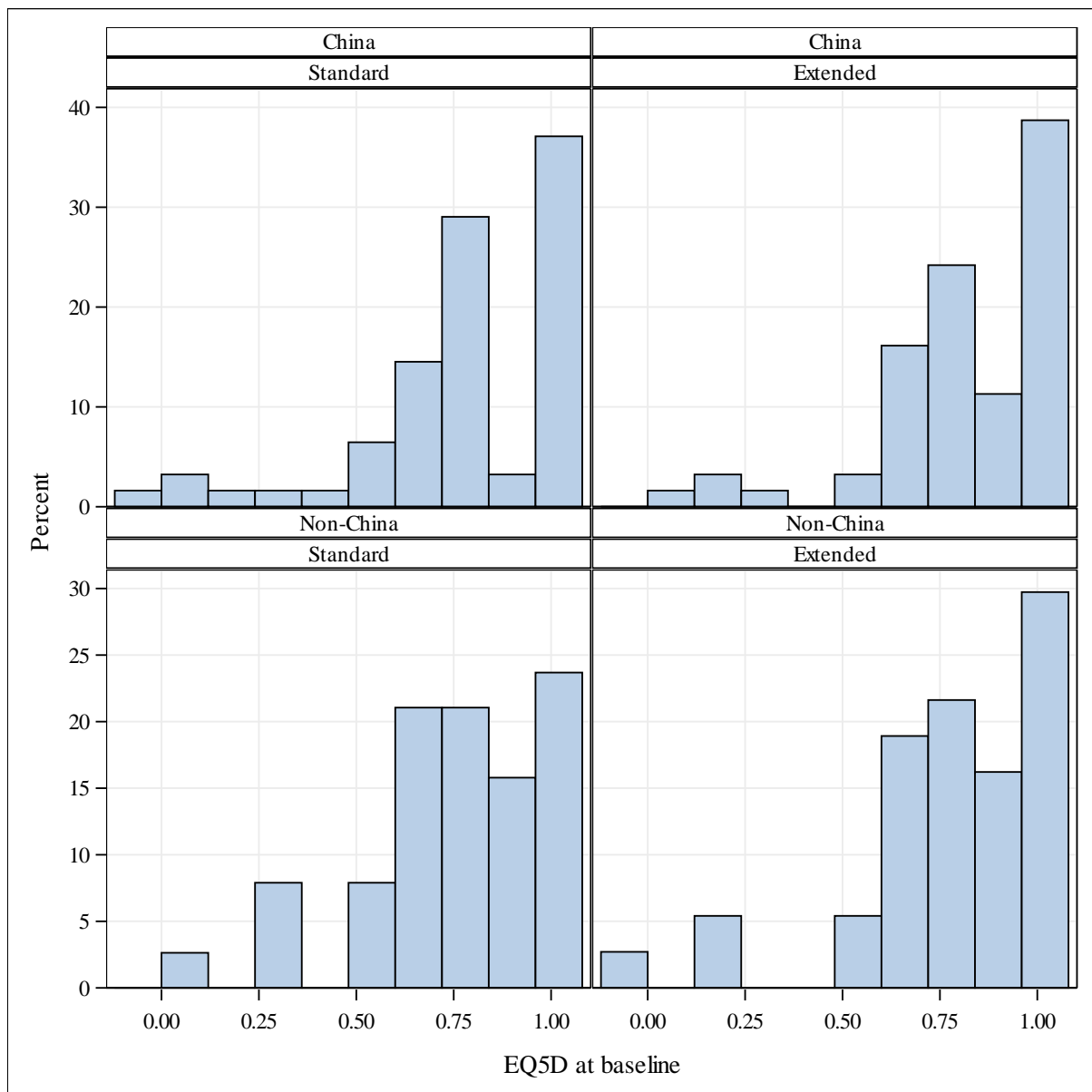
Characteristics	Standard (N = 44)	Extended (N = 51)	Total (N = 95)
Indian	0/44 (0.0%)	0/51 (0.0%)	0/95 (0.0%)
Other	2/44 (4.5%)	1/51 (2.0%)	3/95 (3.2%)
Not reported	0/44 (0.0%)	1/51 (2.0%)	1/95 (1.1%)
Number of dialysis sessions per week			
2	1/44 (2.3%)	0/51 (0.0%)	1/95 (1.1%)
3	39/44 (88.6%)	44/51 (86.3%)	83/95 (87.4%)
4 or more	4/44 (9.1%)	7/51 (13.8%)	11/95 (11.7%)
Total number of hours on dialysis per week			
Mean (SD)	13.4 (2.58)	13.6 (2.50)	13.5 (2.53)
Median (Q1, Q3)	12.0 (12.0, 15.0)	12.0 (12.0, 15.0)	12.0 (12.0, 15.0)
Duration on dialysis at enrolment, median (IQR) in years	2.20 (1.04, 5.19)	2.43 (0.54, 5.35)	2.24 (0.71, 5.35)
Dialysis site at enrolment			
At home	12/44 (27.3%)	13/51 (25.5%)	25/95 (26.3%)
Institution	32/44 (72.7%)	38/51 (74.5%)	70/95 (73.7%)
Intended Dialysis site for study treatment			
Home	6/44 (13.6%)	3/51 (5.9%)	9/95 (9.5%)
Institution (Satellite Centre/Hospital)	38/44 (86.4%)	48/51 (94.1%)	86/95 (90.5%)
Dialysis access			
Native arteriovenous fistula	35/44 (79.5%)	45/51 (88.2%)	80/95 (84.2%)
Synthetic fistula	1/44 (2.3%)	1/51 (2.0%)	2/95 (2.1%)
Tunnelled dialysis catheter	7/44 (15.9%)	4/51 (7.8%)	11/95 (11.6%)
Non-tunnelled dialysis catheter	1/44 (2.3%)	1/51 (2.0%)	2/95 (2.1%)
Dialysis cannulation method			
The Buttonhole technique	8/44 (18.2%)	10/51 (19.6%)	18/95 (18.9%)
The Rope Ladder technique	28/44 (63.6%)	36/51 (70.6%)	64/95 (67.4%)
Dialysis Catheter	8/44 (18.2%)	5/51 (9.8%)	13/95 (13.7%)
Pre-dialysis blood pressure			
Systolic Blood Pressure, mean (SD) in mmHg	143.5 (20.04)	141.9 (15.94)	142.6 (17.87)
Diastolic Blood Pressure, mean (SD) in mmHg	81.3 (13.29)	81.3 (11.85)	81.3 (12.47)
Body Mass Index, median (IQR) in kg/m <sup>2</sup>	24.3 (23.0, 28.9)	24.1 (21.6, 26.6)	24.2 (22.4, 27.7)
Left ventricular mass index <sup>2</sup> , mean (SD) in g/m <sup>2</sup>	103.64 (30.68)	106.48 (36.39)	105.16 (33.72)

**Appendix Table 6. Number (%) of participants with missing data for secondary outcomes**

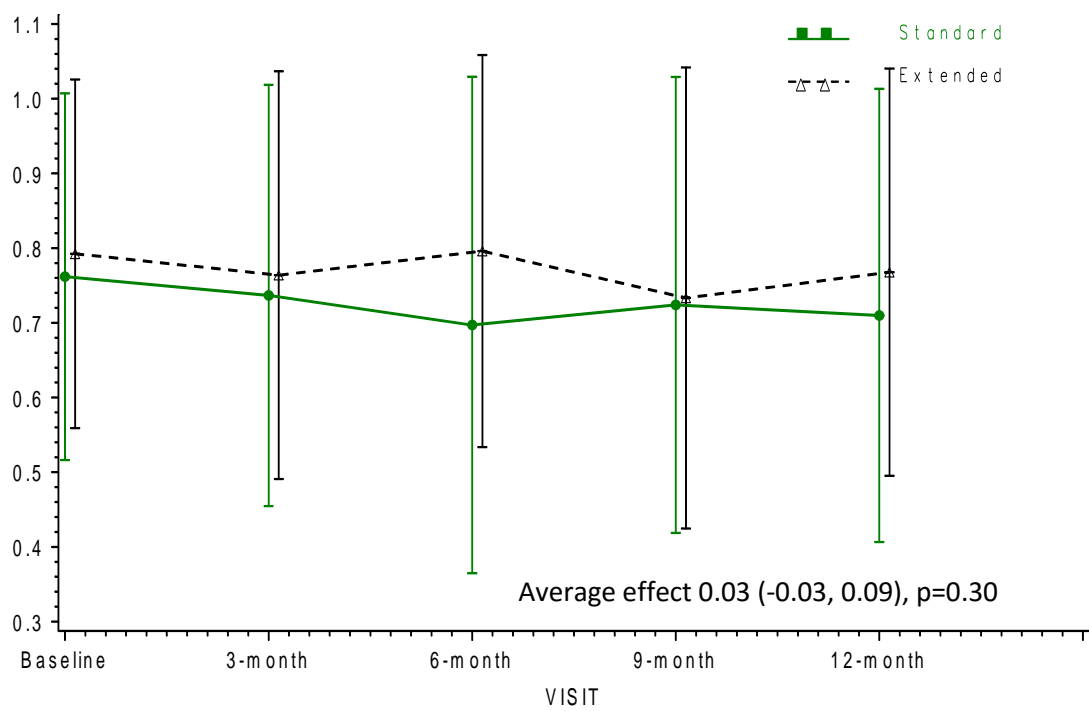
Parameter	No baseline measure	No follow-up measure
	n=200	n=194 <sup>1</sup>
Systolic Blood Pressure (mmHg)	0 (0.0%)	3 (1.5%)
Diastolic Blood Pressure (mmHg)	0 (0.0%)	3 (1.5%)
BP lowering agents (number)	0 (0.0%)	2 (1.0%)
Potassium (meq/L)	3 (1.5%)	2 (1.0%)
Phosphate (mg/dL)	3 (1.5%)	3 (1.5%)
PTH (pg/mL)	25 (12.5%)	6 (3.1%)
Phosphate binders (number of tablets)	0 (0.0%)	2 (1.0%)
Calcium (mg/dl)	3 (1.5%)	3 (1.5%)
Hemoglobin (g/dl)	2 (1.0%)	2 (1.0%)
ESA dose (EPO units)	2 (1.0%)	2 (1.0%)
Ferritin (ng/ml)	46 (23.0%)	27 (13.9%)
Transferrin saturation (%)	65 (32.5%)	45 (23.2%)
Weight (kg)	1 (0.5%)	3 (1.5%)
Waist:hip ratio (cm:cm)	0 (0.0%)	4 (2.1%)
Albumin (g/dL)	22 (11.0%)	15 (7.7%)

1. Numbers eligible for follow-up assessments excludes participants who had withdrawn or died before follow-up assessments

**Appendix Figure 1. Distribution of baseline EQ5D scores in ACTIVE participants according to randomisation and location in China or Australia/Canada/New Zealand**



**Appendix Figure 2. Evolution of EQ5D scores through the study with the average effect from all follow-up visits**



**Appendix Figure 3. Impact of extended dialysis hours on change in left ventricular mass index at 12 months according to prespecified subgroup analyses defined by region, dialysis setting and months on dialysis at baseline**

