CHAPTER 13: HAEMODIALYSIS ADEQUACY

Summary

- Median prescribed spKt/V had increased from 1.3 to 1.5 over the report period, with a significant decrease in patients achieving spKt/V < 1.2.
- While the frequency and duration of dialysis had remained largely the same, there had been an increase in patients dialyzing only twice a week, although they remained a minority (6% in 2002).
- There is a strong trend towards the use of synthetic membranes and bicarbonate-based dialysate. However the number of times of reuse has also increased.
- The elderly, males and diabetics were persistently dialysed to lower Kt/V compared to the rest of the dialysis population.
- Survival analysis identified spKt/V < 1.0 (but not 1.0 - <1.2) as an important risk factor for mortality, while Kt/V > 1.4 did not confer any survival advantage.

Introduction

The term "dialysis adequacy" is usually taken to mean nitrogenous solute removal. Although urea is non-toxic and only represent small solutes, measures of urea removal are often used as surrogates for nitrogenous solute removal. The measures of urea removal most often used in clinical practice are the Urea Reduction Ratio (URR) and the mathematically-related Kt/V urea. The latter was derived from urea-kinetics modeling by Gotch based on data from the National Cooperative Dialysis Study (NCDS) [1]. In this study, patients were randomized to either low or high time-averaged blood urea nitrogen (BUN) and short or long dialysis duration. Low time-averaged BUN was found to result in better clinical outcome, while the benefits of longer dialysis just failed to reach statistical significance. However, further analysis of this study [2] showed that urea removal was an even stronger predictor of outcome. Kt/V represents the clearance of urea (Kt) normalized to the patient's distribution volume for urea (V). Prescribed Kt/V is calculated from the dialyser KoA, dialysis duration and patient's V (usually from anthropometric equations). Delivered Kt/V is usually derived from pre- and post dialysis blood urea. The most commonly used measure of delivered Kt/V is the single pool Kt/V (spKt/V), where post-dialysis urea is sampled within ~15 seconds of slowing the blood flow. This misses the effect of post-dialysis urea rebound and therefore overestimates actual patient urea clearance [3]. However spKt/V and URR are the 2 measures which have been shown in the largest number of studies to predict patient outcome [2, 4-8].

The authors of the NCDS originally suggested spKt/V of 0.8-1.2 as offering adequate dialysis [2]. However, subsequent studies, mainly registry-based, suggested higher spKt/V would be better [4-8]. For example, Held et al [7] found that mortality decreased 7% for every 0.1 increase in spKt/V, but the benefits of further increases beyond 1.3 (corresponding to URR of 70%) did not reach statistical significance. The results of these studies were used as the basis for recommendations by various professional bodies. For instance, the NKF-K/DOQI guidelines recommended a target spKt/V of 1.2 per dialysis for a thrice-a-week haemodialysis regime [9]. The lack of benefits of higher spKt/V was also shown in the HEMO study, a prospective randomized multi-centre study [10]. In this study, patients randomized to the higher dialysis dose group (achieved spKt/V 1.71, URR 75%) did not have better clinical outcome than patients in the standard dialysis dose group (achieved spKt/V 1.32, URR 66%).

More recently, it has been found that urea clearance (Kt) was a better predictor of clinical outcome than Kt normalized to V [11,12]. This is probably because V is strongly correlated with nutritional status, which is itself a good prognostic factor in dialysis patients. Hence, of 2 patients with the same Kt, the one with the larger V (and thus lower Kt/V) is likely to have the better clinical outcome. The lack of benefits at high Kt/V found by Held et al [7] may be because of the inclusion of malnourished patients (with small V) in the highest Kt/V group. Despite its advantages, urea Kt has yet to become a popular measure of dialysis adequacy.

RESULTS

Several factors contributing towards more optimal haemodialysis have shown an improving trend in recent years. Median blood flow rate have increased over the years and is now in the 250-299 ml/min category, whereas that of 1994 was in the 200-249 ml/min category. The proportion of patients with blood flow rates 350 ml/min or higher had also increased from 0% in 1994 to 9% in 2002 (Table 13.01).

However, there appears to be an increasing proportion of patients on twice-a-week haemodialysis (rising from 2% in 1994 to 6% in 2002). This may be due to the increasing numbers of financially marginal patients dialyzing at NGO and private centres. For example, in 2002 Malaysian Dialysis and Transplant Registry Report, the frequency of patients on twice a week dialysis in government, NGO and private dialysis centers were 1%, 3% and 25% respectively [13]. The number of patients dialyzing more than thrice a week remained negligible (Table 13.02).

Similarly, there was no suggestion of increasing dialysis duration from 4 hours, despite a small increase in the proportion of patients on 4.5 hours or more per session in the 1996-2000 period. It is also unclear whether these patients on longer dialysis are dialyzing less frequently (Table 13.03).

There has been a shift towards greater use of synthetic membranes over the report period. The proportion of dialyses using cellulosic membranes had decreased from 76% to 19% between 1994 and 2002 whilst that of synthetic membranes had risen from 1% to 64% over the same period. There was also a smaller decrease in the use of cellulose acetate membranes (from 23% to 17%) (Table 13.04).

Most HD units continue to practise dialyser reuse, although 4% of patients do not practise dialyser reuse in 2002, up from 1 % in 1994. The commonest number of dialyser use was 3 times prior to 1998. In 1998, the commonest number of times of dialyser reuse increased to 6. There has also been increasing number of patients with 8 to 12 reuses, most likely as a consequence of greater use of the more expensive synthetic dialysers (Table 13.05).

The other significant trend over the report period is the move away from acetate-based dialysate towards bicarbonate-based dialysate. The use of bicarbonate-based dialysate increased from 13% in 1994 to 98% in 2002, with a corresponding decrease in the use of acetate-based dialysate (Table 13.06).

Currently, data on delivered Kt/V is not collected in the National Renal Registry dialysis patient notification forms. Therefore all spKt/V reported in this analysis are prescribed Kt/V.

There has been an improvement in median and mean spKt/V from 1.3 in 1994 to 1.5 in 2002. Importantly, the proportion of patients with spKt/V below 1.2 decreased from 40% to 18% over the these same period. The proportion of patients with spKt/V more than or equal to 1.6 increased from 13% to 36% (Table 13.07). However it is not clear whether these patients are on fewer than 3 dialysis sessions a week. This improvement could be attributed to the use of higher prescribed blood flow rates, as shown previously. The use of dialysers with larger KoA's may also have contributed.

The trend of improving spKt/V is seen in all age groups. Younger patients tend to have higher spKt/V than older patients at all periods (Table 13.08). In particular, the median spKt/V in those aged < 20 years has risen to 1.9-2.0 in recent years, possibly due to the inclusion of paediatric patients with a small V. However, even in the oldest age group (age > 60 years), the median spKt/V is 1.5. Better vascular access, ability to tolerate higher blood flow rates and greater effort by physicians to optimize dialysis may account for the difference between age groups.

Subpopulation analysis reveals a difference in spKt/V between certain groups. Female patients consistently achieved higher spKt/V than males, most likely due to their smaller V (Table 13.09). Similarly, non-diabetic patients consistently achieved a spKt/V 0.1-0.2 Kt/V points higher than diabetics (Table 13.10). This may be due to diabetics having suboptimal vascular access resulting in limitations to the blood flow rates. Further analyses of these factors would clarify the causes leading to the differences in Kt/V.

spKt/V was found to have a significant impact on patient survival in this population. Between 1997 and 2002, unadjusted 1-year patient survival for spKt/V of <1, 1.2-<1.4 and ≥1.6 were 88%, 94% and 95% respectively. Corresponding rates for 3-year survival were 66%, 79% and 83% whilst those for 5-year survival were 57%, 64% and 73% respectively (Table 13.11, Fig. 13.11). These rates are significantly better than those reported by other registries. For example, the latest USRDS report reported overall survival rates of 79% at 1 year, 51% at 3 years and 33% at 5 years for haemodialysis patients [14]. This could reflect the stricter acceptance criteria for entry into haemodialysis programmes in Malaysia or under-reporting by under-performing centers.

After adjusting for age, gender, primary diagnosis and time on dialysis, and using the spKt/V 1.2 to <1.4 group as reference, the group with spKt/V <1 still showed a significantly lower 5-year survival. However, the groups with higher spKt/V than the reference group failed to show an increase in 5-year survival rates (Table 1.12, Fig. 1.12). This is in contrast to data from Australia and New Zealand, where there is continuous improvement in survival when groups with increasing URR from ≤ 59% to ≥70% were considered. However, even in the group with the highest URR, one-year patient survival was less than 90% [15].

Table 13.01 Blood Flow Rates in HD Units 1994– 2002

Blood flow rates	1994		1995		1996		1997	
	No.	%	No.	%	No.	%	No.	%
<150 ml/min	2	0	2	0	1	0	2	0
150-199 ml/min	30	3	24	2	20	2	34	2
200-249 ml/min	575	62	604	61	605	50	650	40
250-299 ml/min	288	31	297	30	484	40	735	46
300-349 ml/min	28	3	62	6	82	7	176	11
>=350 ml/min	4	0	7	1	9	1	18	1
Total	927	100	996	100	1201	100	1615	100

Blood flow rates	1998		1999		2000		2001		2002	
	No.	%	No.	%	No.	%	No.	%	No.	%
<150 ml/min	4	0	6	0	9	0	7	0	9	0
150-199 ml/min	36	2	65	2	85	2	69	1	63	1
200-249 ml/min	735	35	963	33	1283	30	1234	25	917	17
250-299 ml/min	969	47	1368	47	1940	46	2230	44	2502	46
300-349 ml/min	298	14	455	16	814	19	1276	25	1486	27
>=350 ml/min	30	1	31	1	94	2	216	4	479	9
Total	2072	100	2888	100	4225	100	5032	100	5456	100

Table 13.02 Number of HD Sessions per week, HD Units 1994 – 2002

HD sessions	1994		1995		1996		1997	
Per week	No.	%	No.	%	No.	%	No.	%
1	3	0	1	0	0	0	1	0
2	23	2	5	0	6	0	6	0
3	923	97	1015	99	1226	99	1666	99
4	2	0	3	0	8	1	9	1
Total	951	100	1024	100	1240	100	1682	100

HD sessions	1998		1999		2000		2001		2002	
Per week	No.	%	No.	%	No.	%	No.	%	No.	%
1	1	0	4	0	8	0	8	0	9	0
2	5	0	153	5	341	8	337	7	325	6
3	2111	100	2813	95	3985	91	4763	92	5250	94
4	2	0	3	0	10	0	50	1	17	0
Total	2119	100	2973	100	4356	100	5161	100	5604	100

Table 13.03 Duration of HD in HD Units 1994 – 2002

Duration of HD	1994		1995		1996		1997	
per session	No.	%	No.	%	No.	%	No.	%
<=3 hours	5	1	0	0	2	0	7	0
-3.5 hours	5	1	4	0	1	0	3	0
-4 hours	924	97	1009	98	1199	97	1595	95
-4.5 hours	4	0	7	1	30	2	70	4
-5 hours	12	1	4	0	8	1	8	0
>5 hours	2	0	1	0	0	0	1	0
Total	952	100	1025	100	1240	100	1684	100

Duration of HD	1998		1999		2000		2001		2002	
per session	No.	%	No.	%	No.	%	No.	%	No.	%
<=3 hours	3	0	4	0	8	0	6	0	18	0
-3.5 hours	18	1	9	0	12	0	33	1	15	0
-4 hours	1994	94	2737	92	4056	93	4958	96	5454	97
-4.5 hours	91	4	160	5	189	4	106	2	63	1
-5 hours	8	0	61	2	77	2	59	1	46	1
>5 hours	3	0	0	0	13	0	0	0	0	0
Total	2117	100	2971	100	4355	100	5162	100	5596	100

Table 13.04 Dialyser membrane types in HD Units 1994 – 2002

Dialyser membrane	1994 No.	1994 %	1995 No.	1995 %	1996 No.	1996 %	1997 No.	1997 %
Cellulosic	718	76	792	80	932	78	1149	73
Cellulose acetate	222	23	183	19	235	20	360	23
Synthetic	10	1	14	1	34	3	74	5
Total	950	100	989	100	1201	100	1583	100

Dialyser membrane	1998 No.	1998 %	1999 No.	1999 %	2000 No.	2000 %	2001 No.	2001 %	2002 No.	2002 %
Cellulosic	1077	57	987	46	1270	40	1145	31	858	19
Cellulose acetate	413	22	489	23	504	16	493	13	740	17
Synthetic	413	22	672	31	1415	44	2022	55	2826	64
Total	1903	100	2148	100	3189	100	3660	100	4424	100

Table 13.05 Dialyser Reuse Frequency in HD Units 1994- 2002

Dialyser reuse Frequency	1994 No.	1994 %	1995 No.	1995 %	1996 No.	1996 %	1997 No.	1997 %
1*	13	1	15	2	19	2	21	1
2	9	1	7	1	10	1	9	1
3	582	64	751	77	761	67	998	63
4	188	21	153	16	175	16	174	11
5	84	9	22	2	121	11	194	12
6	37	4	18	2	31	3	154	10
7	0	0	0	0	0	0	2	0
8	2	0	0	0	1	0	4	0
9	1	0	4	0	10	1	30	2
10	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0
>=13	0	0	0	0	0	0	0	0
Total	916	100	970	100	1128	100	1586	100

Dialyser reuse Frequency	1998 No.	1998 %	1999 No.	1999 %	2000 No.	2000 %	2001 No.	2001 %	2002 No.	2002 %
1*	16	1	65	2	117	3	152	3	183	4
2	5	0	13	0	17	0	15	0	34	1
3	215	11	192	7	205	5	232	5	247	5
4	113	6	250	9	477	12	416	9	331	6
5	137	7	264	10	313	8	357	7	304	6
6	1073	55	1415	51	1731	43	1415	29	1121	21
7	37	2	46	2	69	2	85	2	123	2
8	66	3	122	4	357	9	793	16	850	16
9	109	6	179	6	101	2	132	3	55	1
10	84	4	96	3	246	6	400	8	482	9
11	23	1	6	0	4	0	43	1	36	1
12	64	3	118	4	333	8	470	10	831	16
>=13	0	0	0	0	91	2	331	7	618	12
Total	1942	100	2766	100	4061	100	4841	100	5215	100

1* is single use i.e. no reuse

Table 13.06 Dialysate Buffer used in HD Units 1994 – 2002

Dialysate buffer	1994 No.	1994 %	1995 No.	1995 %	1996 No.	1996 %	1997 No.	1997 %
Acetate	830	87	822	80	648	52	551	33
Bicarbonate	122	13	207	20	603	48	1125	67
Total	952	100	1029	100	1251	100	1676	100

Dialysate buffer	1998 No.	1998 %	1999 No.	1999 %	2000 No.	2000 %	2001 No.	2001 %	2002 No.	2002 %
Acetate	610	29	549	19	381	9	233	5	112	2
Bicarbonate	1475	71	2417	81	3955	91	4900	95	5436	98
Total	2085	100	2966	100	4336	100	5133	100	5548	100

Table 13.07 Distribution of KT/V, HD patients 1994-2002

Year	No of subjects	Mean	SD	Median	LQ	UQ	% patients <1	% patients 1-<1.2	% patients 1.2-<1.4	% patients 1.4-<1.6	% patients ≥1.6
1994	891	1.3	.3	1.3	1.1	1.5	14	26	28	19	13
1995	977	1.3	.3	1.3	1.1	1.5	12	27	27	20	14
1996	1176	1.3	.3	1.3	1.1	1.5	10	25	26	22	17
1997	1560	1.4	.3	1.4	1.2	1.5	9	21	27	22	21
1998	2023	1.4	.3	1.4	1.2	1.6	7	17	27	25	24
1999	2833	1.5	.3	1.5	1.3	1.7	4	13	23	24	35
2000	4090	1.5	.4	1.5	1.3	1.7	4	13	23	24	37
2001	4910	1.5	.4	1.5	1.3	1.7	4	13	23	23	37
2002	5213	1.5	.4	1.5	1.3	1.7	4	14	23	23	36

Table 13.08 Distribution of KT/V in relation to Age, HD patients 1994-2002

Year		Age group (years)							
		<20		20-39		40-59		60	
1994	Mean ± SD	1.6	0.5	1.3	0.3	1.3	0.3	1.2	0.2
	Median ± IQR	1.5	0.6	1.3	0.4	1.2	0.4	1.2	0.3
1995	Mean ± SD	1.6	0.4	1.4	0.3	1.3	0.3	1.2	0.3
	Median ± IQR	1.6	0.6	1.3	0.4	1.2	0.3	1.2	0.3
1996	Mean ± SD	1.5	0.3	1.4	0.3	1.3	0.3	1.3	0.3
	Median ± IQR	1.6	0.5	1.4	0.4	1.3	0.4	1.3	0.3
1997	Mean ± SD	1.6	0.3	1.4	0.3	1.3	0.3	1.3	0.3
	Median ± IQR	1.6	0.3	1.4	0.4	1.3	0.4	1.3	0.4
1998	Mean ± SD	1.7	0.5	1.5	0.3	1.4	0.3	1.3	0.3
	Median ± IQR	1.6	0.6	1.5	0.4	1.4	0.4	1.3	0.4
1999	Mean ± SD	1.9	0.5	1.6	0.3	1.5	0.3	1.5	0.3
	Median ± IQR	1.9	0.7	1.6	0.4	1.4	0.4	1.4	0.4
2000	Mean ± SD	2	0.5	1.6	0.4	1.5	0.3	1.5	0.3
	Median ± IQR	2	0.6	1.6	0.5	1.4	0.4	1.4	0.4
2001	Mean ± SD	2	0.6	1.6	0.4	1.5	0.3	1.5	0.3
	Median ± IQR	1.9	0.7	1.6	0.5	1.4	0.4	1.5	0.4
2002	Mean ± SD	1.9	0.6	1.6	0.4	1.5	0.3	1.5	0.3
	Median ± IQR	1.9	0.8	1.6	0.5	1.4	0.4	1.5	0.4

Table 13.09 Distribution of KT/V in relation to Gender, HD patients 1994-2002

Year		Gender			
		Male		Female	
1994	Mean ± SD	1.2	0.3	1.4	0.3
	Median ± IQR	1.2	0.3	1.4	0.4
1995	Mean ± SD	1.2	0.3	1.4	0.3
	Median ± IQR	1.2	0.3	1.4	0.4
1996	Mean ± SD	1.3	0.2	1.5	0.3
	Median ± IQR	1.2	0.3	1.5	0.4
1997	Mean ± SD	1.3	0.3	1.5	0.3
	Median ± IQR	1.3	0.4	1.5	0.4
1998	Mean ± SD	1.3	0.3	1.5	0.3
	Median ± IQR	1.3	0.4	1.5	0.4
1999	Mean ± SD	1.4	0.3	1.6	0.4
	Median ± IQR	1.4	0.4	1.6	0.5
2000	Mean ± SD	1.4	0.3	1.7	0.4
	Median ± IQR	1.4	0.4	1.6	0.5
2001	Mean ± SD	1.4	0.3	1.6	0.4
	Median ± IQR	1.4	0.4	1.6	0.5
2002	Mean ± SD	1.4	0.3	1.6	0.4
	Median ± IQR	1.4	0.4	1.6	0.5

Table 13.10 Distribution of KT/V in relation to Diabetes mellitus, HD patients 1994-2002

Year		Diabetes mellitus			
		Without DM		With DM	
1994	Mean ± SD	1.3	0.3	1.2	0.2
	Median ± IQR	1.3	0.4	1.1	0.3
1995	Mean ± SD	1.3	0.3	1.2	0.2
	Median ± IQR	1.3	0.4	1.2	0.3
1996	Mean ± SD	1.4	0.3	1.2	0.2
	Median ± IQR	1.3	0.4	1.2	0.3
1997	Mean ± SD	1.4	0.3	1.2	0.2
	Median ± IQR	1.4	0.4	1.2	0.3
1998	Mean ± SD	1.5	0.3	1.3	0.3
	Median ± IQR	1.4	0.4	1.3	0.3
1999	Mean ± SD	1.6	0.4	1.4	0.3
	Median ± IQR	1.5	0.5	1.3	0.3
2000	Mean ± SD	1.6	0.4	1.4	0.3
	Median ± IQR	1.5	0.5	1.4	0.3
2001	Mean ± SD	1.6	0.4	1.4	0.3
	Median ± IQR	1.5	0.5	1.4	0.4
2002	Mean ± SD	1.6	0.4	1.4	0.3
	Median ± IQR	1.5	0.5	1.4	0.4

Figure 13.11 Unadjusted five-year patient survival in relation to KT/V, HD patients 1997-2002

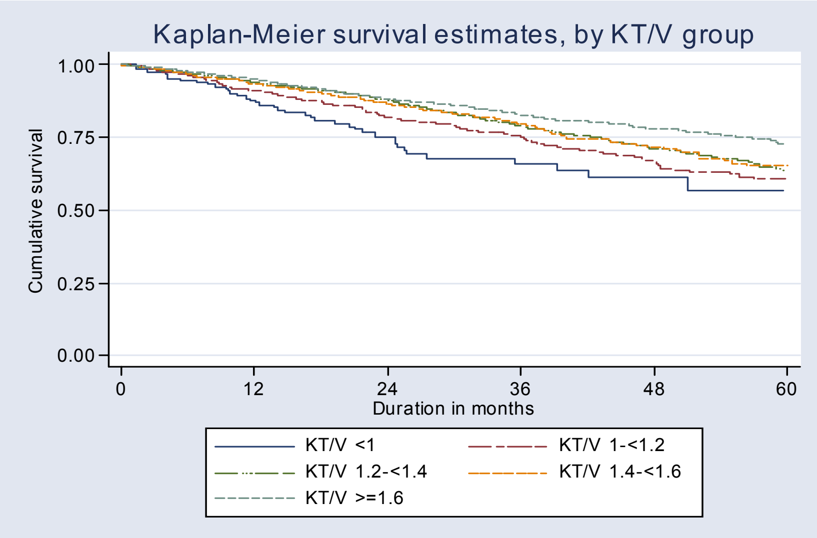

Table 13.12 Adjusted five-year patient survival in relation to KT/V, HD patients 1997-2002

KT/V	n	Hazard ratio	95% CI	p-value
<1	164	1.86	(1.34, 2.58)	0.000
1-<1.2	690	1.17	(0.97, 1.41)	0.096
1.2-<1.4	2133	1.00	-	-
1.4-<1.6	740	1.04	(0.86, 1.26)	0.691
≥ 1.6	2131	1.01	(0.87, 1.18)	0.888

Figure 13.12 Adjusted five-year patient survival in relation to KT/V, HD patients 1997-2002
(Adjusted for age, gender, primary diagnosis and time on RRT)

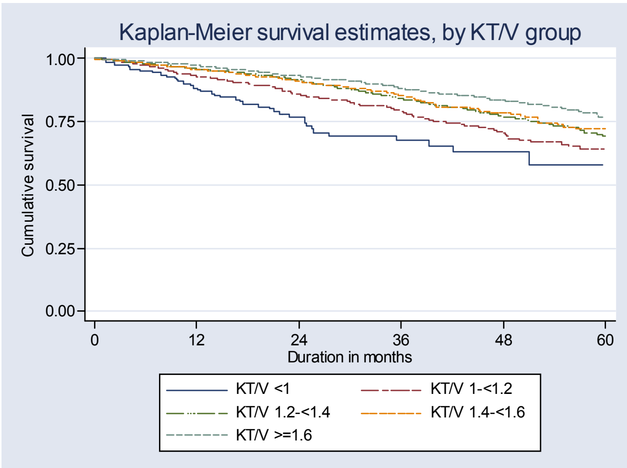

Table 13.11 Unadjusted five-year patient survival in relation to KT/V, HD patients 1997-2002

KT/V	<1		1-<1.2		1.2-<1.4		1.4-<1.6		≥1.6	
Interval (months)	% survival	SE	% survival	SE	% survival	SE	% survival	SE	% survival	SE
6	95	2	96	1	97	0	97	1	98	0
12	88	3	91	1	94	1	94	1	95	0
24	75	4	82	2	88	1	86	1	89	1
36	66	5	75	2	79	1	79	2	83	1
48	61	6	67	3	71	1	72	2	78	1
60	57	7	61	3	64	2	65	3	73	2

SE=standard error

Recommendations for future reports

1. The response rates from haemodialysis centres should be further improved to minimize the effect of under-reporting by centres offering suboptimal dialysis.
2. Analysis of dialysis parameters should distinguish between patients dialyzing 3 times a week from those dialyzing less so that a more balanced conclusion can be reached.
3. Data based consistently on delivered spKt/V, with standardized methods of blood sampling, would increase the value of our analysis.
4. Analysis of trends specific to centre type (government, NGO or private) should be done to identify factors influencing their dialysis practices and outcomes, and the changes in response to the sociopolitical and economic climate.
5. Analysis of dialyser KoA should be done to supplement data from dialyser membrane type in better identifying trends in dialyser usage.
6. Analysis of factors affecting delivered Kt/V should be done to identify areas for further improvement.
7. Data on dialysis adequacy for CAPD is not currently requested by the National Renal Registry. This should be rectified.

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