UK Renal Registry 17th Annual Report: Chapter 6 Adequacy of Haemodialysis in UK Adult Patients in 2013: National and Centre-specific Analyses

Catriona Shaw[a], Retha Steenkamp[a], Andrew Davenport[b]

[a]UK Renal Registry, Bristol, UK; [b]Royal Free Hospital, London, UK

Key Words
Adequacy · Haemodialysis · Urea reduction ratio

Summary

- Data suitable for urea reduction ratio (URR) analyses were available in 15,223 (75.3%) of the 20,214 patients receiving haemodialysis (HD) in the UK on the 30/9/2013.
- In 2013, 88.6% of prevalent HD patients achieved a URR >65%. The between centre range of prevalent patients achieving this target was wide (77.1–97.6%).
- The median URR in 2013 was 75.0%.
- URR was greater in those with longer dialysis vintage. Ninety one percent of patients who had survived on renal replacement therapy (RRT) for more than two years achieved a URR >65% compared with only 74.2% of those on RRT for only six months.
- Large variation between centres in the percentage of patients achieving the UK Renal Association's (RA) URR guideline persists.

Introduction

Amongst patients with established renal failure (ERF), the delivered dose of HD [1] has been reported in observational studies to potentially influence survival [2–4]. The delivered dose of HD depends on treatment (duration and frequency of dialysis, dialyser size, dialysate and blood flow rate) and patient characteristics (size, weight, haematocrit and vascular access) [5]. The two widely accepted measures of urea clearance are Kt/V, the ratio between the product of urea clearance (K, in ml/min) and dialysis session duration (t, in minutes) divided by the volume of distribution of urea in the body (V, in ml) and URR which is derived solely from the percentage fall in serum urea (URR) during a dialysis treatment. Whilst Kt/V is a more accurate descriptor of urea clearance, its calculation is more complex and requires additional data items not commonly reported by most UK renal centres [6, 7]. The UKRR has historically presented analyses based on URR rather than Kt/V for comparative audit of haemodialysis adequacy as these data are more widely available. However, URR does not take into account the rebound in serum urea concentration at the end of dialysis, and so may over estimate delivered dialysis dose, particularly when higher blood pump speeds are used.

Based on published evidence, clinical practice guidelines have been developed by various national and regional organisations [8–11]. There is considerable uniformity between them with regard to the recommendations for minimum dose of dialysis although there are differences in the methodology advised. Table 6.1 lists the recommended RA audit measures which are relevant to the haemodialysis population and whether the audit measure is currently reported on in the UK Renal Registry (UKRR) annual report [9].

The main objective of this chapter is to determine the extent to which patients undergoing HD treatment for established renal failure in the UK received the dose of HD, as measured by URR, recommended in the UK RA current clinical practice guidelines [9].

Methods

Seventy-one renal centres in the UK submitted data electronically to the UKRR on a quarterly basis . The majority of these centres have satellite units but for the purposes of this study the data from the renal centres and their associated satellite units were amalgamated. Data from two groups of patients were analysed. Firstly, analysis was undertaken using data from the prevalent adult HD patient population as of the 30th September 2013. For this analysis, data for URR were taken from the 3rd quarter of 2013 unless that data point was missing in which case data from the 2nd quarter were taken. The prevalent population only included patients receiving HD who were alive on 30th September 2013. Data from those patients who had died before that date have not been included in the analysis. The second analysis involved adult incident patients who had commenced treatment with HD during 2012. For these patients, analysis was undertaken using the last recorded URR in the quarter in which the patient had started dialysis. The incident HD patient cohort was followed up

Table 6.1 Summary of recommended Renal Association Audit Measures relevant to haemodialysis adequacy [9]

RA Audit Measure	Included in UKRR annual report?	Reason for non-inclusion
Haemodialysis Adequacy Audit Measures		
Audit measure: The proportion of patients in the main renal unit and its satellite units who are on twice weekly haemodialysis	No	Varying levels of reporting between centres
Audit measure: Cumulative frequency curves of urea reduction ratio measured using a standard method of post-dialysis sampling	Yes, but data not presented in the cumulative frequency format	
Audit measure: The proportion of patient non-attendances for haemodialysis sessions and the proportion of dialysis sessions shortened at the patient's request	No	Data not available
Audit measure: The proportion of thrice weekly haemodialysis sessions which have prescribed treatment times less than 4 hours	No	Varying levels of reporting between centres
Audit measure: The proportion of hospital (main and satellite unit) and home haemodialysis patients who are prescribed more frequent than thrice weekly haemodialysis	Yes	Not for home haemodialysis patients

for one year and the last recorded URR in the quarter after one year follow-up was used for this analysis.

Data from patients known to be receiving more or less than thrice weekly HD were omitted from analysis for both the incident and prevalent population. Patients for whom data recording the number of dialysis sessions per week were missing, were assumed to be dialysing thrice weekly. However, because not all centres report frequency of HD, it is possible that data from a small number of patients receiving HD at a different frequency were included in the analyses. Home HD patients were excluded from the analysis.

Analyses of the data from both groups of patients included calculation of the median URR and of the proportion of patients who had achieved the RA guideline (as outlined below) in each of the renal centres as well as for the country as a whole. The median URR and proportion of patients who achieved the RA guideline were also calculated separately for males and females. The number of dialysis sessions per week and the time per dialysis session is shown by renal centre.

All patients with data were included in the statistical analyses at a national level, although centres with fewer than 20 patients, or providing less than 50% data completeness were excluded from the comparison between centres. The number preceding the centre name in each figure indicates the percentage of missing data for that centre.

The UK RA clinical practice guidelines in operation at the time these data were collected were as follows:

HD should take place at least three times per week in nearly all patients. Reduction of dialysis frequency to twice per week because of insufficient dialysis facilities is unacceptable.

Every patient receiving thrice weekly HD should have consistently:

- ***either URR >65%***
- ***or equilibrated Kt/V (eKt/V) of >1.2 (or single pool Kt/V of >1.3) calculated from pre- and post-dialysis urea values, duration of dialysis and weight loss during dialysis).***

To achieve a URR above 65% or eKt/V above 1.2 consistently in the vast majority of the HD population clinicians should aim for a minimum target URR of 70% or minimum eKt/V of 1.4 in individual patients.

The duration of thrice weekly HD in adult patients with minimal residual renal function should not be reduced below 4 hours without careful consideration.

Patients receiving HD twice weekly for reasons of geography should receive a higher sessional dose of HD. If this cannot be achieved, then it should be recognised that there is a compromise between the practicalities of HD and the patient's long-term health.

Measurement of the 'dose' or 'adequacy' of HD should be performed monthly in all hospital HD patients and may be performed less frequently in home HD patients. All dialysis units should collect and report this data to their regional network and the UKRR.

Post-dialysis blood samples should be collected either by the slow-flow method, the simplified stop-flow method, or the stop dialysate flow method. The method used should remain consistent within renal units and should be reported to the Registry.

The RA clinical practice guidelines for HD dose apply specifically to patients undergoing thrice weekly HD. In these patients it is recommended that blood for biochemical measurement (including pre-dialysis urea for URR) should be taken before the mid-week dialysis session [9].

Results

Data completeness

Sixty four of the 71 renal centres submitted HD dose (URR) data to the UKRR (table 6.2). Data were available

Table 6.2. Percentage completeness of URR data returns for prevalent patients on HD by centre, on 30/9/2013

Centre	% completeness	Centre	% completeness
B Heart	99.7	Sheff	96.0
B QEH	94.8	Shrew	91.6
Basldn	98.6	Stevng	98.1
Bradfd	98.9	Sthend	100.0
Brightn	2.9	Stoke	73.4
Bristol	100.0	Sund	2.5
Camb	98.0	Truro	78.3
Carlis	100.0	Wirral	0.0
Carsh	91.9	Wolve	94.2
Chelms	97.8	York	99.1
Colchr	82.9		
Covnt	98.5	**N Ireland**	
Derby	91.2	Antrim	99.1
Donc	100.0	Belfast	98.9
Dorset	99.6	Newry	78.1
Dudley	95.3	Ulster	98.9
Exeter	99.7	West NI	91.0
Glouc	100.0		
Hull	99.7	**Scotland**	
Ipswi	100.0	Abrdn	99.0
Kent	90.3	Airdrie	97.7
L Barts	0.0	D & Gall	91.9
L Guys	69.5	Dundee	95.5
L Kings	0.0	Edinb	99.6
L Rfree	0.0	Glasgw	97.0
L St.G	0.0	Inverns	94.1
L West	94.1	Klmarnk	91.3
Leeds	100.0	Krkcldy	95.7
Leic	99.6		
Liv Ain	0.0	**Wales**	
Liv Roy	0.0	Bangor	100.0
M RI	22.6	Cardff	95.0
Middlbr	99.0	Clwyd	96.9
Newc	10.7	Swanse	71.9
Norwch	98.2	Wrexm	90.3
Nottm	93.5		
Oxford	94.8	**England**	71.9
Plymth	95.6	**N Ireland**	94.6
Ports	97.9	**Scotland**	96.8
Prestn	85.4	**Wales**	87.7
Redng	6.7	**UK**	75.3
Salford	80.6		

for 75.3% ($n = 15,223$) of the total prevalent population ($n = 20,214$) treated with HD who met the inclusion criteria for these analyses.

Fifty-one centres reported URR data on more than 90% of patients. Five centres reported URR data on less than 50% of prevalent patients (Manchester RI, Newcastle, Reading, Brighton and Sunderland). URR data were not received from seven centres (London Barts, London Kings, London Royal Free, London St Georges, Liverpool Aintree, Liverpool Royal Infirmary and Wirral).

Several centres had a reduction in the completeness of URR data submitted to the UKRR in 2013 compared with 2012 (data not shown). These changes may represent changes in data extraction, or a move by centres to utilising Kt/V rather than URR as the preferred measure of dialysis dose.

Of the total incident patient population ($n = 4,348$) who started HD during 2012 and meeting the inclusion criteria for URR analyses, 48.9% ($n = 2,125$) had URR data available during the first quarter of treatment (data not shown).

Percentage completeness of data returns on the number of HD sessions varied across centres (table 6.3). Ten centres in England and two centres in Wales returned no data on this variable. All centres in Northern Ireland returned data in over 95% of their HD population. All centres in Scotland returned data in over 90% of their HD population.

For those centres that did return data, three dialysis sessions a week was most prevalent, although a few centres reported >10% of the HD population undergoing a frequency of HD more or less than three sessions a week (table 6.3). For example, Salford reported 16.5% of their prevalent haemodialysis population having more than three sessions a week whereas Southend reported that 15.0% of their population in 2013 had fewer than three sessions per week.

Wide between centre variation in completeness of data on dialysis session time was also evident (table 6.4). In

Table 6.3. Number of dialysis sessions for prevalent patients on HD by centre, on 30/9/2013

Centre	Percentage completeness	Frequency of dialysis/week %		
		<3 sessions	3 sessions	>3 sessions
England				
B Heart	91.7	5.7	93.5	0.8
B QEH	0.0			
Basldn	99.3	1.4	94.6	4.1
Bradfd	96.8	3.9	95.6	0.6
Brightn	100.0	0.0	99.1	0.9
Bristol	100.0	4.8	94.8	0.5
Camb	100.0	8.8	89.4	1.8
Carlis	85.2	7.7	92.3	0.0
Carsh	0.0			
Chelms	100.0	9.0	91.0	0.0
Colchr	97.1	0.0	100.0	0.0
Covnt	1.8	0.0	100.0	0.0
Derby	76.4	0.0	100.0	0.0
Donc	99.3	0.7	99.3	0.0
Dorset	99.6	2.5	97.1	0.4
Dudley	100.0	0.7	98.7	0.7
Exeter	100.0	3.3	95.6	1.1
Glouc	0.0			
Hull	1.4	0.0	100.0	0.0
Ipswi	87.8	3.0	97.0	0.0
Kent	98.3	3.3	95.3	1.5
L Barts	0.0			
L Guys	0.0			
L Kings	100.0	0.0	100.0	0.0
L Rfree	0.0			
L St.G	82.3	0.5	99.5	0.0
L West	45.1	0.7	98.5	0.8
Leeds	99.1	5.2	94.3	0.5
Leic	99.4	0.9	99.1	0.0
Liv Ain	99.3	0.7	97.4	2.0

Table 6.3. Continued

Centre	Percentage completeness	Frequency of dialysis/week %		
		<3 sessions	3 sessions	>3 sessions
Liv Roy	98.3	0.7	88.7	10.6
M RI	38.1	1.9	98.1	0.0
Middlbr	15.4	0.0	97.9	2.1
Newc	100.0	1.7	97.4	0.9
Norwch	98.6	0.7	97.8	1.4
Nottm	99.7	0.9	99.1	0.0
Oxford	0.0			
Plymth	0.0			
Ports	99.2	6.1	91.9	2.0
Prestn	0.0			
Redng	100.0	0.4	99.6	0.0
Salford	98.7	1.6	81.9	16.5
Sheff	99.4	3.5	96.5	0.0
Shrew	99.4	5.5	93.3	1.2
Stevng	98.9	5.3	93.6	1.1
Sthend	100.0	15.0	85.0	0.0
Stoke	100.0	0.4	90.6	9.0
Sund	98.3	0.0	90.9	9.1
Truro	95.7	9.0	87.2	3.8
Wirral	97.3	2.2	90.0	7.8
Wolve	0.0			
York	86.3	2.0	90.1	7.9
N Ireland				
Antrim	100.0	0.9	99.1	0.0
Belfast	99.0	0.5	96.8	2.6
Newry	100.0	4.7	95.3	0.0
Ulster	100.0	1.0	96.9	2.1
West NI	99.1	0.9	91.7	7.4
Scotland				
Abrdn	99.0	1.5	97.0	1.5
Airdrie	97.7	0.0	100.0	0.0
D & Gall	95.5	2.4	83.3	14.3
Dundee	96.3	0.0	94.9	5.1
Edinb	97.1	0.0	98.7	1.3
Glasgw	93.1	0.4	99.0	0.6
Inverns	94.3	0.0	96.0	4.0
Klmarnk	96.1	0.8	99.2	0.0
Krkcldy	94.2	0.0	100.0	0.0
Wales				
Bangor	85.7	1.9	96.3	1.9
Cardff	0.0			
Clwyd	97.0	1.5	95.4	3.1
Swanse	0.0			
Wrexm	100.0	2.1	96.9	1.0
England	**59.8**	**2.8**	**95.1**	**2.0**
N Ireland	**99.5**	**1.3**	**96.1**	**2.5**
Scotland	**95.6**	**0.4**	**98.0**	**1.6**
Wales	**23.0**	**1.9**	**96.3**	**1.9**
UK	**62.2**	**2.4**	**95.6**	**2.0**

Blank cells denote no data returned by that centre

Table 6.4. Time per dialysis session for prevalent patients on HD by centre, on 30/9/2013

Centre	Percentage completeness	Percentage per dialysis session		
		<3.5 hours	3.5–5 hours	>5 hours
England				
B Heart	81.0	5.1	91.0	3.9
B QEH	0.0			
Basldn	99.3	15.0	83.7	1.4
Bradfd	97.3	6.6	93.4	0.0
Brightn	99.4	2.5	97.5	0.0
Bristol	100.0	6.1	93.9	0.0
Camb	0.0			
Carlis	85.2	11.5	88.5	0.0
Carsh	0.0			
Chelms	100.0	4.0	96.0	0.0
Colchr	97.1	0.0	100.0	0.0
Covnt	6.5	40.9	59.1	0.0
Derby	76.4	0.7	99.3	0.0
Donc	99.3	9.9	90.1	0.0
Dorset	99.6	3.7	96.3	0.0
Dudley	100.0	6.6	93.4	0.0
Exeter	100.0	19.7	80.3	0.0
Glouc	0.0			
Hull	2.4	28.6	71.4	0.0
Ipswi	87.8	1.0	99.0	0.0
Kent	98.3	13.0	86.4	0.6
L Barts	0.0			
L Guys	15.5	0.0	100.0	0.0
L Kings	100.0	19.0	81.1	0.0
L Rfree	0.0			
L St.G	72.4	0.5	99.5	0.0
L West	45.4	4.4	94.2	1.5
Leeds	99.8	5.8	94.2	0.0
Leic	88.1	1.7	98.1	0.2
Liv Ain	100.0	11.1	88.9	0.0
Liv Roy	99.7	15.2	84.8	0.0
M RI	38.1	3.7	95.0	1.2
Middlbr	100.0	22.6	77.1	0.3
Newc	100.0	7.4	90.9	1.7
Norwch	98.6	18.8	81.2	0.0
Nottm	15.1	10.2	89.8	0.0
Oxford	0.0			
Plymth	0.0			
Ports	0.0			
Prestn	0.6	0.0	100.0	0.0
Redng	97.6	1.2	98.4	0.4
Salford	94.3	7.1	92.6	0.3
Sheff	82.2	52.8	46.9	0.2
Shrew	99.4	15.2	84.8	0.0
Stevng	98.9	51.1	48.7	0.3
Sthend	100.0	20.6	79.4	0.0
Stoke	100.0	6.5	92.8	0.7
Sund	88.2	10.2	89.8	0.0
Truro	90.6	22.2	77.0	0.8
Wirral	99.5	18.5	81.0	0.5
Wolve	0.0			
York	88.0	4.9	95.2	0.0

Table 6.4. Continued

Centre	Percentage completeness	Percentage per dialysis session		
		<3.5 hours	3.5–5 hours	>5 hours
N Ireland				
Antrim	100.0	3.5	96.5	0.0
Belfast	99.5	16.8	83.2	0.0
Newry	100.0	9.3	90.7	0.0
Ulster	100.0	5.2	94.9	0.0
West NI	99.1	13.9	86.1	0.0
Scotland				
Abrdn	99.0	1.5	96.6	2.0
Airdrie	97.7	5.3	94.7	0.0
D & Gall	97.7	7.0	93.0	0.0
Dundee	96.3	5.7	93.7	0.6
Edinb	97.5	9.0	88.9	2.1
Glasgw	93.4	0.4	94.2	5.4
Inverns	94.3	4.0	96.0	0.0
Klmarnk	96.1	0.0	92.7	7.3
Krkcldy	94.9	13.0	85.5	1.5
Wales				
Bangor	85.7	9.3	90.7	0.0
Cardff	0.0			
Clwyd	97.0	38.5	61.5	0.0
Swanse	0.0			
Wrexm	99.0	5.3	94.7	0.0
England	**54.1**	**12.7**	**86.8**	**0.4**
N Ireland	**99.7**	**10.8**	**89.2**	**0.0**
Scotland	**95.9**	**4.1**	**92.9**	**3.0**
Wales	**22.9**	**16.4**	**83.6**	**0.0**
UK	**57.3**	**11.5**	**87.7**	**0.7**

Blank cells denote no data returned by that centre

centres that reported data, the most frequently reported dialysis session length was 3.5–5 hours.

Achieved URR

For prevalent patients, the median URR (75.0% for UK, centre range 71.0–83.0%) and percentage of patients attaining the RA guideline of a URR >65% (88.6% for the UK, centre range 77.1–97.6%) are shown in figures 6.1a and 6.2 respectively. The UK median URR in women was 78.0% (centre range 73.0–85.0%) compared with a UK median in men of 74.0% (centre range 69.0–81.0%) (figures 6.1b, 6.1c).

There continued to be variation between renal centres in the percentage of prevalent patients with a URR of >65%, with 22 centres attaining the RA clinical practice guideline in >90% of patients and 37 centres reporting attainment of the guideline in 70%–90% of patients (figure 6.2).

Changes in URR over time

The change in the percentage attainment of the current RA clinical practice guidelines (URR >65%) and the median URR for the UK from 2000 to 2013 is shown in figure 6.3. The proportion of patients attaining the RA guideline increased from 69% to 89% whilst the median URR has risen from 69% to 75% during the same time period. There has been no substantial change in the median URR between 2011 and 2013 in the UK.

Variation of achieved URR with time on dialysis

The proportion of patients who attained the RA guideline for HD was greater in those who had been on RRT for the longest time (figure 6.4). In 2013, of those dialysed for less than six months, 74% had a URR >65%, whilst 91% of patients who had survived and continued on RRT for more than two years had a URR within the guideline target. In all strata of time on dialysis, there

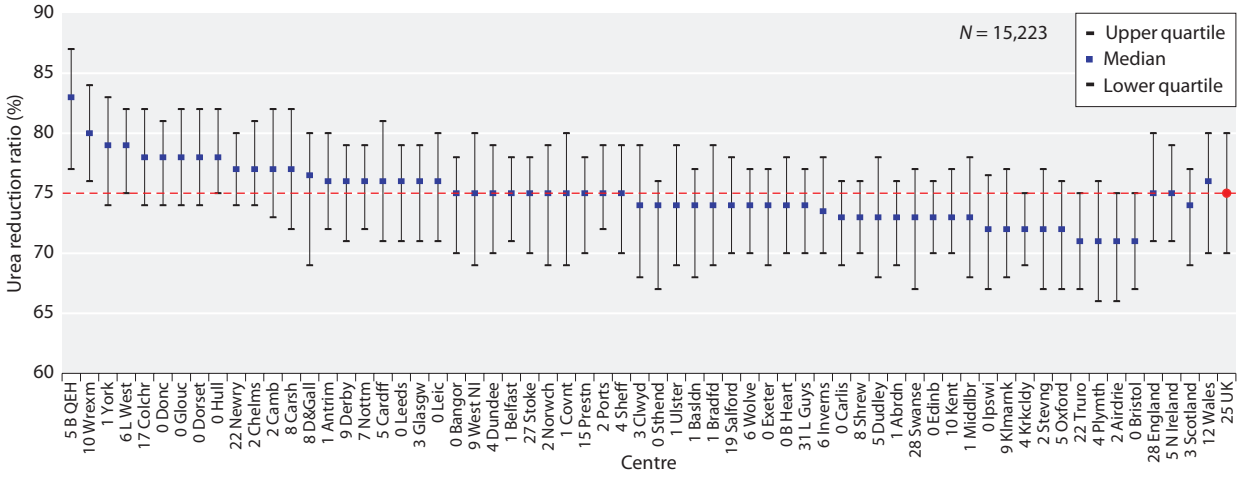

Fig. 6.1a. Median URR achieved in prevalent patients on HD by centre, 30/9/2013

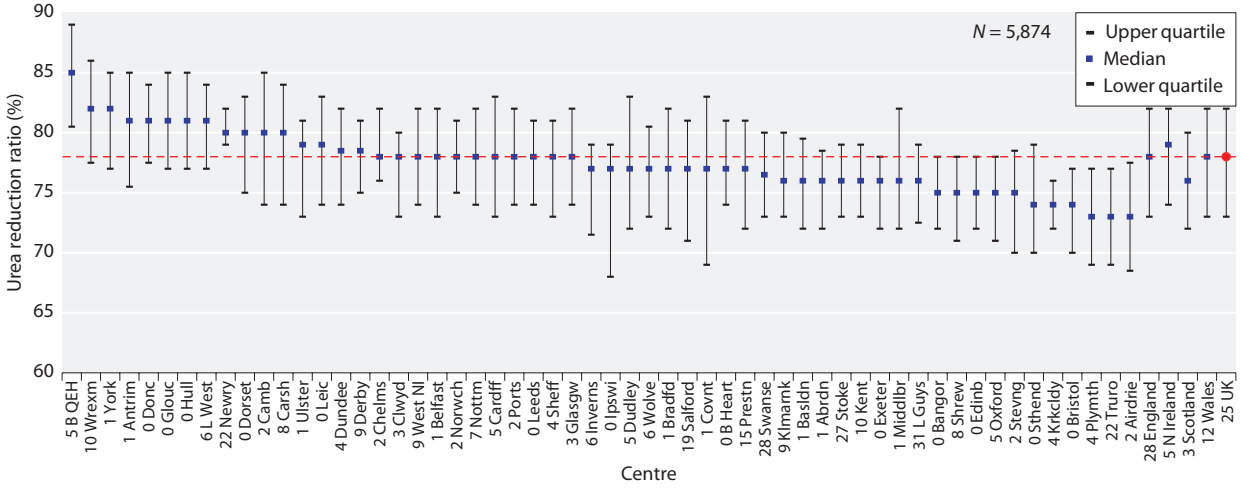

Fig. 6.1b. Median URR achieved in female prevalent patients on HD by centre, 30/9/2013

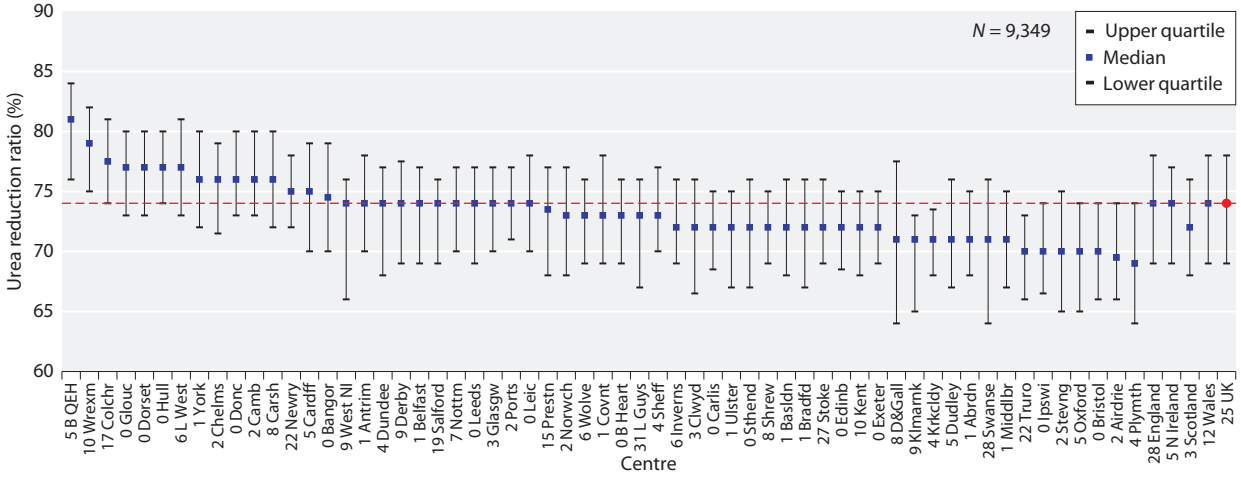

Fig. 6.1c. Median URR achieved in male prevalent patients on HD by centre, 30/9/2013

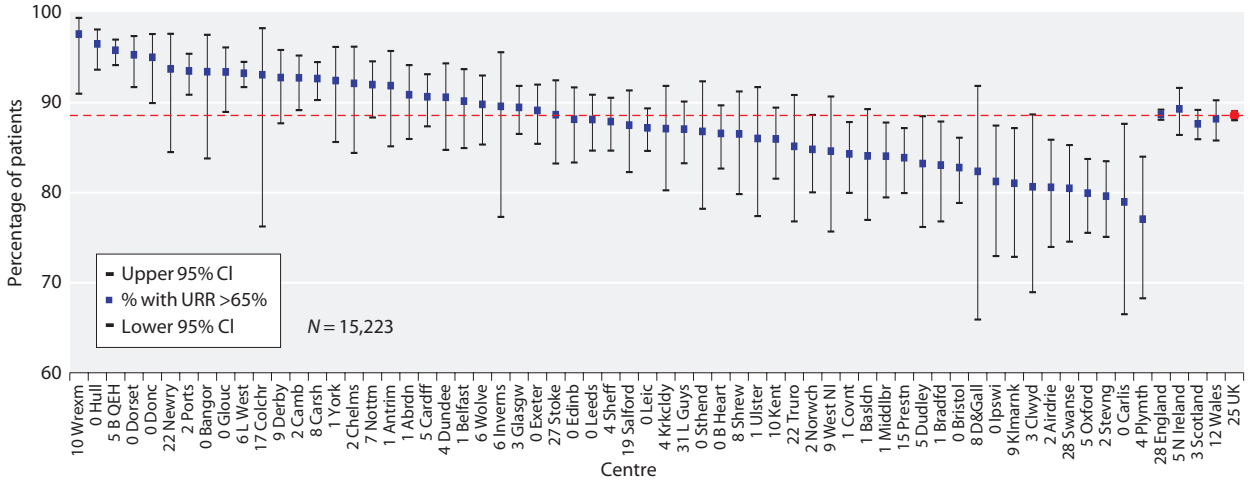

Fig. 6.2. Percentage of prevalent patients with URR >65% on HD by centre, 30/9/2013

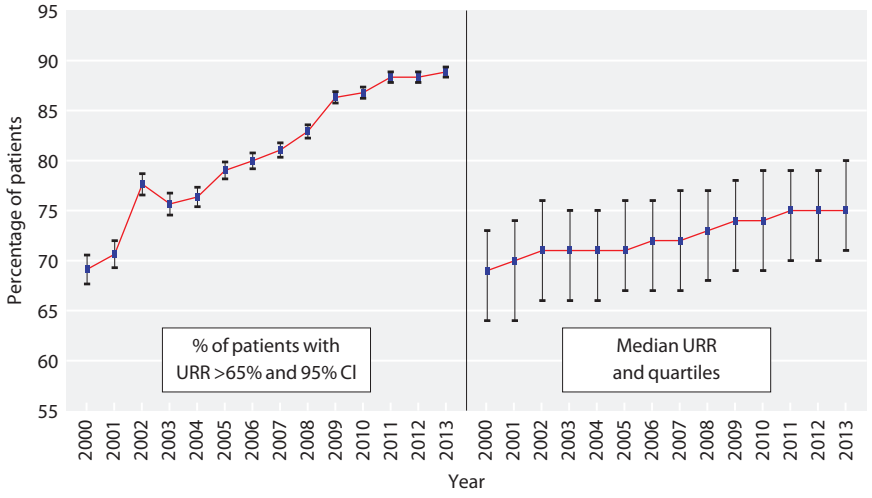

Fig. 6.3. Change in the percentage of prevalent patients on HD with URR >65% and the median URR between 2000 and 2013 in the UK

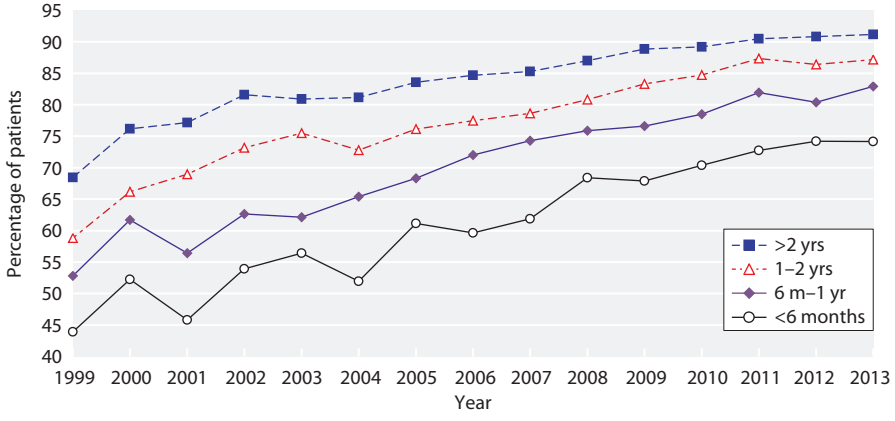

Fig. 6.4. Percentage of prevalent patients on HD achieving URR >65% by time on RRT between 1999 and 2013

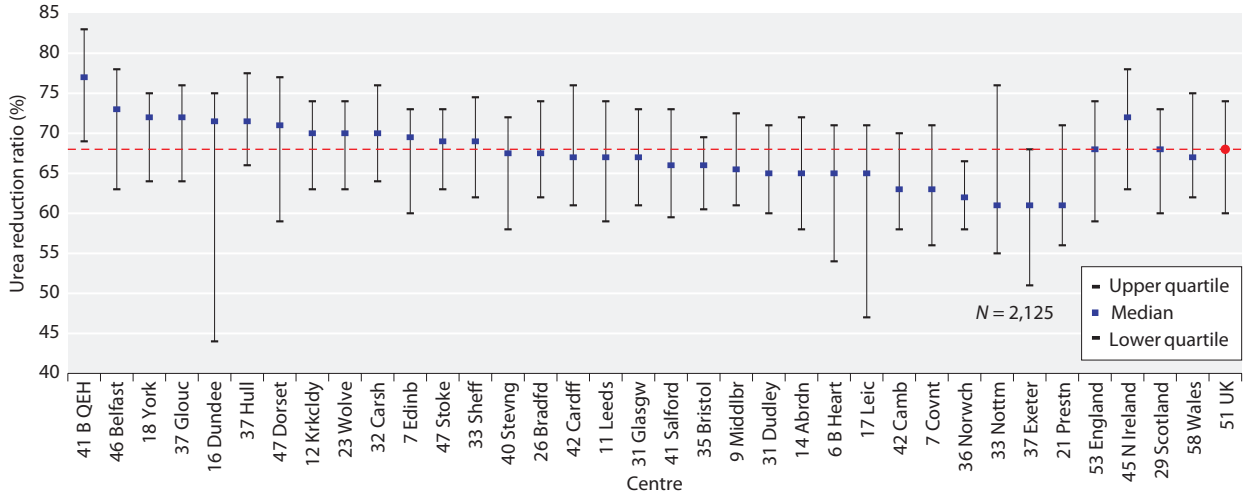

Fig. 6.5a. Median URR in the first quarter of starting RRT in incident patients who started haemodialysis in 2012

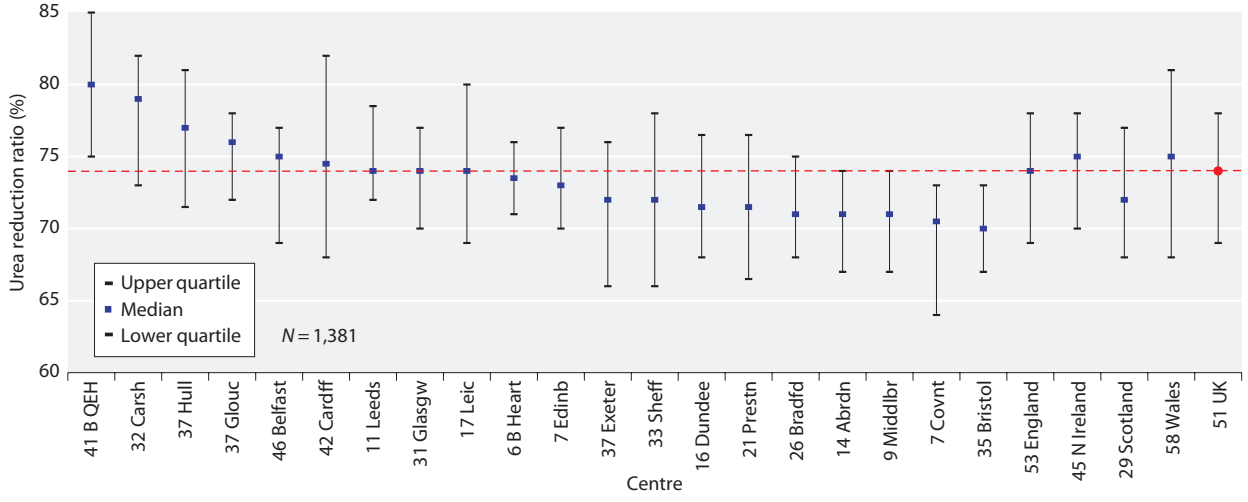

Fig. 6.5b. Median URR one year after starting RRT for patients who started haemodialysis in 2012

has been an improvement in the proportion of patients receiving the target dose of HD over the last 14 years.

The median URR during the first quarter of starting HD treatment of the incident HD population in the UK in 2012 was 68% (centre range 61–77%) (figure 6.5a). At the end of one year for this incident cohort, the median URR was higher (median URR 74%, centre range 70–80%) (figure 6.5b).

Conclusions

The dose of delivered HD is recognised as potentially having an important influence on outcome in ERF patients treated with low flux HD. Patient well being has been shown to depend on achieving a minimum urea clearance target, but it remains unclear as to whether higher clearance targets add benefit [1–3]. It is therefore reassuring that the proportion of UK patients achieving the RA guideline for URR has increased in the last decade, with over 88% of the prevalent HD population achieving the URR guideline in 2013, with a median URR of 75%. This increment will not only reflect improvements in practice and delivery of dialysis, but also enhanced coverage and quality of the data collected by the UKRR and renal centres over the years.

Post hoc analyses of the HEMO study and observational studies have suggested that women may benefit from a higher dialysis dose than men [12, 13]. Current

RA guidelines do not differentiate on the basis of gender [9]. It is an interesting observation that the UK median URR achieved in women was higher than in men in this analysis, a similar finding to the analyses presented in last year's annual report. This may however simply reflect differences in dietary intake and lower pre-dialysis serum urea values in women, and as such does not necessarily imply improved dialysis clearance for women [14, 15].

In the prevalent haemodialysis population there continues to be a wide range (77.1–97.6%) of achievement of the RA guideline for URR between different centres which is likely to reflect genuine differences in HD dose with both individual and centre level contributors. Understanding more fully individual renal centre practice would be informative, as although most centres do not formally measure residual renal function, centres may adjust sessional times based on urine output. In the incident population, the variation in the between centre median URR within the first quarter for incident patients may represent variation in dialysis prescription practice for patients starting RRT. Some renal centres may use an incremental dialysis approach, whilst other centres use a standardised 'full-dose' approach to dialysis prescription, irrespective of residual function. Increasing URR with dialysis vintage in the prevalent patient group would support the suggestion that some centres operate an incremental dialysis policy, increasing dialysis dosing as residual renal function falls. Although observational evidence supports that preservation of residual renal function is associated with improved survival [16], maintaining patients overhydrated to try and preserve residual renal function [17] may increase cardiovascular mortality. How much individualisation of dialysis prescription based on residual renal function is practiced across UK renal centres and how this correlates with outcomes, remains to be determined. Similarly, it is not known whether the decline in residual renal function is affected by differences in centre practice approach to initiating dialysis. Varied completeness of data returns across other important factors such as dialysis session information also limits the interpretation of the data. Although RA guidelines recommend standardised methods for urea sampling, inconsistency in sampling methodology for the post-dialysis urea sample may also play a part in the variations reported [9].

Debate continues as to the toxicity of urea, and how representative urea clearance is of other azotaemic toxin clearances. In addition, the dialysis prescription should also encompass volume control, sodium and divalent cation balance and correct metabolic acidosis. As such basing and evaluating HD dose simply on urea clearance has been criticised by some [13] arguing that patient outcomes are improved by longer treatment times independent of urea removal [5, 18–23] and that clearance of 'middle molecules' have an important impact [24, 25]. However, no consensus has yet emerged on alternative markers of HD adequacy. The UKRR has historically reported URR, predominantly for logistical reasons with the URR being the easiest measure to calculate, and the measure of dialysis adequacy that is most complete when returned to the UKRR. However, limitations of the URR must be recognised.

The new UKRR dataset, recently distributed to renal units and to be embedded by 2016, should help contribute to further improvements in both URR data capture, as well as Kt/V reporting in addition to data on dialysis prescription practice.

Conflicts of interest: none

References

1 Gotch FA, Sargent JA: A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). Kidney Int 1985;28:526–534

2 Owen WF, Lew NL, Liu Y, Lowrie EG, Lazarus JM: The Urea Reduction Ratio and Serum Albumin Concentration as Predictors of Mortality in Patients Undergoing Hemodialysis. N Engl J Med 1993;329:1001–1006

3 Held PJ, Port FK, Wolfe RA, Stannard DC, Carroll CE, Daugirdas JT, Bloembergen WE, Greer JW, Hakim RM: The dose of hemodialysis and patient mortality. Kidney Int 1996; 50:550–556

4 Tentori F, Hunt WC, Rohrscheib M, Zhu M, Stidley CA, Servilla K, Miskulin D, Meyer KB, Bedrick EJ, Johnson HK, Zager PG: Which Targets in Clinical Practice Guidelines Are Associated with Improved Survival in a Large Dialysis Organization? J Am Soc Nephrol 2007;18:2377–2384

5 Locatelli F, Buoncristiani U, Canaud B, Kohler H, Petitclerc T, Zucchelli P: Dialysis dose and frequency. Nephrol Dial Transplant 2005;20:285–296

6 Depner TA: Assessing adequacy of hemodialysis: urea modeling. Kidney Int 1994;45:1522–1535

7 Kumar S, Khosravi M, Massart A, Potluri M, Davenport A. The effects of racial differences on body composition and total body water measured by multifrequency bioelectrical impedance analysis influence delivered Kt/V dialysis dosing. Nephron Clin Pract. 2013;124(1–2):60–6

8 Vanbelleghem H, Vanholder R, Levin NW, Becker G, Craig JC, Ito S, Lau J, Locatelli F, Zoccali C, Solez K, Hales M, Lameire N, Eknoyan G: The Kidney Disease: Improving Global Outcomes website: Comparison of guidelines as a tool for harmonization. Kidney Int 2007;71: 1054–1061

9 UK Renal Association Clinical Practice Guidelines Committee. Haemodialysis, 2009 http://www.renal.org/Clinical/GuidelinesSection/Haemodialysis.aspx

10 European Best Practice Guidelines Expert Group on Haemodialysis. Nephrol Dial Transplant 2002: 17(suppl 7):S16–S31
11 NKF-KDOQI clinical practice guidelines; update 2006. Am J Kidney Dis 2006: 48(suppl 1):S2–S90
12 Depner T, Daugirdas J, Greene T, Allon M, Beck G, Chumlea C, Delmez J, Gotch F, Kusek J, Levin N, Macon E, Milford E, Owen W, Star R, Toto R, Eknoyan G, Hemodialysis Study Group Dialysis dose and the effect of gender and body size on outcome in the HEMO Study. Kidney Int. 2004;65(4):1386
13 Port FK, Wolfe RA, Hulbert-Shearon TE, McCullough KP, Ashby VB, Held PJ. High dialysis dose is associated with lower mortality among women but not among men. Am J Kidney Dis. 2004;43(6):1014
14 Lowrie EG: The Kinetic Behaviors of Urea and Other Marker Molecules During Hemodialysis. Am J Kidney Dis 2007;50:181–183
15 Spalding EM, Chandna SM, Davenport A, Farrington K. Kt/V underestimates the haemodialysis dose in women and small men. Kidney Int 2008; 74: 348–355
16 Hanson JA, Hulbert-Shearon TE, Ojo AO, et al: Prescription of twice-weekly hemodialysis in the USA. Am J Nephrol 19:625–633, 1999
17 McCafferty K, Fan S, Davenport A Extracellular volume expansion, measured by multifrequency bioimpedance, does not help preserve residual renal function in peritoneal dialysis patients. Kidney Int. 2014;85(1):151–7
18 Vanholder R, Eloot S, Van Biesen W: Do we need new indicators of dialysis adequacy based on middle-molecule removal? Nature Clinical Practice Nephrology 2008;4:174–175
19 Tattersall J, Martin-Malo A, Pedrini L, Basci A, Canaud B, Fouque D, Haage P, Konner K, Kooman J, Pizzarelli F, Tordoir J, Vennegoor M, Wanner C, ter Wee P, Vanholder R: EBPG guideline on dialysis strategies. Nephrol Dial Transplant 2007;22:ii5–21
20 Saran R, Bragg-Gresham JL, Levin NW, Twardowski ZJ, Wizemann V, Saito A, Kimata N, Gillespie BW, Combe C, Bommer J, Akiba T, Mapes DL, Young EW, Port FK: Longer treatment time and slower ultrafiltration in hemodialysis: Associations with reduced mortality in the DOPPS. Kidney Int 2006;69:1222–1228
21 Marshall MR, Byrne BG, Kerr PG, McDonald SP: Associations of hemodialysis dose and session length with mortality risk in Australian and New Zealand patients. Kidney Int 2006;69:1229–1236
22 Eloot S, Van Biesen W, Dhondt A, Van de Wynkele H, Glorieux G, Verdonck P, Vanholder R: Impact of hemodialysis duration on the removal of uremic retention solutes. Kidney Int 2007;73:765–770
23 Basile C, Lomonte C: Dialysis time is the crucial factor in the adequacy of hemodialysis. Kidney Int 2008;74:965–966
24 Eloot S, Torremans A, De Smet R, Marescau B, De Deyn PP, Verdonck P, Vanholder R: Complex Compartmental Behavior of Small Water-Soluble Uremic Retention Solutes: Evaluation by Direct Measurements in Plasma and Erythrocytes. Am J Kidney Dis 2007;50:279–288
25 Davenport A. How best to improve survival in haemodialysis patients: solute clearance or volume control? Kidney Int. 2011;80(10):1018–20